Uniform Medical Plan coverage limits

Updates effective 10/1/2017

The benefit coverage limits listed below apply to these UMP plans:
Uniform Medical Plan Classic (UMP Classic)
UMP Consumer-Directed Health Plan (UMP CDHP)
  - UMP Plus–Puget Sound High Value Network
  - UMP Plus–UW Medicine Accountable Care Network

Some services listed under these benefits have coverage limits. These limits are either determined by a Health Technology Clinical Committee (HTCC) decision or a Regence BlueShield medical policy. The table below does not include every limit or exclusion under this benefit. For more details, refer to your plan’s Certificate of Coverage.

### Surgery

<table>
<thead>
<tr>
<th>These services or supplies have coverage limits</th>
<th>The rules or policies that define the coverage limits</th>
<th>Limit applies to these codes (chosen by your provider to bill for services)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ablation of Primary and Metastatic Liver Tumors</td>
<td>Regence Medical Policy Sur204</td>
<td>• 47370, 47371, 47380, 47381, 47382, 47383</td>
</tr>
<tr>
<td>Autologous Fat Grafting to the Breast and Adipose-derived Stem Cells</td>
<td>Regence Medical Policy Sur182</td>
<td>• 19366, 11950, 11951, 11952, 11954</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Code 19366 is considered investigational when used for autologous fat grafting and adipose-derived stem cells for augmentation or reconstruction of the breast.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• NOTE: Code 19366 requires pre-authorization for all services</td>
</tr>
<tr>
<td>Bariatric Surgery</td>
<td>HTCC decision</td>
<td>• 43644, 43770, 43771, 43772, 43773, 43774, 43775, 43846, 43848, 43860, 43886, 43887, 43888</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Bariatric surgery</strong> and HTCC guidelines apply, in order to establish eligibility for surgery and medical necessity.</td>
</tr>
<tr>
<td>Medical Procedure</td>
<td>Code(s)</td>
<td></td>
</tr>
<tr>
<td>--------------------------------------------------------</td>
<td>----------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Cardiac Stenting</td>
<td>HTCC decision</td>
<td></td>
</tr>
<tr>
<td></td>
<td>92928, 92933, 92937, 92941, 92943</td>
<td></td>
</tr>
<tr>
<td>Carotid Artery Stenting</td>
<td>HTCC decision</td>
<td></td>
</tr>
<tr>
<td></td>
<td>37215, 37216, 37217, 37246, 37247</td>
<td></td>
</tr>
<tr>
<td>Catheter Ablation for Procedures for SVTA including Atrial Flutter/Fibrillation</td>
<td>HTCC decision</td>
<td></td>
</tr>
<tr>
<td></td>
<td>93653, 93655, 93656, 93657</td>
<td></td>
</tr>
<tr>
<td>Cochlear Implant</td>
<td>For Bilateral Cochlear Implants, UMP is subject to HTCC decision</td>
<td></td>
</tr>
<tr>
<td></td>
<td>69930</td>
<td></td>
</tr>
<tr>
<td></td>
<td>L8614, L8619, L8627, L8628</td>
<td></td>
</tr>
<tr>
<td></td>
<td>For Unilateral Cochlear Implant, UMP follows Regence Medical Policy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>11920, 11921, 11922, 15788, 15789, 15792, 15793, 15820, 15821, 15822, 15823, 15830, 17106, 17107, 17108, 17360, 19355, 21244, 21245, 21246, 21248, 21249, 21295, 21296, 21740, 21742, 21743, 30120, 30400, 30410, 30420, 30430, 30435, 30450, 41510, 49250, 49560, 49565, 49654, 49656, 54360, 57291, 57292, 57295, 57296, 57426, 67900, 67901, 67902, 67903, 67904, 67906, 67908, 67909, 67950, 69300, G0429, Q2026, Q2028</td>
<td></td>
</tr>
<tr>
<td>Cosmetic and Reconstructive Surgery</td>
<td>Regence Medical Policy Sur12</td>
<td></td>
</tr>
<tr>
<td></td>
<td>19366: This code always requires pre-authorization regardless of diagnosis. In addition, please see the Autologous Fat Grafting to Breast and Adipose-derived Stem Cells section.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pre-authorization is not required for breast reconstruction and nipple/areola reconstruction following mastectomy for breast cancer.</td>
<td></td>
</tr>
</tbody>
</table>

October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
<table>
<thead>
<tr>
<th>Procedure</th>
<th>Policy Reference</th>
<th>Codes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transgender services</td>
<td>• Transgender services must also meet transgender policy requirements</td>
<td></td>
</tr>
<tr>
<td>Cryosurgical Ablation of Miscellaneous Solid Organ and Breast Tumors</td>
<td>Regence Medical Policy Sur132</td>
<td>• 31641, 50542</td>
</tr>
<tr>
<td>Deep Brain Stimulation</td>
<td>Regence Medical Policy Sur84</td>
<td>• 61850, 61860, 61863, 61864, 61867, 61868, 61885, 61886, C1820, L8679, L8680, L8685, L8686, L8687, L8688, L8682, L8683</td>
</tr>
<tr>
<td>Endometrial Ablation</td>
<td>Regence Medical Policy Sur01</td>
<td>• 58353, 58356, 58563</td>
</tr>
<tr>
<td>Endovascular Angioplasty and/or Stenting for Intracranial Arterial Disease (Atherosclerosis and Aneurysms)</td>
<td>Regence Medical Policy Sur141</td>
<td>• 61630, 61635</td>
</tr>
<tr>
<td>Extracorporeal Circulation Membrane Oxygenation (ECMO) for the Treatment of Respiratory Failure in Adults</td>
<td>HTCC decision</td>
<td>• 33946, 33945, 33947, 33948, 33949, 33952, 33954, 33956, 33958, 33962, 33964, 33966, 33984, 33986, 33987, 33988, 33989, ECMO for UMP is subject to HTCC Decision for initiation. Regence Medical Policy Sur141 is used for continued use criteria not addressed in the HTCC. Regence requires the facility to specifically notify Regence when ECMO is initiated on a Regence member. We will initiate concurrent review upon this notification. Please see the Inpatient Admission section for further information.</td>
</tr>
<tr>
<td>Facets Neurotomy</td>
<td>HTCC decision</td>
<td>• 64633, 64634, 64635, 64636</td>
</tr>
<tr>
<td>Gastric Electrical Stimulation</td>
<td>Regence Medical Policy Sur111</td>
<td>• 43647, 43881, 64590</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• E0765</td>
</tr>
</tbody>
</table>
Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.

<table>
<thead>
<tr>
<th>Procedure/Condition</th>
<th>Medical Plan/Website</th>
<th>ICD Codes</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastroesophageal Reflux Surgery</td>
<td>Regence Medical Policy Sur186</td>
<td>C1767, L8679, L8680, L8685, L8686, L8687, L8688</td>
<td>-</td>
</tr>
</tbody>
</table>
| Hysterectomy surgery for members with the following cancer diagnoses does not require pre-authorization. | MCG | D06.0-D06.9, C79.60-C79.62, C57.00-C57.8, C58, C79.60-C79.62, C79.82, D06.0-D06.9, D49.59 | • 58150, 58152 - MCG S-650  
• 58260, 58262, 58263, 58267, 58270, 58275, 58280, 58290, 58291, 58292, 58293, 58294 - MCG S-660  
• 58550, 58552, 58553, 58554, 58570, 58571, 58572, 58573 - MCG S-665  
• 58200 and 58210 do not require surgery pre-authorization  
• 58240 does not require surgery pre-authorization |
| Hysterectomy surgery for members without the above listed diagnoses require pre-authorization | MCG | N81.2-N81.4, N81.85 | - |
| Implantable Bone Conduction and Bone-Anchored Hearing Aids | Regence Medical Policy Sur121 | L8690, L8691, L8692 | • 69714, 69710, 69715, 69717, 69718 |
| Implantable Cardiac Defibrillators | Regence Medical Policy Sur17 | 33270, 33271 | • 33230, 33231, 33240, 33249, 33270, 33271 |

Visit MCG’s website at careguidelines.com/products/ for information on purchasing their criteria, or contact us and we will be happy to provide you with a copy of the specific guideline.

Any inpatient request requires pre-authorization for level of care and length of stay.

Hysterectomy for the indication of gender dysphoria is addressed in the Transgender Services Medical Policy.

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage.

Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
<table>
<thead>
<tr>
<th>Procedure / Service</th>
<th>Reference</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanical Embolectomy for Treatment of Acute Stroke</td>
<td><a href="#">Regence Medical Policy Sur158</a></td>
<td>• C1721, C1722, C1882 Pre-authorization is not required for members age 17 and younger</td>
</tr>
<tr>
<td>Microwave Tumor Ablation</td>
<td><a href="#">Regence Medical Policy Sur189</a></td>
<td>• 37184, 37185, 61645 Pre-authorization is not required; however, these codes will be reviewed post-service prepayment</td>
</tr>
<tr>
<td>Negative Pressure Wound Therapy for Home Use (NPWT)</td>
<td><a href="#">HTCC decision</a></td>
<td>• Effective January 1, 2018: 97605, 97606, 97607, 98608, A6550, E2402</td>
</tr>
<tr>
<td>Occipital Nerve Stimulation and Posterior Tibial Nerve Stimulation</td>
<td><a href="#">Regence Medical Policy Sur174</a></td>
<td>• 61885, 61886, 64553, 64555, 64568, 64575, 64585, 64590, 0466T • C1820, L8679, L8680, L8682, L8683, L8685, L8686, L8687, L8688 Occipital Nerve Stimulation is considered investigational for all indications, including but not limited to headaches NOTE: These codes may overlap with the codes in the Vagus Nerve Stimulation Medical Policy so to ensure proper adjudication of your claim, please call for preauth on all of the above codes.</td>
</tr>
<tr>
<td>Orthognathic Surgery</td>
<td><a href="#">Regence Medical Policy Sur137</a></td>
<td>• 21085, 21110, 21120, 21121, 21122, 21123, 21125, 21127, 21141, 21142, 21143, 21145, 21146, 21147, 21150, 21151, 21154, 21155, 21159, 21160, 21188, 21193, 21194, 21195, 21196, 21198, 21206, 21208, 21209, 21210, 21215, 21230, 21295, 21296 • Codes 21145, 21196, 21198 do not require pre-authorization when the procedure is performed for</td>
</tr>
</tbody>
</table>

October 1, 2017
These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
<table>
<thead>
<tr>
<th>Procedure</th>
<th>Code(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteochondral Allograft and Autograft Transplantation (OAT)</td>
<td>HTCC decision</td>
</tr>
<tr>
<td></td>
<td>• 27415, 27416, 29866, 29867</td>
</tr>
<tr>
<td></td>
<td>• J7330, S2112</td>
</tr>
<tr>
<td>Ovarian, Internal Iliac and Gonadal Vein Embolization, Ablation,</td>
<td>Regence Medical Policy Sur147</td>
</tr>
<tr>
<td>and Sclerotherapy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 37241</td>
</tr>
<tr>
<td>Percutaneous Angioplasty and Stenting of Veins</td>
<td>Regence Medical Policy Sur109</td>
</tr>
<tr>
<td></td>
<td>• 37238, 37239, 37248, 37249</td>
</tr>
<tr>
<td>Percutaneous Tibial Nerve Stimulation</td>
<td>Regence Medical Policy Sur154</td>
</tr>
<tr>
<td></td>
<td>• L8680</td>
</tr>
<tr>
<td>Radiofrequency Ablation of Tumors (RFA)</td>
<td>Regence Medical Policy Sur92</td>
</tr>
<tr>
<td></td>
<td>• 20982, 31641, 32998, 50542, 50592</td>
</tr>
<tr>
<td>Reconstructive Breast Surgery/Mastopexy, and Management of Breast Implants</td>
<td>Regence Medical Policy Sur40</td>
</tr>
<tr>
<td></td>
<td>• 11920, 11921, 19316, 19318, 19324, 19325, 19328, 19330, 19340, 19342,</td>
</tr>
<tr>
<td></td>
<td>19350, 19355, 19370, 19371</td>
</tr>
<tr>
<td></td>
<td>• L8600</td>
</tr>
<tr>
<td></td>
<td>Pre-authorization is not required for breast reconstruction and</td>
</tr>
<tr>
<td></td>
<td>nipple/areola reconstruction following mastectomy for breast cancer.</td>
</tr>
<tr>
<td></td>
<td>Code 19366: This code always requires pre-authorization regardless of</td>
</tr>
<tr>
<td></td>
<td>diagnosis. In addition, please see the Autologous Fat Grafting to the</td>
</tr>
<tr>
<td></td>
<td>Breast and Adipose-derived Stem Cells section.</td>
</tr>
<tr>
<td>Reduction Mammaryoplasty</td>
<td>Regence Medical Policy Sur60</td>
</tr>
<tr>
<td></td>
<td>• 19318</td>
</tr>
</tbody>
</table>

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage.
Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
<table>
<thead>
<tr>
<th>Procedure</th>
<th>Code(s)</th>
<th>Additional Information</th>
</tr>
</thead>
</table>
| Sacral Nerve Modulation/Stimulation for Pelvic Floor Dysfunction         | Regence Medical Policy Sur134                | • 64561, 64581, 64585, 64590  
  • C1767, L8679, L8680, L8682, L8683, L8685, L8686, L8687, L8688 |
| Sacroiliac Joint Fusion                                                  | Regence Medical Policy Sur193                | • 27280                |
| Spinal Cord and Dorsal Root Ganglion Stimulation                        | Regence Medical Policy Sur45                 | • 63650, 63655, 63685  
  • C1820, C1822, L8679, L8680, L8685, L8686, L8687, L8688 |
|                                                                          |                                              | Spinal cord stimulation for the treatment of chronic neuropathic pain is not a covered benefit, per HTCC decision when associated diagnosis codes are included: G60.9, M47.20-M47.28, M54.10-M54.13, M54.5, G89.28-G89.29, M47.811-M47.819, M54.16-M54.17, M79.2, G89.4, M50.10-M50.13, M54.30-M54.32, M96.1, M50.121-M50.123, M54.40-M54.42, M51.14-M51.17 |
|                                                                          |                                              | If treatment is for other than this indication, Regence Medical Policy applies. |
| Spinal Injections                                                        | HTCC decision                                | • CPT 64633, 64634, 64635  
  and 64636 may be subject to HTCC decision; therefore, they require preauthorization.  
  • CPT 62292 for Therapeutic Medial Branch Nerve Block, Intradiscal and Facet Spinal injections are not a covered benefit.  
  • CPT 64490, 64491, 64492, 64493, 64494, 64495 may be subject to HTCC decision. Pre-authorization is not required. Claims should be submitted with the Spinal Injection Additional Information Form to certify that the provider is billing for an allowed service.  
  • This coverage policy does not apply to those with systemic |
<table>
<thead>
<tr>
<th>Procedure</th>
<th>Code Listings</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spinal Surgery – Artificial intervertebral disc re-review</td>
<td>HTCC decision</td>
<td>• 22856, 22858, 22861, 22864&lt;br&gt;• 0095T, 0098T</td>
</tr>
<tr>
<td>Spinal Surgery - Lumbar Fusion</td>
<td>HTCC decision</td>
<td>• 22533, 22558, 22612, 22630, 22633, 22853, 22854, 22859&lt;br&gt;• Lumbar Fusion for degenerative disc disease uncomplicated by comorbidities is not a covered benefit per HTCC decision; this includes diagnosis codes M5135, M5136 and M5137. This decision does not apply to patients with the following conditions: radiculopathy, spondylolisthesis (&gt;grade 1), severe spinal stenosis, acute trauma or systemic disease affecting spine, e.g., malignancy.&lt;br&gt;• UMP is subject to HTCC decision for Bone Morphogenic Protein:&lt;br&gt;  o Bone morphogenetic protein-2 (rhBMP-2) and bone morphogenetic protein-7 (rhBMP-7)&lt;br&gt;  o Note: Bone morphogenetic protein-7 (rhBMP-7) is not a covered benefit</td>
</tr>
<tr>
<td>Spinal Surgery - Cervical Fusion for Degenerative Disc Disease</td>
<td>HTCC decision</td>
<td>• 22551, 22552, 22554, 22853, 22854, 22859, 22600</td>
</tr>
<tr>
<td>Spinal Surgery - Cervical Fusion</td>
<td>MCG</td>
<td>• 22551, 22552, 22554 - MCG ORG S-320&lt;br&gt;• 22600 - MCG ORG S-330</td>
</tr>
</tbody>
</table>

inflammatory disease such as ankylosing spondylitis, psoriatic arthritis or enteropathic arthritis.
<table>
<thead>
<tr>
<th>Condition</th>
<th>Reference</th>
<th>Codes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stereotactic Radiation Surgery and Stereotactic Body Radiation Therapy</td>
<td>HTCC decision</td>
<td>32701, 61796, 61797, 61798, 61799, 61800, 63620, 63621, 77371, 77372, 77373, 77432, 77435</td>
</tr>
<tr>
<td></td>
<td></td>
<td>G0339, G0340</td>
</tr>
<tr>
<td>Surgical Treatments for Hyperhidrosis</td>
<td>Regence Medical Policy Sur165</td>
<td>32664, 64818, 69676</td>
</tr>
<tr>
<td>Sleep Apnea Diagnosis and Treatment</td>
<td>HTCC decision</td>
<td>21121, 21122, 21141, 21145, 21196, 21198, 21199, 21685, 41120, 41500, 42140, 42145, 42160, 64568, 0466T</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Codes 21145, 21195, 21198, 41120, 42160 do not require pre-authorization when the procedure is performed for oral cancer dx codes: C01, C02-C02.9, C03-C03.9, C04-C04.9, C05-C05.9, C06, C06.2-C06.9, C09-C09.9, C10-C10.0, C41-C41.1, C46.2, D00-D00.00, D10, D10.1-D10.9, D16.4-D16.5, D37-D37.0, D49-D49.0</td>
</tr>
<tr>
<td>Temporomandibular Joint (TMJ) Surgical Interventions</td>
<td>MCG</td>
<td>21010 - MCG A-0522, 21050 - MCG A-0521, 29800, 29804 - MCG A-0492, 21240, 21242, 21243 - MCG A-0523</td>
</tr>
<tr>
<td>Transesophageal Endoscopic Therapies for Gastroesophageal Reflux Disease (GERD)</td>
<td>Regence Medical Policy M-SUR110</td>
<td>43192, 43210, 43236</td>
</tr>
<tr>
<td>Vagus/Vagal Nerve Stimulation</td>
<td>Regence Medical Policy Sur74</td>
<td>UMP is subject to HTCC Decision: 61885, 61886, 64560, 64568, 0466T</td>
</tr>
</tbody>
</table>

Note: For Botox injections, please see the Pharmacy policy.

October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
<table>
<thead>
<tr>
<th>Treatment</th>
<th>Policy Reference</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varicose Vein Treatment</td>
<td>Regence Medical Policy Sur104</td>
<td>• Effective January 1, 2018: UMP is subject to <a href="#">HTCC Decision</a>. 36470, 36471, 36475, 36476, 36478, 36479, 37700, 37718, 37722, 37735, 37760, 37761, 37765, 37766, 37780, 37785, S2202</td>
</tr>
</tbody>
</table>

Note: Vagal Nerve Stimulation for the treatment of epilepsy and depression are subject to [HTCC decision](#). If treatment is for other than these indications, our policy applies.
Ablation of Primary and Metastatic Liver Tumors

Effective: October 1, 2017

Next Review: June 2018
Last Review: June 2017

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Ablation is a method of locoregional therapy used treat cancerous lesions, including hepatocellular carcinoma and hepatic metastases from other primary cancers.

MEDICAL POLICY CRITERIA

Note: This policy addresses locoregional therapies, specifically, percutaneous ethanol injection, cryoablation, radiofrequency and microwave ablation for primary and metastatic liver tumors. Please see Cross References for other ablative techniques and indications.

I. Percutaneous ethanol injection, cryoablation, radiofrequency and microwave local ablative techniques may be considered medically necessary for treatment of liver tumors when either of the following (A. or B.) are met:

   A. In patients not currently awaiting liver transplantation, and one or more of the following criteria are met (1., 2., or 3.):

      1. Unresectable primary liver tumors [hepatocellular carcinoma (HCC)] when all of the following criteria (a-d) are met:
a. The tumor(s) is 5 cm or less in diameter; and  

b. There are no more than 3 hepatic lesions; and  
c. There is documentation that the tumor(s) is unresectable (e.g., due to comorbidities or an estimate of inadequate liver volume following resection); and  
d. The goal of treatment is curative, defined as complete ablation of all tumor foci.

2. Hepatic metastases from colorectal tumors, including but not limited to adenocarcinoma when all of the following criteria (a.-e.) are met  
a. The metastatic tumor(s) is 5 cm or less in diameter; and  
b. There are no more than 5 hepatic lesions; and  
c. There is documentation that the tumor(s) is unresectable (e.g., due to comorbidities, or an estimate of inadequate liver volume following resection; and  
d. No extrahepatic metastatic disease is present; and  
e. The goal of treatment is curative, defined as complete resection/ablation of all tumor foci.

3. Hepatic metastases from neuroendocrine tumors when all of the following criteria (a.-c.) are met:  
a. The disease is symptomatic; and  
b. Systemic therapy has failed to control symptoms; and  
c. There is documentation that the tumor(s) is unresectable (e.g., due to comorbidities or an estimate of inadequate liver volume following resection)  

B. As a bridge to liver transplantation when the intent is to prevent tumor progression or decrease tumor size to achieve or maintain a patient’s candidacy for liver transplant  

II. Percutaneous ethanol injection, cryoablation, radiofrequency and microwave ablation are considered investigational as a treatment for all other benign or malignant liver tumors that do not meet the medical necessity criteria above, including but not limited to the following:  

A. In the absence of contraindications for surgical resection  
B. More than 3 HCC tumors or 5 metastatic colorectal tumors in the liver  
C. Metastases to the liver from organ tumors other than colorectal or the following neuroendocrine tumors:  
   1. Asymptomatic neuroendocrine tumors  
   2. Neuroendocrine tumors with symptoms controlled by systemic therapy  
D. Metastatic or primary liver tumors larger than 5 cm in diameter  
E. Debulking procedures with a goal of less than complete resection/ablation  

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage.  
Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

POLICY GUIDELINES

REQUIRED DOCUMENTATION

It is critical that the list of information below is submitted for review to determine if the policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome.

1. Specific description of the tumor(s) targeted for treatment including the following:
   - Tumor type (primary vs. metastatic; primary tumor type)
   - The location of tumor(s)
   - The number and size(s) of lesion(s) being treated
2. Rationale for the determination that the patient is not a surgical candidate or the tumor is unresectable
3. Whether the goal of treatment is curative or palliative
4. Comorbidities and any contraindicated treatments (e.g., surgery; radiation therapy)
5. Prior treatments, if any, and tumor response
6. Documentation of whether this treatment is to preserve organ function
7. Include documentation of the presence or absence of extra-hepatic disease

CROSS REFERENCES

1. Radioembolization for Primary and Metastatic Tumors of the Liver, Medicine, Policy No. 140
2. Radiofrequency Ablation of Tumors (RFA), Surgery, Policy No. 92
3. Cryosurgical Ablation of Miscellaneous Solid Tumors, Surgery, Policy No. 132
4. Magnetic Resonance (MR) Guided Focused Ultrasound (MRgFUS) and High Intensity Focused Ultrasound (HIFU) Ablation, Surgery, Policy No. 139
5. Microwave Tumor Ablation, Surgery, Policy No. 189

BACKGROUND

ABLATIVE TECHNIQUES

THERMAL ABLATION

Radiofrequency Ablation

Radiofrequency ablation (RFA) is one of a number of locoregional thermal ablation therapies to treat various benign or malignant tumors. RFA kills cells (cancerous and normal) by applying a heat-generating rapidly alternating radiofrequency current through probes inserted into the tumor. The cells killed by RFA are not removed but are gradually replaced by fibrosis and scar tissue. If there is local recurrence, it occurs at the edge of this scar tissue and, in some cases, may be retreated. RFA can be performed as an open surgical procedure, laparoscopically, or percutaneously with ultrasound or computed tomography (CT) guidance. The goals of RFA may include 1) controlling local tumor growth and preventing recurrence; 2) palliating symptoms; and 3) extending survival duration for patients with certain cancerous tumors.

Reports have been published on use of RFA to treat renal cell carcinomas, breast cancer, pulmonary (including primary and metastatic lung tumors), bone, and other tumors including
those that are non-cancerous (benign). Well-established local or systemic treatment alternatives are available for each of these tumor types.

Radiofrequency ablation (RFA) has been investigated as a treatment for unresectable hepatic tumors, both as primary treatment and as a bridge to liver transplant. In the latter setting, RFA is being tested to determine whether it can reduce the incidence of tumor progression in patients awaiting transplantation and thus maintain patients’ candidacy for liver ablation, transhepatic arterial chemoembolization, microwave coagulation, percutaneous ethanol injection, and radioembolization (yttrium-90 microspheres).

**Microwave Ablation**

Microwave ablation (MWA) is a technique in which the use of microwave energy induces an ultra-high speed, 915 MHz or 2.450 MHz (2.45 GHz), alternating electric field which causes water molecule rotation and the creation of heat. This results in thermal coagulation and localized tissue necrosis. In MWA, a single microwave antenna or multiple antennas connected to a generator are inserted directly into the tumor or tissue to be ablated; energy from the antennas generates friction and heat. The local heat coagulates the tissue adjacent to the probe, resulting in a small, approximately 2-3 cm elliptical area (5 x 3 cm) of tissue ablation. In tumors greater than 2 cm in diameter, 2-3 antennas may be used simultaneously to increase the targeted area of MWA and shorten operative time. Multiple antennas may also be used simultaneously to ablate multiple tumors. Tissue ablation occurs quickly, within 1 minute after a pulse of energy, and multiple pulses may be delivered within a treatment session depending on the size of the tumor. The cells killed by MWA are typically not removed but are gradually replaced by fibrosis and scar tissue. If there is local recurrence, it occurs at the edges. Treatment may be repeated as needed. MWA may be used to: 1) control local tumor growth and prevent recurrence; 2) palliate symptoms; and 3) extend survival duration.

Complications from MWA are usually considered mild and may include pain and fever. Other potential complications associated with MWA include those caused by heat damage to normal tissue adjacent to the tumor (e.g., intestinal damage during MWA of the kidney or liver), structural damage along the probe track (e.g., pneumothorax as a consequence of procedures on the lung), liver enzyme elevation, liver abscess, ascites, pleural effusion, diaphragm injury or secondary tumors if cells seed during probe removal. MWA should be avoided in pregnant patients since potential risks to the patient and/or fetus have not been established and in patients with implanted electronic devices such as implantable pacemakers that may be adversely affected by microwave power output.

MWA is an ablative technique similar to radiofrequency or cryosurgical ablation; however, MWA may have some advantages. In MWA, the heating process is active, which produces higher temperatures than the passive heating of radiofrequency ablation and should allow for more complete thermal ablation in a shorter period of time. The higher temperatures reached with MWA (over 100° C) can overcome the “heat sink” effect in which tissue cooling occurs from nearby blood flow in large vessels potentially resulting in incomplete tumor ablation. MWA does not rely on the conduction of electricity for heating, and therefore, does not have electrical current flow through patients and does not require grounding pads be used during the procedure to prevent skin burns. Unlike radiofrequency ablation, MWA does not produce electric noise, which allows ultrasound guidance to occur during the procedure without
interference. Finally, MWA can be completed in less time than radiofrequency ablation since multiple antennas can be used simultaneously.

Regulatory Status

There are several devices cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process for MWA. Covidien’s (a subsidiary of Tyco Healthcare) Evident Microwave Ablation System has 510(k) clearance for soft tissue ablation, including partial or complete ablation of non-resectable liver tumors. The following devices have 510(k) clearance for MWA of (unspecified) soft tissue:

- BSD Medical Corporation’s MicroThermX® Microwave Ablation System (MTX-180);
- Valleylab’s (a subsidiary of Covidien) VivaWave® Microwave Ablation System;
- Vivant’s (acquired by Valleylab in 2005) Tri-Loop™ Microwave Ablation Probe;
- MicroSurgeon Microwave Soft Tissue Ablation Device;
- Microsulis Medical’s Acculis Accu2i; and
- NeuWave Medical’s Certus 140™

FDA determined that these devices were substantially equivalent to existing radiofrequency and MWA devices. FDA product code: NEY.

CRYOSURGICAL ABLATION

Cryosurgical ablation (also called cryosurgery, cryotherapy, or cryoablation) kills cells (cancerous and normal) by freezing target tissues, most often by inserting a probe into the tumor through which coolant is circulated. Cryosurgery may be performed as an open surgical technique or as a closed procedure under laparoscopic or ultrasound guidance.

The goals of cryosurgery may include the following:

- Destruction or shrinkage of tumor tissue
- Controlling local tumor growth and preventing recurrence
- Palliating symptoms
- Extending survival duration for patients with certain tumors.

Potential complications associated with cryosurgery in any organ include the following:

- Hypothermic damage to normal tissue adjacent to the tumor (e.g., nerve damage)
- Structural damage along the probe track
- Secondary tumors if cancerous cells are seeded during probe removal.

Regulatory Status

There are several cryoablation devices cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process for use in open, minimally invasive or endoscopic surgical procedures in the areas of general surgery, urology, gynecology, oncology, neurology, dermatology, proctology, thoracic surgery and ear, nose and throat. Examples include:

- Cryocare® Surgical System by Endocare;
- CryoGen Cryosurgical System by Cryosurgical, Inc.;
- CryoHit® by Galil Medical;
• IceRod® CX, IcePearl® 2.1 CX and IceFORCE® 2.1 CX Cryoablation Needles by Galil Medical;
• SeedNet™ System by Galil Medical;
• Visica® System by Sanarus Medical;
• Visual-ICE® Cryoablation System by Galil;
• ERBECRYO 2® Cryosurgical Unit, ERBE USA Incorporated

PERCUTANEOUS ETHANOL INJECTION

Using a needle, percutaneous ethanol injection (PEI) delivers an injection of 95 percent ethanol directly into a tumor. Multiple treatment sessions may be performed in order to achieve tumor destruction. Prior to RFA, PEI was the most widely accepted, minimally invasive method to treat hepatocellular carcinoma. Like other local ablative techniques, PEI is most successful in small HCC tumors when resection is not an option.

LIVER (HEPATIC) TUMORS

Hepatic tumors can arise either as primary liver cancer (such as hepatocellular carcinoma, HCC) or by metastasis to the liver from other primary cancer sites. Local therapy for hepatic metastasis may be indicated when there is no extrahepatic disease, which rarely occurs for patients with primary cancers other than colorectal carcinoma or certain neuroendocrine malignancies. At present, surgical resection with adequate margins or liver transplantation constitutes the only treatments available with demonstrated curative potential. Partial liver resection, hepatectomy, is considered the gold standard. However, the majority of hepatic tumors are unresectable at diagnosis, due either to their anatomic location, size, number of lesions, or underlying liver reserve.

Locoregional therapies are proposed as a treatment for unresectable hepatic tumors, both as primary treatment, palliative treatment, and as a bridge to liver transplant. In the case of liver transplants, it is hoped that locoregional ablative techniques will reduce the incidence of tumor progression while awaiting transplantation and thus maintain a patient’s candidacy for liver transplant during the wait time for a donor organ.

EVIDENCE SUMMARY

RADIOFREQUENCY ABLATION

RFA AS A PRIMARY TREATMENT OF UNRESECTABLE HEPATOCELLULAR CANCER

Systematic Reviews

A 2003 TEC Assessment addressed radiofrequency ablation (RFA) in the treatment of unresectable primary or metastatic liver tumors. Since that time, many systematic reviews and meta-analyses have been published on RFA for hepatocellular cancer (HCC). Some are discussed below.

In 2016, Lan et al published a network meta-analysis comparing different interventional treatments for early stage HCC. A total of 21 RCTs were included that compared transhepatic arterial chemoembolization (TACE), RFA, percutaneous ethanol injection (PEI), and hepatic resection, or combinations of treatments. These studies were all rated at a low-to-moderate risk of bias, with lack of blinding being the most substantial limitation. The primary...
outcome measures were overall survival (OS) at 1, 3, and 5 years posttreatment. The treatments and combinations of treatments were rank-ordered by results on OS. At each time point, the combination of RFA plus TACE was the number 1 ranked treatment. The combination of RFA plus TACE ranked second highest at 1 and 3 years, and was third highest at 5 years, with hepatic resection ranked second at 5 years. RFA alone was ranked as the fourth highest treatment at 1 year and the fifth highest treatment at 3 and 5 years.

In a 2013 Cochrane review, Weis et al reviewed studies on RFA for HCC versus other interventions.[3] Moderate-quality evidence demonstrated hepatic resection had superior survival outcomes compared with RFA; however, resection might have greater rates of complications and longer hospital stays. Other systematic reviews and meta-analyses have also found superior survival with hepatic resection but higher rates of complications than RFA.[4-7] This finding reinforces the use of RFA only for unresectable HCC. The Cochrane review also reported finding moderate quality evidence demonstrating superior survival with RFA over PEI.[3] Evidence on RFA versus acetic acid injection, microwave ablation, or laser ablation was insufficient to draw conclusions.[3]

Randomized and nonrandomized trials in the 1990s reported that PEI could safely achieve complete necrosis in small HCCs, with 5-year survival rates of 32% to 38%.[8,9] A systematic review of randomized trials for HCC treated with percutaneous ablation therapies was conducted by Cho et al.[9] The authors identified 4 RCTs (total N=652 patients) that compared RFA with PEI. The reviewers concluded that RFA demonstrated significantly improved 3-year survival in patients with HCC compared with ethanol injections. Most patients in these studies had 1 tumor, and more than 75% of the tumors were 3 cm or smaller in size. The 3-year survival with RFA ranged from 63% to 81%.

In a 2013, Shen et al reported on a systematic review of 4 RCTs and quasi-RCTs (total N=766 patients), to compare RFA with PEI for treatment of HCC nodules up to 3 cm.[10] OS was significantly longer for RFA than for PEI at 3 years (hazard ratio [HR], 0.66; 95% confidence interval [CI], 0.48 to 0.90; p=0.009), and local recurrence risk was lower with RFA (HR=0.38; 95% CI, 0.15 to 0.96, p=0.040). However, there was no difference in distant intrahepatic recurrence, and RFA resulted in more complications.

In 2012, Xu et al reported on a meta-analysis of 13 studies that compared RFA with surgical resection for early HCC.[11] Only 2 studies were RCTs. Surgical resection was done in 1233 patients and RFA was used in 1302 patients. Surgical resection patients had significantly longer OS rates at 1, 3 and 5 years than RFA patients (odds ratio [OR], 0.60; 95% CI, 0.42 to 0.86, OR=0.49; 95% CI, 0.36 to 0.65; OR=0.60; 95% CI, 0.43 to 0.84), respectively. When only HCC tumors of 3 cm or less were analyzed, resection still had significantly better OS than RFA at 1, 3, and 5 years. Recurrence rates were also significantly lower in the surgical resection group at 1, 3, and 5 years than in the RFA group (OR=1.48; 95% CI, 1.05 to 2.08; OR=1.76; 95% CI, 1.49 to 2.08; OR=1.68; 95% CI, 1.21 to 2.34; all respectively). Local recurrence rates did not differ significantly between procedures. Complication rates were higher with resection than with RFA (OR=6.25; 95% CI, 3.12 to 12.52; p=0.000), but, in a subanalysis of HCC 3 cm or less, complication rates were significantly lower with resection than RFA.

Tiong and Maddern conducted a systematic review of the literature from 2000 to 2010 and a meta-analysis of survival and disease recurrence after RFA for HCC.[12] Studies reporting on patients with HCC who were treated with RFA, either in comparison to or in combination with other interventions (eg, surgery, PEI), were eligible for inclusion. Outcome data collected were
OS, disease-free survival (DFS), and disease recurrence rates. Only RCTs, quasi-RCTs, and nonrandomized comparative studies with more than 12 months of follow-up were included. Forty-three articles, including 12 RCTs, were included in the review. Most articles reported the use of RFA for unresectable HCC, often in combination with other treatments (eg, PEI, TACE, surgery). Meta-analysis of 5 RCTs showed that RFA was better than PEI, with higher OS and DFS rates. Data on RFA compared with microwave ablation were inconclusive. The reviewers concluded that RFA can achieve good clinical outcomes for unresectable HCC.

In a 2013 meta-analysis comparing RFA with cryoablation for HCC, Huang et al evaluated 3 prospective studies and 1 retrospective study.[13] Included in the studies were 180 RFA and 253 cryoablation patients. RFA was significantly superior to cryoablation in rates of complications (OR=2.80; 95% CI, 1.54 to 5.09), local recurrence of patient (OR=4.02; 95% CI, 1.93 to 8.39), and local recurrence of tumor (OR=1.96, 95% CI, 1.12 to 3.42). However, mortality did not differ significantly (OR=2.21; 95% CI, 0.45 to 10.8) between groups.

**Randomized Controlled Trials**

Feng et al. randomized patients with HCC with up to 2 nodules with nodular diameter of less than 4 cm to either surgical resection (n=84) or RFA (n=84).[14] This study population differed from that of many other RCTs in that the tumors were resectable. There were no statistically significant differences between the groups for overall survival or recurrence-free survival. The authors concluded that RFA provided therapeutic effects similar to surgical resection, but that RFA of small HCCs in certain sites was more likely to be incomplete, making surgical resection the better option in those cases.

**Nonrandomized Studies**

A large body of case series, meta-analyses, and retrospective evidence has been published on RFA as a treatment of unresectable primary liver tumors.[15-21] These articles reported disease-free survival rates consistent with those reported in the randomized controlled trials.

**RFA AS A PRIMARY TREATMENT OF INTRAHEPATIC CHOLANGIOCARCINOMAS**

Cholangiocarcinomas are tumors that originate in the bile duct epithelium; 90% are adenocarcinomas. Intrahepatic cholangiocarcinomas (ICC) are located within the hepatic parenchyma. They may also be referred to as peripheral cholangiocarcinomas. Extrahepatic cholangiocarcinomas (ECC) are more common than intrahepatic cholangiocarcinoma and are located within the extrahepatic bile duct. ECC are reviewed under Complete resection with negative margin is potential curative, though recurrence is common and most cases are unresectable due to advanced disease when diagnosed. For unresectable or metastatic cholangiocarcinomas at any location, the primary treatment may include chemotherapy, treatment within a clinical trial, or best supportive care. RFA and other locoregional therapies may be an option. Biliary drainage with biliary stenting may be warranted for unresectable or metastatic extrahepatic disease. Liver transplantation is potentially curative in carefully selected patients with lymph node negative, nondisseminated locally advanced hilar cholangiocarcinomas and otherwise normal biliary and hepatic function or underlying liver disease precluding surgery.

A number of small (n<20) retrospective analyses and case series have been published for ablation of ICC.[22-30] These studies consistently reported high technical effectiveness with early tumor necrosis, and a low rate of major adverse effects.
RFA AS A PRIMARY TREATMENT OF UNRESECTABLE LIVER METASTASES OF COLORECTAL AND NEUROENDOCRINE ORIGIN

Colon Cancer

More than half of patients with colorectal cancer (CRC) will develop liver metastases, generally with a poor prognosis. A median survival of 21 months has been observed in patients with a single CRC liver metastasis; those with several unilobar lesions have median survival of 15 months; and those with disseminated metastases have median survival of less than 1 year. A number of first-line systemic chemotherapy regimens have been used to treat metastatic CRC, with a 2-year survival rate of 25% for those treated with 5-fluorouracil (5-FU) or 5-FU plus leucovorin. With the introduction of newer agents (eg, irinotecan, oxaliplatin) and targeted drugs (eg, cetuximab, bevacizumab), 2-year survival rates have increased to between 30% and 39%, with marked improvement in OS. Because the liver is often the only site of metastases from CRC, however, locoregional therapies have been investigated. Surgical resection is considered the criterion standard for treatment of CRC liver metastases, with 5-year actuarial survival rates that historically range from 28% to 38%, but may reach 58% in appropriately selected, resectable patients without widely disseminated disease. However, only 10% to 25% of patients with CRC metastases are eligible for surgical resection because of the extent and location of the lesions within the liver or because of the presence of comorbid conditions or disseminated disease. Unresectable cases or those for whom surgery is contraindicated typically are treated with systemic chemotherapy, with poor results and considerable adverse effects.

Alternatively, RFA has been proposed to treat metastatic CRC in the liver. Early clinical experience with RFA comprised case series to establish feasibility, safety, tolerability, and local therapeutic efficacy in short-term follow-up. A 2006 literature review encompassing 6 case series (total N=446 patients) showed that RFA of unresectable CRC metastases was associated with 1-, 2-, and 3-year survival rates that ranged from 87% to 99%, 69% to 77%, and 37% to 58%, respectively. While these results suggested RFA may have clinical benefit in this setting, a primary caveat is the definition of the term “unresectable” in the different series and that different surgeons may have different opinions on this issue. Further, differences in lesion size, number, distribution, prior treatments, RFA technology, and physician experience may affect results, making it difficult to compare results of different studies.

Systematic Reviews

A 2012 systematic review by Cirocchi et al analyzed 17 nonrandomized studies and an meeting abstract of an RCT on RFA for CRC liver metastases. The RCT reported PFS was significantly higher in 60 patients receiving RFA plus chemotherapy than in 59 patients receiving only chemotherapy. The RCT did not report OS. This Cochrane review found different types of vulnerability in all reviewed studies. Of main concern was the imbalance in patient characteristics across studies reviewed, as well as heterogeneity in the interventions, comparisons, and outcomes. Therefore, the reviewers concluded the evidence was insufficient to recommend RFA for CRC liver metastasis. In a 2014 Health Technology Assessment, Loveman et al also found insufficient evidence to draw conclusions on the clinical effectiveness of ablative therapies, including RFA, for liver metastases.

In 2012, Weng et al reported a meta-analysis comparing RFA with liver resection for the treatment of CRC liver metastases. One prospective study and 12 retrospective studies
were included in the analysis. OS at 3 and 5 years was significantly longer in liver resection than in RFA (relative risk [RR], 1.377; 95% CI, 1.246 to 1.522; RR=1.474; 95% CI, 1.284 to 1.692, respectively). DFS was also significantly longer in liver resection than RFA at 3 and 5 years (RR=1.735; 95% CI, 1.483 to 2.029; RR=2.227; 95% CI, 1.823 to 2.720, respectively). While postoperative morbidity with liver resection was significantly higher than with RFA (RR=2.495; 95% CI, 1.881 to 3.308), mortality did not differ significantly between treatments. Liver resection also performed significantly better than RFA when data were analyzed in 3 subgroups: tumors less than 3 cm, solitary tumor, and open or laparoscopic approach. However, hospital stays were significantly shorter (9.2 days vs 3.9 days, p<0.01) and rates of complications lower (18.3% vs 3.9%, p<0.01) with RFA than liver resection. Interpretation of the meta-analysis is limited by the retrospective nature of most studies.

A 2011 systematic review by Pathak et al assessed the long-term outcome and complication rates of various ablative therapies used in the management of colorectal liver metastases.[37] The literature search was from 1994 to 2010, and study inclusion criteria were minimum 1-year follow-up and more than 10 patients. In all, 226 studies were identified, 75 of which met inclusion criteria. Most studies were single-arm, single-center, retrospective, and prospective. There was wide variability in patient groups, adjuvant therapies, and management approaches within individual studies. Several studies combined results for colorectal and non–colorectal metastases, often reporting combined outcomes. End points were not always reported uniformly, with varying definitions of survival time, recurrence time, and complication rates. Cryotherapy (26 studies) had local recurrence rates of 12% to 39%, with mean 1-, 3-, and 5-year survival rates of 84%, 37%, and 17%, respectively. The major complication rate ranged from 7% to 66%. Microwave ablation (13 studies) had a local recurrence rate of 5% to 13%, with a mean 1-, 3-, and 5-year survival of 73%, 30%, and 16%, respectively, and a major complication rate ranging from 3% to 16%. RFA (36 studies) had a local recurrence rate of 10% to 31%, with a mean 1-, 3-, and 5-year survival of 85%, 36%, and 24%, respectively, with major complication rate ranging from 0% to 33%. The authors concluded that ablative therapies offer significantly improved survival compared with palliative chemotherapy alone, with 5-year survival rates of 17% to 24%, and that complication rates of commonly used techniques are low.

A review by Guenette and Dupuy in 2010 summarized the literature on the use of RFA for colorectal hepatic metastases.[38] Approximately 17 studies with more than 50 patients treated with RFA for colorectal hepatic metastases reported survival. Average tumor size, reported in 15 studies, ranged from 2.1 to 4.2 cm. Five-year OS, reported in 12 studies, ranged from 2% to 55.3% (mean, 24.5%). The largest study series (Lencioni et al) included in the review consisted of 423 patients, with average tumor size of 2.7 cm, 4 or fewer metastases, each 5 cm or less in greatest dimension, and no extrahepatic disease.[33] OS in the Lencioni study at 1, 3, and 5 years was 86%, 47%, and 24%, respectively. Guenette and Dupuy concluded that 5-year survival rates following RFA were similar to those following resection but that long-term data associated with RFA and colorectal hepatic metastases were sparse, randomized trials have failed recruitment, and patients with resectable disease should undergo resection if possible. However, given the efficacy of RFA compared with chemotherapy alone, they noted that RFA should be considered as a primary treatment option in patients with unresectable disease.

**Randomized Controlled Trials**

No additional RCTs not included in systematic reviews were identified.
Nonrandomized Studies

Nonrandomized studies in which RFA was compared to resection or systemic chemotherapy in patients with localized CRC metastases and no evidence of additional metastatic disease have been conducted. In 2016, Hof et al compared outcomes from RFA or hepatic resection in patients with hepatic metastases from CRC.[39] There were 431 patients included from an institutional database. All patients underwent locoregional treatment for hepatic metastases from CRC. Initial treatment was either hepatic resection (n=261), open RFA (n=26), percutaneous RFA (n=75), or a combination of resection plus RFA (n=69). Mean follow-up was 38.6 months. The overall recurrence rate was 83.5% (152/182) in patients treated with RFA compared to 66.6% (201/302) in patients treated with hepatic resection (p<0.001). The 5-year OS estimate by Kaplan-Meier analysis was 51.9% for RFA and 53.0% for hepatic resection (p=0.98).

Abdalla et al examined recurrence and survival rates for clinically similar patients treated with hepatic resection only (n=190), resection plus RFA (n=101), RFA only (n=57, open laparotomy by hepatobiliary surgeon), and systemic chemotherapy alone (n=70).[40] In the key relevant comparison, RFA versus chemotherapy in chemotherapy-naive patients with nonresectable CRC metastases (median, 1 lesion per patient; range, 1-8; median tumor size, 2.5 cm), OS at 4 years was 22% in the RFA group and 10% in the chemotherapy group (p=0.005). Median survival was estimated at 25 months in the RFA group and 17 months in the chemotherapy group (p not reported). Recurrence at a median follow-up of 21 months was 44% in the RFA group and 11% in the resection-only group (p<0.001), although the proportion of patients with distant recurrence as a component of failure was similar (41% resection vs 40% RFA, p=NS).

In a second trial, a consecutive series of well-defined, previously untreated patients (N=201) without extrahepatic disease underwent laparotomy to determine therapeutic approach.[41] Three groups were identified: those amenable to hepatic resection (n=117); those for whom resection plus local ablation were indicated (RFA, n=27; cryoablation, n=18); and those deemed unresectable and unsuitable for local ablation (n=39) who received systemic chemotherapy. Median OS was 61 months (95% CI, 41 to 81 months) in resected patients (median, 1 tumor per patient; range, 1-9; median diameter, 3.8 cm), 31 months (95% CI, 20 to 42 months) in locally ablated patients (median, 4 tumors per patient; range, 1-19; median diameter, 3 cm per lesion), and 26 months (95% CI, 17 to 35 months) in the chemotherapy patients (median, 4 tumors per patient; range, 1-17; median diameter, 4 cm per lesion; p=NS, ablated vs chemotherapy). Results from 2 validated quality-of-life instruments (EuroQol-5D, EORTC QLQ C-30) showed that patients treated by local ablation returned to baseline values within 3 months, whereas those treated with chemotherapy remained significantly lower (ie, worse quality of life) than baseline over 12 months posttreatment (p<0.05).

In 2011, Van Tilborg et al reported long-term results in 100 patients with unresectable colorectal liver metastases who underwent a total of 126 RFA sessions (237 lesions).[42] Lesion size ranged from 0.2 to 8.3 cm (mean 2.4 cm). Mean follow-up time was 29 months (range, 6-93 months). Major complications (including abscess, hemorrhage, grounding pad burns, and diaphragm perforation) occurred in 8 patients. Factors that determined the success of the procedure included lesion size and the number and location of the lesions. Local tumor site recurrence was 5.6% for tumors less than 3 cm, 19.5% for tumors 3 to 5 cm, and 41.2% for those greater than 5 cm. Centrally located lesions recurred more often than peripheral, at 21.4% versus 6.5%, respectively (p=0.009). Mean survival time from the time of RFA was 56 months (95% CI, 45 to 67 months).
NEUROENDOCRINE TUMORS

Unlike the above liver tumors, the treatment benefit for RFA of neuroendocrine metastases in the liver is related to symptom control rather than survival or local recurrence. Therefore, patient selection and outcome measures in related studies focused on the level of symptoms rather than lesion size, number, and location. The primary treatment of symptomatic neuroendocrine tumor (NET) metastases is chemotherapy.

Systematic Reviews

Most reports of RFA treatment for neuroendocrine liver metastases include small numbers of patients or subsets of patients in reports of more than 1 ablative method or very small subsets of larger case series of patients with various diagnoses. A systematic review of RFA as treatment for unresectable metastases from neuroendocrine tumors was published in 2015.[43] Seven unique studies (total N=301 patients) included in the review, all were retrospective case series from a single institution. The most common tumor type was carcinoid (59%), followed by nonfunctional pancreatic tumors (21%) and functional pancreatic tumors (13%). There were 2 periprocedural deaths (rate, 0.7%), and the overall rate of complications was 10% (including hemorrhage, abscess, viscus perforation, bile leak, biliopleural fistula, transient liver insufficiency, pneumothorax, grounding pad burn, urinary retention, pneumonia, pleural effusion). Improvement in symptoms was reported in 92% (117/127) of symptomatic patients, with a median duration of symptom relief ranging from 14 to 27 months. There was a high degree of variability in the length of follow-up and surveillance used for follow-up, and a wide range of local recurrence rates, from less than 5% to 50%. The reported 5-year survival rates ranged from 57% to 80%.

Nonrandomized Studies

Berber and Siperstein analyzed a large series of liver tumors treated with RFA.[44] Of 1032 tumors in the study, 295 were neuroendocrine tumor metastases. The mean number of lesions treated was 5.6 (range, 1-16) and mean lesion size was 2.3 cm (range, 0.5-10.0 cm). Local recurrence rates were lower in patients with neuroendocrine tumors than in patients with other tumor types: neuroendocrine tumors (19/295 [6%]), colorectal metastases (161/480 [24%]), non–colorectal, non–neuroendocrine metastases (28/126 [22%]), and HCC (23/131 [18%]). In patients with neuroendocrine tumors, 58% of the recurrences were evident at 1 year and 100% at 2 years versus 83% at 1 year and 97% at 2 years for colorectal metastases. Eight neuroendocrine tumors were eligible for repeat RFA; 7 were retreated, and 1 was not. Symptom control and survival were not reported.

Mazzaglia et al report on a series gathered over 10 years for 63 patients with neuroendocrine metastases who were treated with 80 sessions of LRFA.[45] Tumor types were 36 carcinoid, 18 pancreatic islet cell, and 9 medullary thyroid cancer. Indications for study enrollment were liver metastases from neuroendocrine tumors, enlarging liver lesions, worsening of symptoms, and/or failure to respond to other treatment modalities and predominance of disease in the liver; patients with additional minor extrahepatic disease were not excluded. RFA was performed 1.6 years (range, 0.1-7.8 years) after diagnosis of liver metastases. Fourteen patients had repeat sessions for disease progression. The mean number of lesions treated at the first RFA session was 6 and the mean tumor size was 2.3 cm. One week after surgery, 92% of patients had at least partial symptom relief and 70% had complete relief. Symptom control lasted 11 months. Median survival times were 11 years postdiagnosis of the primary
tumor, 5.5 years postdiagnosis of the neuroendocrine hepatic metastases, and 3.9 years after the first RFA treatment.

Elias et al report on 16 patients who underwent a 1-step procedure comprising a combination of hepatectomy and RFA for treatment of gastroenteropancreatic endocrine tumors.[46] A mean of 15 liver tumors per patient were surgically removed, and a mean of 12 were ablated using RFA. Three-year survival and DFS rates were similar to those observed in the authors’ preliminary series of 47 patients who had hepatectomy with a median of 7 liver tumors per patient. Venkatesan et al reported on 6 patients treated for pheochromocytoma metastases.[47] Complete ablation was achieved in 6 of 7 metastases. Mean follow-up was 12.3 months (range, 2.5-28 months).

RFA AS A PRIMARY TREATMENT OF UNRESECTABLE LIVER METASTASES OF OTHER ORIGIN

Breast Cancer

A number of case series have reported on use of RFA to treat breast cancer liver metastases. In 2014, Veltri et al analyzed 45 women treated with RFA for 87 breast cancer liver metastases (mean size, 23 mm).[48] Complete ablation was seen on initial follow-up in 90% of tumors, but tumor recurrence occurred in 19.7% within 8 months. RFA did not impact OS, which at 1 year was 90% and at 3 years was 44%.

In a retrospective review, Meloni et al assessed local control and intermediate- and long-term survival in 52 patients.[49] Inclusion criteria were fewer than 5 tumors, maximum tumor diameter of 5 cm, and disease confined to the liver or stable with medical therapy. Complete tumor necrosis was achieved in 97% of tumors. Median time to follow-up from diagnosis of liver metastasis and from RFA was 37.2 and 19.1 months, respectively. Local tumor progression occurred in 25% of patients, and new intrahepatic metastases developed in 53%. Median OS, from the time of first liver metastasis diagnosis, was 42 months, and 5-year survival was 32%. Patients with tumors 2.5 cm in diameter or larger had worse prognoses than those with smaller tumors. The authors concluded that these survival rates were comparable to those reported in the literature for surgery or laser ablation. In another series of 43 breast cancer patients with 111 liver metastases, technical success (tumor ablation) was achieved in 107 (96%) metastases.[50] During follow-up, local tumor progression was observed in 15 metastases. Estimated median OS was 58.6 months. Survival was significantly lower among patients with extrahepatic disease, with the exception of skeletal metastases.

A series of 19 patients was reported by Lawes et al.[51] Eight patients had disease confined to the liver, with 11 also having stable extrahepatic disease. At the time of the report, 7 patients, with disease confined to the liver at presentation, were alive, as were 6 with extrahepatic disease; median follow-up after RFA was 15 months (range, 0-77 months). Survival at 30 months was 41.6%. RFA failed to control hepatic disease in 3 patients.

Sarcoma

Jones et al evaluated RFA in a series of patients with sarcoma.[52] Thirteen gastrointestinal stromal tumor (GIST) patients and 12 with other histologic subtypes received RFA for metastatic disease in the liver: 12 responded to the first RFA procedure and 1 achieved stable disease. Two GIST patients received RFA on 2 occasions for separate lesions within the liver, and both responded to the second RFA procedure. Of the other subtypes, 7 underwent RFA to
liver lesions, 5 of whom responded to RFA, 1 progressed, and 1 was not assessable at the time of analysis. RFA was well-tolerated in this series of sarcoma patients. RFA may have a role in patients with GIST who have progression in a single metastasis but stable disease elsewhere. The authors advised conducting further larger studies to better define the role of this technique in this patient population.

A case series of 66 patients who underwent hepatic resection (n=35), resection and RFA (n=18), or RFA alone (n=13) was reported by Pawlik et al.[53] After a median follow-up of 35.8 months, 44 patients had recurrence (intrahepatic only, n=16; extrahepatic only, n=11; both, n=17). The 1-, 3-, and 5-year OS rates were 91.5%, 65.4%, and 27.1%, respectively. The authors recommended that patients with metastatic disease who can be rendered surgically free of disease be considered for potential hepatic resection.

**RFA AS A TREATMENT OF UNRESECTABLE HCC TUMORS IN THE TRANSPLANT SETTING**

The goal of RFA prior to transplantation is to maintain a patient’s eligibility for liver transplant by either downsizing a large tumor or by preventing progression of a smaller tumor. The literature related to locoregional therapy for HCC in the transplant setting can be divided into 3 objectives:

- Prevention of tumor progression while on the waiting list
- Downgrading HCC prior to transplantation
- To reduce risk of post-transplantation tumor recurrence in patients with T3 tumors

Assessment of the effects of pre-transplantation RFA on these objectives would, ideally, include clinical trials that compare the recurrence-free survival of patients who received pretransplant locoregional therapies with those who did not and to study recurrence-free survival in patients who received locoregional therapies to downsize larger tumor(s) or to prevent progression of smaller tumor(s) in order to meet transplant waiting list criteria.

The current published evidence is limited to case series and retrospective reviews which are considered unreliable due to methodologic limitations such as lack of randomization and lack of a control group for comparison.[54-62] In addition to these limitations, current studies targeted only a subset of candidates for liver transplant to treat HCC. Because only patients with adequate liver reserves were offered treatment, it cannot be determined whether any reported increase in recurrence-free survival was related to the pretransplant locoregional therapy or liver reserve status. It is unknown whether patients with adequate liver reserves have improved outcomes regardless of pretransplant management.

**United Network for Organ Sharing policy**

The United Network for Organ Sharing (UNOS) recognizes pretransplant locoregional therapies including RFA as a component of patient management during the waiting period for a donor liver.[63] In allocating donor organs, UNOS sought to balance risk of death on the waiting list against risk of recurrence after transplant. For HCC, part of this balance included tumor size and number of nodules as follows:

- **T1:** 1 nodule 1.9 cm or smaller
- **T2:** 1 nodule between 2.0–5.0 cm, or 2 or 3 nodules each smaller than 3.0 cm
- **T3:** 1 nodule larger than 5.0 cm, or 2 or 3 nodules with at least 1 larger than 3.0 cm

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
Patients with T1 lesions were considered at low risk of death on the waiting list, while those with T3 lesions were considered at high risk of post-transplant recurrence. Patients with T2 tumors were considered to have an increased risk of dying while on the waiting list compared with T1 lesions, and an acceptable risk of post-transplant tumor recurrence. Therefore, the UNOS criteria prioritized T2 HCC. In addition, patients could be removed from the waiting list if they were determined to be unsuitable for transplantation based on progression of HCC. Thus these criteria provide incentives to use locoregional therapies to maintain T2 classification.

The UNOS allocation system provides incentives to use locoregional therapies in 2 different settings:

To downsize T3 tumors to T2 status to meet the UNOS criteria for additional allocation points; or to prevent progress of T2 tumors while on the waiting list to maintain the UNOS allocation points.

These two indications are discussed further here. It should be noted that the UNOS policy addresses the role of locoregional therapy in the pretransplant setting as follows:

Organ Procurement and Transplant Network (OPTN) Class 5T (Treated) nodules are defined as any OPTN Class 5 or biopsy-proven HCC lesion that was automatically approved upon initial application or extension and has subsequently undergone loco-regional treatment. OPTN Class 5T nodules qualify for continued priority points predicated on the pre-treatment classification of the nodule(s) and are defined as:

- Past loco-regional treatment for HCC (OPTN class 5 lesion or biopsy proven prior to ablation).
- Evidence of persistent/recurrent HCC such as nodular or crescentic extra-zonal or intra-zonal enhancing tissue on late arterial imaging (relative to hepatic parenchyma) may be present.

OPTN guidelines also indicate “candidates whose tumors have been ablated after previously meeting the criteria for additional MELD/PELD points (OPTN Class 5T) will continue to receive additional MELD/PELD points (equivalent to a 10-percentage point increase in candidate mortality) every 3 months without RRB review, even if the estimated size of residual viable tumor falls below stage T2 criteria."

Candidates with HCC not meeting transplant criteria, “including those with downsized tumors whose original or presenting tumor was greater than a stage T2, must be referred to the applicable RRB [Regional Review Board] for prospective review in order to receive additional priority.”[63]

ADVERSE EVENTS

Complication rates for RFA of liver tumors are reported in approximately 7% of patients, as compared with that of open liver resection which may be as high as 22%.[64]

Specific complications reported in the literature to date include the following:[42,44,64-67]

1. Hemorrhage
2. Liver Abscess
3. Liver infarction
4. Liver failure

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.

October 1, 2017

Back to Top
5. Cutaneous burn
6. Diaphragm perforation
7. Bowel perforation
8. Seeding of the needle tract with cancer cells
9. Hydrothorax or hemothorax requiring drainage
10. Bile duct injury
11. Death

MICROWAVE ABLATION

MWA AS A TREATMENT OF HEPATOCELLULAR CARCINOMA (HCC)

Systematic Reviews

In 2016, Facciorusso and colleagues reported results from a systematic review and meta-analysis of one RCT and six retrospective studies (N=774) comparing RFA and MWA for the treatment of unresectable hepatocellular carcinoma (HCC).[68] The authors found a non-significant trend of higher complete response rates in the patients treated with MWA (odds ratio (OR) = 1.12, 95% confidence interval (CI) 0.67-1.88, p = 0.67). Overall local recurrence was similar between the two treatment groups (OR 1.01, 95% CI 0.53-1.87, p = 0.98) but MWA outperformed RFA in cases of larger nodules (OR 0.46, 95% CI 0.24-0.89, p = 0.02). 3-year survival was higher after RFA without statistically significant difference (OR 0.95, 95% CI 0.58-1.57, p = 0.85). Major complications were more frequent, although not significantly, in MWA patients (OR 1.63, 95% CI 0.88-3.03, p = 0.12).

Chinnaratha et al published a meta-analysis of randomized controlled trials (RCTs) and observational studies that compared the effectiveness and safety of radiofrequency ablation (RFA) to MWA in patients with primary hepatocellular carcinoma (HCC).[69] MEDLINE, EMBASE, and Cochrane Central databases were searched between January 1980 and May 2014 for human studies comparing the 2 technologies. The primary outcome was the risk of local tumor progression (LTP); secondary outcomes were complete ablation, overall survival (OS), and major adverse events. Odds ratios (ORs) were combined across studies using a random-effects model. Ten studies (2 prospective, 8 retrospective) were included. The overall LTP rate was 14% (176/1298). There was no difference in LTP rates between RFA and MWA (OR=1.01; 95% CI, 0.67 to 1.50; p=0.9). The complete ablation rate, 1- and 3- year OS, and major adverse events were similar between the 2 modalities (p>0.05 for all). Subgroup analysis showed LTP rates were lower with MWA for treatment of larger tumors (OR=1.88; 95% CI, 1.10 to 3.23; p=0.02). No significant publication bias was detected nor was interstudy heterogeneity (I²<50%, p>0.1) observed for any measured outcomes.

In 2011, Bertot and colleagues conducted a systematic review evaluating mortality and complication rates of ablation techniques for primary and secondary liver tumors.[70] This review included 2 studies using MWA totaling 1,185 patients.[71,72] The pooled mortality rate for MWA was 0.23% (95% confidence interval [CI]: 0.0–0.58%). Major complication rates were 4.6% for MWA (calculated by using a random effects model since there was significant heterogeneity). The authors concluded that percutaneous ablation techniques, including MWA, are safe and have acceptable complication rates for the treatment of liver tumors.
In 2009, Ong and colleagues conducted a systematic review of studies on MWA for primary and secondary liver tumors.\textsuperscript{73} Based on the results from 25 clinical studies, the authors concluded that MWA was an effective and safe technique for liver tumor ablation with low complication rates and survival rates comparable to hepatic resection. However, rates of local recurrence after MWA were noted to be higher than hepatic resection. In most studies of MWA, hepatocellular carcinoma recurrence rates were approximately 10% but were also noted to be as high as 50%, which the authors indicated could be addressed with further ablation. Survival rates in the studies on MWA for hepatocellular carcinoma were as high as 92% at 3 years and 72% at 5 years, which was noted to be comparable to radiofrequency ablation (RFA) and percutaneous ethanol injections. Pain and fever were the most frequently reported complications, but complications increased when there were more tumors, larger tumors, and more microwave antennas used. The authors concluded that MWA may be a promising option for the treatment of HCC tumors but should be reserved for patients not amenable to hepatic resection. The authors also noted further randomized clinical trials are warranted to compare MWA to other ablation procedures.

**Randomized Controlled Trials (RCTs)**

In 2002, Shibata and colleagues reported on 72 consecutive patients with 94 small hepatocellular carcinoma (HCC) nodules randomized to receive either percutaneous MWA or RFA performed by a single surgeon.\textsuperscript{74} No significant differences were identified between the 2 treatment group characteristics, e.g., sex, age, nodule size, Child-Pugh cirrhosis class and number of nodules. In the radiofrequency ablation group, complete therapeutic effect was seen in 46 (96%) of 48 nodules (mean size 2.3 cm, range 1.0-3.7) versus 41 (89%) of 46 nodules (mean size 2.2 cm, range 0.9-3.4) treated with percutaneous MWA (p=0.26). Treatment outcomes were not significantly different between the percutaneous MWA and radiofrequency ablation groups in the rates of untreated disease (follow-up range of 6-27 months [8 of 46 nodules vs. 4 of 48 nodules, respectively]), and major complication rates (4 vs. 1, respectively). Major complications included one case of segmental hepatic infarction in the radiofrequency ablation group. In the MWA group, major complications included one case of each of the following: liver abscess, cholangitis with intrahepatic bile duct dilatation, subcutaneous abscess with skin burn and subcapsular hematoma. Life-threatening complications were not experienced. The number of treatment sessions required per nodule in the radiofrequency ablation group was significantly lower than in the percutaneous MWA group (1.1 vs. 2.4; p<0.001). However, treatment time per session was significantly shorter in the MWA group (33 minutes ± 11) than the radiofrequency ablation group (53 minutes ± 16).

In 2006, Taniai and colleagues reported on 30 patients with multiple HCC tumors who underwent reduction hepatectomy with postoperative transcatheter arterial embolization.\textsuperscript{75} Prior to surgery, patients were randomly assigned to receive no intraoperative adjuvant therapy (n=15) or intraoperative adjuvant therapy with either MWA (n=10) or radiofrequency ablation (n=5) of satellite lesions. No significant differences in characteristics were identified between the two treatment groups of no intraoperative adjuvant therapy vs. intraoperative adjuvant therapy, e.g., sex, age, nodule size (maximum tumor size 42.7 mm ± 23.5 vs. 37.8 mm ± 16, respectively), Child-Pugh cirrhosis class and number of nodules. Cumulative survival rates at 3 and 5 years were not significantly different in the group that did not receive intraoperative adjuvant therapy (35.0% and 0%, respectively) versus the intraoperative adjuvant therapy group (35.7% and 7.7%, respectively). A-fetoprotein, number of tumors,
maximum tumor size and clinical stage, but not intraoperative adjuvant therapy, were identified
as independent prognostic survival factors.

Nonrandomized Studies

In addition to the studies noted above, a number of nonrandomized studies have been
published on the use of MWA in patients with hepatocellular carcinoma. Several examples are
cited, below. The results of these studies should be interpreted with caution due to the
following limitations:

- Results from small sample sizes (n<100), limit the ability to rule out the role of chance
  as an explanation of study findings.[76-83]
- Results from studies with short-term follow-up (<1 year) are not adequate to determine
  the durability of the treatment effect.[76,84,85]
- A lack of comparison group, without which it is not possible to account for the many
types of bias that can affect study outcomes.[71,72,82-91]

Given the limitations noted above, nonrandomized studies do not provide reliable data to
demonstrate the efficacy of MWA treatment in patients with HCC.

MWA AS A TREATMENT OF HEPATIC METASTASIS

The literature search identified several systematic reviews[35,37,70,73,92] on MWA for hepatic
metastases and a single RCT.

Systematic Reviews

A 2014 Health Technology Assessment[35] and a 2013 Cochrane review[92] also identified only
one RCT on ablation for liver metastasis, Shibata et al.[93] The reviewers found insufficient
evidence to determine any benefits of MWA for liver metastasis over surgical resection.

In 2013, Vogl and colleagues reviewed evidence regarding RFA, laser-induced thermotherapy
(LITT) and MWA treatment of breast cancer liver metastasis.[94] Local tumor response,
progression and survival rates were evaluated. Authors reported positive response rates of 63
% to 97 % in RF-ablated lesions, 98.2 % in LITT-treated lesions and 34.5-62.5 % in MWA
lesions. Median survival was 10.9-60 months with RFA, 51-54 months with LITT and 41.8
months with MWA. Five-year survival rates were 27-30 %, 35 % and 29 %, respectively. Local
tumor progression ranged from 13.5 % to 58 % using RFA, 2.9 % with LITT and 9.6 % with
MWA. The authors called for additional, large RCTs to further explore the benefits of ablation
therapies.

In the Ong review described above[73], local recurrence rates for liver metastases after
treatment with MWA averaged approximately 15% but varied between 0 and 50% in the 7
studies reviewed that addressed liver metastases. As noted above, Ong and colleagues
concluded MWA may be a promising treatment option for the treatment of liver tumors but
should be reserved for patients not amenable to hepatic resection.

In 2011, Pathak and colleagues also conducted a systematic review of ablation techniques for
colorectal liver metastases, which included 13 studies on MWA, totaling 406 patients with a
minimum of 1-year follow-up.\textsuperscript{[37]} Mean survival rates were 73\%, 30\% and 16\% and ranged from 40–91.4\%, 0–57\% and 14–32\% at 1-, 3- and 5-years’ follow-up, all respectively. Minor and major complication rates were considered acceptable and ranged from 6.7–90.5\% and 0–19\%, respectively. Local recurrence rates ranged from 2-14\%. The authors acknowledged limitations in the available studies but concluded survival rates for MWA are more favorable than for palliative chemotherapy alone.

**Randomized Controlled Trials (RCTs)**

Only one RCT comparing the use of MWA for hepatic metastases to the gold standard of surgical resection was identified. In 2000, Shibata et al. reported on a trial of 30 patients with hepatic metastases from colorectal cancer randomly assigned without stratification to treatment with either MWA after laparotomy (n=14) or hepatectomy (n=16).\textsuperscript{[93]} The study began with 40 patients, but 10 patients were excluded because the researchers discovered intraoperatively that these patients did not meet study criteria due to having extensive metastasis or equal to or greater than 10 tumors. The treatment groups of MWA vs. hepatectomy were not significantly different in age (mean age 61 in both groups) number of tumors (mean 4.1 vs. 3.0, respectively) or tumor size (mean 27 mm vs. 34 mm, respectively). The authors reported no significant differences in survival rates following MWA or hepatectomy (27 months vs. 25 months, respectively) and mean disease-free survival (11.3 vs. 13.3 months, respectively). However, intraoperative blood loss was significantly lower and no blood transfusions were required in the MWA group whereas 6 patients in the hepatectomy group required blood transfusions. Complications in the microwave group consisted of one hepatic abscess and one bile duct fistula. In the hepatectomy group, complications were one intestinal obstruction, one bile duct fistula and one wound infection.

**Nonrandomized Studies**

Several nonrandomized trials regarding MWA treatment in patients with liver metastases were identified; however, these studies were limited by a lack of comparison group,\textsuperscript{[95-97]} short-term follow-up\textsuperscript{[95,96]} and small sample size.\textsuperscript{[95,97]} These limitations preclude reaching a conclusion regarding MWA treatment in this patient population.

**CRYOSURGICAL ABLATION**

The evidence regarding cryoablation as a treatment for hepatocellular carcinoma (HCC) remains controversial. However, use of cryotherapy for HCC became a standard of care and published research increased through the late 1990’s and early 2000’s. Awad published a systematic Cochrane Review in 2009, noting that the literature consisted of two prospective cohort studies and two retrospective cohort studies.\textsuperscript{[98]} Overall, the Review concluded that the evidence is not sufficient to evaluate potential harms and benefits; large well-designed randomized clinical trials (RCTs) are feasible and necessary to define the role of cryotherapy in the treatment of HCC.

Since the 2009 Cochrane Systematic Review, Wang (2015) reported results from one RCT comparing the safety and efficacy of cryotherapy vs RFA.\textsuperscript{[99]} One hundred eighty participants were randomized to each group, with no significant differences found at baseline between the arms, with the exception of number of tumors – 10.56\% of the cryo group participants had two tumors at enrollment, compared to 5\% in the RFA group. Participants were followed for 5-
years, and there were no differences in local recurrence, new recurrence, overall survival, or tumor-free survival. At the end of follow-up, 52 patients (28.9%) in the CRYO group and 55 patients (30.6%) in the RFA group died. The causes of death included HCC progression in 44 (24.4%), hepatic failure in five (2.8%), and variceal bleeding in three (1.7%) in the CRYO group, and HCC progression in 47 (26.1%), hepatic failure in four (2.2%), variceal bleeding in two (1.1%), and refractory ascites-induced renal failure in two (1.1%) in the RFA group. Overall, the authors concluded that patients with Child-Pugh class A-B cirrhosis and HCC lesions less than or equal to 4 cm and no more than two lesions in total, percutaneous cryoablation and RFA are equally safe and effective ablation treatments. For HCC 3.1-4.0 cm, cryoablation was associated with a lower rate of local tumor progression than RFA.

PERCUTANEOUS ETHANOL INJECTION

Like RFA, percutaneous ethanol injection (PEI) is most often considered a treatment option for patients with small HCC lesions who are not resection candidates. RFA and PEI are the most commonly performed ablation therapies.

Weis (2015) published a Cochrane Systematic Review that evaluated the harms and benefits of percutaneous ethanol injection (PEI) and percutaneous acetic acid injection (PAI) in adults with early HCC defined by Milam criteria, i.e., one cancer nodule up to 5 cm in diameter or up to three cancer nodules up to 3 cm in diameter compared with no intervention, sham intervention, each other, other percutaneous interventions, or surgery. One randomised trial compared PEI versus surgery; we included 76 participants in the analyses. There was no significant difference in the overall survival (HR 1.57; 95% CI 0.53 to 4.61) and recurrence-free survival (HR 1.35; 95% CI 0.69 to 2.63). No serious adverse events were reported in the PEI group while three postoperative deaths occurred in the surgery group. Given the data on PEI were available for only one RCT, the authors concluded there is insufficient evidence to determine whether PEI versus surgery was more effective for early HCC.

In a number of RCT’s, the safety and efficacy of RFA and PEI have been investigated in the treatment of Child-Pugh class A patients with early stage HCC tumors. Complication rates were relatively low for both methods.

PRACTICE GUIDELINE SUMMARY

National Comprehensive Cancer Network (NCCN)

The NCCN guidelines for hepatocellular carcinoma (v.2.2017) recommend ablation be considered in patients who are not candidates for surgical curative treatments, or as part of a strategy to bridge patients for other curative therapies. (category 2A)

The NCCN guidelines for rectal (v.3.2017) and colon (v.2.2017) cancer metastatic to the liver state that “Ablative techniques may be considered alone or in conjunction with resection. All original sites of disease need to be amenable to ablation or resection.” (category 2A).

The NCCN guidelines for neuroendocrine tumors (v.2.2016) state that “…ablative therapies such as radiofrequency ablation (RFA) or cryoablation may be considered if near-complete treatment of tumor burden can be achieved (category 2B). For unresectable liver metastases, … (arterial embolization, chemoembolization, or radioembolization [category 2B]) is recommended.”
AMERICAN COLLEGE OF RADIOLOGY (ACR)

The 2014 ACR Appropriateness Criteria® for metastatic rectal cancer states that RFA “yields excellent local control of small (<3 cm) CRC liver metastases.”[111]

The 2011 ACR Appropriateness Criteria® considered RFA by percutaneous, open, or laparoscopic methods effective for treatment of small (<5 cm) HCC tumors.[112] While ablative therapy is most effective for these small HCCs, moderate success has also been described with tumors <7 cm. With larger tumor number and/or size, “the operator may want to focus on arterial-based therapies and adjuvant or neoadjuvant therapy.”

AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES (AASLD)

The 2011 update of the practice guideline from the American Association for the Study of Liver Diseases (AASLD) considered RFA a safe and effective therapy for unresectable HCC or as a bridge to liver transplantation.[113]

SUMMARY

For primary tumors of the liver, and hepatic metastases from colorectal tumors or neuroendocrine tumors, there is limited research regarding locoregional ablative therapies, however, treatment options are limited in this population. Clinical practice guidelines based on research recommend ablative therapies in carefully selected patients. Therefore, percutaneous ethanol injection, cryoablation, radiofrequency and microwave ablation may be considered medically necessary when policy criteria are met. Due to a lack of research and clinical practice guidelines, percutaneous ethanol injection, cryoablation, radiofrequency and microwave ablation are considered investigational when criteria are not met.

REFERENCES

1. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Radiofrequency ablation of unresectable hepatic tumors. TEC Assessments 2003: Volume 18, Tab 13. PMID:


67. Wong, SL, Mangu, PB, Choti, MA, et al. American Society of Clinical Oncology 2009 clinical evidence review on radiofrequency ablation of hepatic metastases from...


114. BlueCross BlueShield Association Medical Policy Reference Manual "Radiofrequency Ablation of Primary or Metastatic Liver Tumors." Policy No. 7.01.91


### CODES

<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>47370</td>
<td>Laparoscopy, surgical, ablation of one or more liver tumor(s); radiofrequency</td>
</tr>
<tr>
<td></td>
<td>47371</td>
<td>Laparoscopy, surgical, ablation of 1 or more liver tumor(s); cryosurgical</td>
</tr>
<tr>
<td></td>
<td>47380</td>
<td>Ablation, open, of one or more liver tumor(s); radiofrequency</td>
</tr>
<tr>
<td></td>
<td>47381</td>
<td>Ablation, open, of 1 or more liver tumor(s); cryosurgical</td>
</tr>
<tr>
<td></td>
<td>47382</td>
<td>Ablation, 1 or more liver tumor(s), percutaneous, radiofrequency</td>
</tr>
<tr>
<td></td>
<td>47383</td>
<td>Ablation, 1 or more liver tumor(s), percutaneous, cryoablation</td>
</tr>
<tr>
<td></td>
<td>47399</td>
<td>Unlisted procedure, liver</td>
</tr>
<tr>
<td>HCPCS</td>
<td>None</td>
<td></td>
</tr>
</tbody>
</table>

**Date of Origin:** June 2017
Medical Policy Manual

**Topic:** Autologous Fat Grafting to the Breast and Adipose-derived Stem Cells  
**Date of Origin:** November 2011

**Section:** Surgery  
**Last Reviewed Date:** December 2016

**Policy No:** 182  
**Effective Date:** January 1, 2017

**IMPORTANT REMINDER**

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

**DESCRIPTION**

Autologous fat grafting to the breast has been used as an adjunct to reconstructive breast surgery, for post-mastectomy pain and in irradiated skin. Adipose-derived stem cells have been proposed as a supplement to the fat graft in an attempt to improve graft survival.

**Background**

**Adipose Tissue Physiology in Fat Grafting**

Harvesting of adipose tissue by liposuction is relatively easy, minimally invasive, and associated with minimal patient discomfort and morbidity. Small amounts (100-200 mL) can be obtained under local anesthesia. The most common technique, called the Coleman technique, also involves a purification step which involves centrifugation to remove blood, fluid and ruptured adipocytes.

Adipose tissue is a highly vascularized tissue, and adipocytes are in direct contact with adjacent capillary vessels. In free fat grafting, direct diffusion of nutrients from plasma in the surrounding bed and subsequent revascularization usually occurs within 48 hours and are essential for graft survival. If the local environment does not undergo revascularization, the grafted fat tissue eventually undergoes
necrosis, one complication after fat grafting. Other complications include oil cyst formation, indurations in either the subcutis or breast parenchyma, calcification, and severe breast deformity.[1]

Indications for autologous fat grafting to the breast

Autologous fat grafting to the breast has been proposed for indications which include breast augmentation and following oncologic surgery. Proposed indications following oncologic surgery include as an adjunct to reconstruction post mastectomy or lumpectomy for contour deformities and improved shape and volume of the breast, for post mastectomy pain syndrome (neuropathic pain), and for irradiated skin to soften the skin and restore it to non-irradiated appearance and consistency.

Adipose-derived Stem Cells (ADSCs)

Stem cell biology, and the related field of regenerative medicine, involves multipotent stem cells that exist within a variety of tissues, including bone marrow and adipose tissue. Studies have shown that 1 gram of adipose tissue yields approximately 5 x 10^3 stem cells, which is up to 500 times greater than the number of mesenchymal stem cells in 1 gram of bone marrow.[1] Stem cells, because of their pluripotentiality and unlimited capacity for self-renewal, offer promise for tissue engineering and advances in reconstructive procedures. Adipose tissue in particular represents an abundant and easily accessible source of adipose-derived stem cells (ADSCs), which can differentiate along multiple mesodermal lineages.[1] ADSCs may allow for improved graft survival and generation of new fat tissue after transfer from another site.

This identification of several potentially beneficial therapeutic properties of ADSC has led to proposed novel techniques of fat grafting in conjunction with ADSC therapy for breast fat grafting, including the differentiation of ADSC into adipocytes as a reservoir for adipose tissue turnover, the differentiation of ADSC into endothelial cells and the subsequent increase in blood supply to the grafted fat tissue, thereby decreasing the rate of graft resorption, the release of angiogenic growth factors by ADSC and the induction of angiogenesis, protection of the graft from ischemic reperfusion injury by ADSC, and acceleration of wound healing at the recipient site.[1]

Current methods for isolating ADSCs can involve various processes, which may include centrifugation and enzymatic techniques that rely on collagenase digestion followed by centrifugal separation to isolate the stem cells from primary adipocytes. Isolated ADSCs can be expanded in monolayer on standard tissue culture plastic with a basal medium containing 10% fetal bovine serum,[2] and newly developed culture conditions provide an environment within which the study of ADSCs can be done without the interference of animal serum. They also allow rapid expansion of autologous ADSCs in culture for use in human clinical trials. A standard expansion method has not yet been established.

Yoshimura et al., in an effort to address the problems of unpredictability and low rates of fat graft survival, developed a technique known as cell-assisted lipotransfer (CAL), which produces autogenous fat rich in ADSCs.[3] In CAL, half of the lipoaspirate is centrifuged to obtain a fraction of concentrated ADSCs, while the other half is washed, enzymatically digested, filtered, and spun down to an ADSC-rich pellet. The latter is then mixed with the former, converting a relatively ADSC-poor aspirated fat to ADSC-rich fat.

Regulatory Status

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
A point-of care system is available for concentrating ADSCs from mature fat. The Celution™ system (Cytori Therapeutics, Inc.) is designed to transfer a patient’s own adipose tissue from one part of the body to another in the same surgical procedure. The system received 510(k) marketing clearance from the U.S. Food and Drug Administration as a cell saver device. The system is cleared for the collection, concentration, washing and re-infusion of a patient’s own cells for applications that may include, but are not limited to, cardiovascular, plastic and reconstructive, orthopedic, vascular, and urological surgeries and procedures.

MEDICAL POLICY CRITERIA

Note: This policy does not address free flap autologous fat grafting with micro vascularization. Further, this policy does not address the use of autologous fat tissue in aesthetic breast augmentation (i.e., cosmesis).

The use of autologous fat grafting to the breast, with or without supplemented adipose-derived stem cells is considered investigational.

SCIENTIFIC EVIDENCE

Literature Review

In order to understand the impact on health outcomes of fat grafting to the breast, with or without supplemented adipose-derived stem cells, prospective clinical trials are needed, comparing fat grafting to standard reconstructive procedures. These comparisons are necessary in order to understand the safety and efficacy of the procedures and to determine whether fat grafting offers advantages over conventional surgical procedures with respect to complications, durability, post-procedure ability to detect cancer, and cosmesis.

Autologous Fat Grafting in Breast Reconstruction

The evidence published on the use of autologous fat grafting in breast reconstruction consists only of case series and nonrandomized comparative studies. There have not been any randomized controlled trials published to date. This evidence review will focus on systematic reviews and recent key prospective comparative studies.

Systematic Reviews

Several systematic reviews have been published on autologous fat grafting in breast reconstruction. Below is a summary of key reviews that include similar nonrandomized studies.

In 2015, Charvet et al. conducted a systematic review to assess the oncologic safety of breast fat grafting, including 16 clinical studies (N=2100 patients). Studies with less than 25 patients and/or less than 12 months follow-up after breast fat grafting were excluded. The overall rate of locoregional breast cancer recurrence after fat grafting was 2.2% (47 patients). Two clinical studies, including 60 and 137 patients, after an average of at least 90 months, showed recurrence rates of 3.3-3.6%. These rates are similar to women undergoing standard breast reconstructive procedures without fat grafting (60 month follow-up, 4.1% recurrence). The authors concluded that there is not enough good data to indicate that...
breast fat grafting is oncologically safe in breast cancer patients. The current good quality studies published to date suggest there is no increased risk of cancer associated with fat grafting, but these are limited by lack of standardization of surgical technique and fat harvest method, retrospective analysis, and insufficient long-term follow-up. Although prospective randomized trials are desirable, they will likely not occur. Well-controlled cohort studies with sufficiently long follow-up of a minimum of 120 months demonstrating similar findings that there is no increased cancer risk associated with fat grafting are desirable.

In 2014, Agha et al. conducted a comprehensive, good quality systematic review of the evidence with meta-analysis of oncologic outcomes. The review evaluated women with breast cancer undergoing reconstruction after surgery. A total of 35 nonrandomized studies were included (3623 patients and 4138 breasts) with a median follow-up of 18 months. No RCTs were identified for inclusion in the review. Most studies were determined to be of low quality with only six cohort studies and three comparative studies assessed as moderate quality. It is important to note that there were differences in techniques, patient populations, and indications across studies. Post-operative complications were 7.3% with fat necrosis (4.4%) being the most common. The weighted mean cancer recurrence rate at a median 24.6 months was 4.4%. For the moderate quality studies only, there were no significant difference in cancer recurrence rates for autologous fat grafting compared to control groups (5.3% compared to 4.7%, p=0.10). Biopsy of subsequent breast lumps was needed in 2.7% of patients. The interval mammogram was needed in 11.5% of patients. The authors concluded that high quality studies are needed that report long term data for oncological outcomes and the current evidence review is limited by the low quality of studies with methodological limitations.

In 2014, Tsoi et al. compared the safety of tissue expander/implant reconstruction with that of autologous abdominal tissue reconstruction in a systematic review. Fourteen observational studies were identified that included more than 3000 reconstructed breasts. Significant differences were found between these two approaches. The relative risk associated with reconstructive failure favored autologous abdominal tissue (relative risk, 0.14; 95 percent CI, 0.06 to 0.32; I = 0 percent). Surgical-site infection was significantly lower in autologous abdominal tissue reconstruction compared with tissue expander/implant (relative risk, 0.37; 95 percent CI, 0.25 to 0.55; I = 0 percent), although skin or flap necrosis was higher in autologous abdominal tissue reconstruction compared with tissue expander/implant (relative risk, 2.79; 95 percent CI, 1.87 to 4.17). Studies were of low to moderate quality according to the Newcastle-Ottawa scale. The authors concluded that with the lack of long-term safety studies on different approaches to breast reconstruction, additional long-term comparative studies are needed to support evidence-based decision-making.

A 2013 systematic review by Krastev et al. examined the evidence of the oncological risks associated with autologous fat grafting in breast cancer patients. The review included trials with female patients who underwent either mastectomy or breast conserving therapy (BCT) and subsequent breast reconstruction including autologous fat grafting. The oncologic safety of the fat grafting procedure was assessed by locoregional recurrence rates. The trials included one retrospective cohort study, one multicenter study of case series without controls, two smaller cohorts and several case series. Although 20 trials met the inclusion criteria for the review, only nine reported oncologic recurrence rates. The level of evidence was rated as low due to lack of control groups, lack of randomization, their retrospective nature and small sample sizes. Across the studies there was variation in invasive versus in situ carcinomas and the percentage of patients who underwent radiation therapy before fat grafting. The mean interval between surgery and fat grafting varied across studies between 1 and 6.5 years, and mean follow-up varied between 1 and 5 years. The largest study in the review by Petit et al. was a multicenter study which reported locoregional recurrence rates of 1.35% and 2.19% per year for the mastectomy and
BCT groups, respectively.[9] The authors of the systematic review stated that the highest level of evidence currently available on the oncologic safety of fat grafting to the breast is a retrospective cohort analysis by Petit et al. which was included in the review, and deemed to be level 2b evidence.[10] The cohort analysis included 321 consecutive patients operated for a primary breast cancer between 1997 and 2008 who subsequently underwent fat grafting for reconstructive purpose. For each patient, two matched controls with similar characteristics were selected who had not undergone fat transfer. There were no significant differences between the fat grafting and control groups in locoregional or distant cancer recurrence. The authors of the systematic review concluded that it is still unclear whether fat grafting to the breast promotes locoregional recurrence, and that larger prospective trials with longer follow-up are needed.

In a 2013 critical review, authors critically assessed the current body of literature in fat grafting to provide a framework to guide application and comparison.[11] Authors included 103 articles in their review; headings included donor site, effect of infiltration solution, harvest method, effect of centrifugation, reinjection method, supplementation, the role of adipose-derived stem cells, and scaffolding. Authors concluded that there is no consensus on the optimum technique of autologous fat grafting in both reconstructive and cosmetic surgery due to the array of research methods and short follow-up durations.

A 2012 systematic review by Claro et al. examined the clinical applicability and safety of autologous fat grafting to the breast for reconstruction by identifying clinical complications, radiographic changes and incidence of primary or recurrent breast cancer.[12] Although the review also included patients who underwent fat grafting for augmentation, there were 41 studies that included 3646 patients who underwent grafting for reconstruction. The reconstruction was mainly for partial breast reconstruction and/or correction of breast deformities, but also included patients who underwent total breast reconstruction and for postradiation radiodermatitis. The majority of the studies were graded as low or very low quality. Complication results were not reported separately for the studies that included fat grafting for augmentation versus reconstruction. Clinical complications were 3.9% and consisted mainly of induration and/or palpable nodularity and radiographic abnormalities occurred in 13%, most commonly as cysts. Local recurrence of breast cancer was evaluated in three studies, of which only one was prospective. The three studies included 616 patients with a mean follow-up of 45.2 months. Fourteen recurrent cancers were reported (2.3%), all in women whose initial treatment was mastectomy. The authors concluded that fat grafting to the breast is associated with few complications with no evidence of interference with follow-up after treatment for breast cancer, and that the rate of breast cancer recurrence in the women who had fat grafting to the breast was similar to published rates for patients undergoing mastectomy who did not receive fat grafting, but that confirmation of the oncological safety awaits the results of controlled trials.

A 2012 literature review by Saint-Cyr and colleagues on the role of fat grafting in reconstructive and cosmetic breast surgery included articles published between 2001 and 2011.[13] Due to the heterogeneity of the studies, a formal meta-analysis was not completed. Out of 19 chosen studies, 11 had patients receiving autologous fat transplantation as an adjunct to breast reconstruction, five studies enrolled patients receiving the procedure for strictly cosmetic purposes, and three studies used fat grafting for both reconstructive and cosmetic purposes. In the studies included in the review, follow-up intervals ranged from 2 weeks to 19.1 years. The number of sessions employed per patient ranged from 1 to 7, with the intervals of time between sessions, when reported, ranging from 21 to 263 days. The review found it difficult to correlate patient or surgeon satisfaction with volume stability or complication rate as there was not a standardized method of documenting clinical success, postoperative volume stability, or follow-up intervals used to report complications; however, the majority of studies yielded results that

October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
were satisfactory or better. For fat grafting used in the setting of radiation (four studies), two studies reported a significant decrease in the LENT-SOMA scores in 95 to 100% of patients. Postoperative volume analysis was only performed in three studies. Postoperative infections, all managed with antibiotics, were reported in four of the studies. Among the 19 selected studies in the literature review, the methods used in the harvesting, processing, and injection of the adipose tissue varied widely. The authors of this review concluded that large prospective studies with well-defined follow-up measures are needed to more clearly demonstrate specific risks and answer questions concerning the amount of adipose resorption and long-term stability of the fat grafts used for reconstructive and cosmetic purposes.

**Randomized Controlled Trials**

There were no randomized controlled trials identified.

**Nonrandomized Studies**

There are a large number of nonrandomized studies, most of which were included in the previously summarized systematic reviews that contribute to the body of knowledge concerning autologous fat grafting and may be used to provide direction for future research.[14-23] Key studies published after the systematic reviews are described below.

In 2016, Kronowitz et al. conducted a matched controlled clinical trial to assess if lipofilling increases the risk of breast cancer recurrence.[5] The authors identified cases who underwent mastectomy for breast cancer or breast cancer risk reduction (719 breasts) or benign disease (305 cancer-free breasts) followed by breast reconstruction with lipofilling as an adjunct or primary procedure. Matched controls with breast cancer treated with mastectomy followed by reconstruction without lipofilling (670 breasts) were compared to cases. Mean follow-up times after mastectomy were 60 months for cases, 44 months for controls, and 73 months for cancer-free breasts. The cumulative 5-year locoregional recurrence rates were 1.6% and 4.1% for cases and controls, respectively. Systemic recurrence occurred in 2.4% of cases and 3.6% of controls (p = 0.514). The increase in locoregional recurrence or systemic recurrence were not significantly different between cases who had received lipofilling versus controls who had not.

Similar nonsignificant differences between cases and controls were reported in a smaller prospective study published by Mestak et al.[24]

**Autologous Fat Grafting and the Use of Adipose-derived Stem Cells (ADSC)**

**Systematic Reviews**

In 2016, Zhou et al. conducted a systematic review to evaluate the safety and efficacy of cell-assisted lipotransfer (CAL), including seventeen articles (N=387) for all indications, including breast.[25] For all indications combined, the pooled fat survival rate was significantly higher in the CAL group than in the nonlipotransfer group (60% vs. 45%, p = 0.0096). Complication incidence was similar in the two groups. In breast fat grafting fat survival was improved by only 9% in the CAL group, which was not statistically significant. In addition, lipotransfer in breast cases was associated with a higher complication incidence compared with other indications (p < 0.001).

**Nonrandomized Studies**
In 2016, Jung et al. conducted a small single-arm, prospective study to evaluate the impact of ADSCs, using CAL, on graft survival, including five patients.[26] One year after CAL, breast volume had decreased to 47% of the initial postoperative volume. The ratio of ADSC cell count to grafted fat volume showed no correlation with graft survival. The addition of SVF cells did not appear to improve the retention of grafted fat in these patients. Skin tension may be an important factor influencing the absorption pattern of grafted fat.

In 2013, Peltoniemi et al. conducted a prospective comparative study to evaluate if stem cell enrichment is important for success in lipofilling for cosmetic breast augmentation.[27] A total of 18 women underwent breast augmentation, with 10 of the cases including transferred lipoaspirate enriched with ADSCs using the Cytori Celution(®) system MRI-based volumetric analysis was done preoperatively and six months post-procedure. MRI analysis revealed mean graft survival was not significantly different between groups (54% in nonADSC group vs. 50% in the ADSC-enrichment patients). After centrifugation survival was not significantly different between groups (79% in nonADSC group vs. 74% in the ADSC-enrichment patients. The investigators concluded that they did not see any advantage in stem cell enrichment by the Celution(®) system in cosmetic fat transplantation to the breast.

In 2012, Pérez-Cano et al. conducted a single-arm, prospective, multicenter clinical trial of 71 women who underwent breast conserving surgery for breast cancer and autologous adipose-derived regenerative cell (ADRC)-enriched fat grafting for reconstruction of defects ≤150 mL (the RESTORE-2 trial).[28] Trial endpoints included patient and investigator satisfaction with functional and cosmetic results and improvement in overall breast deformity at 12 months post-procedure. Female patients (18-75 years of age) presenting with partial mastectomy defects and without breast prosthesis were eligible. The RESTORE-2 protocol allowed for up to two treatment sessions and 24 patients elected to undergo a second procedure following the six-month follow-up visit. Of the 67 patients treated, 50 reported satisfaction with treatment results through 12 months. Sixty-one patients underwent radiation therapy as part of their treatment; two patients did not receive radiation and the status of radiation treatment was not known for the other 4 patients. Using the same metric, investigators reported satisfaction with 57 out of 67 patients. There were no serious adverse events associated with the ADRC-enriched fat graft injection procedure. There were no reported local cancer recurrences. The LENT-SOMA scale included investigator and patient assessment of post-radiation signs and symptoms. The investigators of the trial found that LENT-SOMA was insufficiently sensitive to adequately reflect the clinical improvements seen in the trial population. Patients with LENT-SOMA III and IV scores (most severe symptoms) were excluded during screening, which may have contributed to the subtle LENT-SOMA score changes observed in the trial. The investigators reported improvement from baseline through 12 months in the degree of retraction or atrophy in 29 out of 67 patients, while 34 patients had no change and 4 patients reported worse symptoms. Post-radiation fibrosis at 12 months was reported as improved in 29 patients, while 35 patients had no change and 3 patients reported worse symptoms. Management of atrophy was reported as improved in 17 patients, with 48 patients having no change and 2 patients reporting worse symptoms. Improvement in these measures reached statistical significance. The authors concluded that future comparative studies are needed to determine the incremental benefit of ADRC-enriched fat grafting as compared to traditional fat grafting in various clinical circumstances.

In 2011, Kamakura and Ito reported on the use of ADSC enriched fat grafting for breast augmentation in a prospective, nonrandomized open-label study of 20 Japanese women.[29] After the adipose tissue was harvested by liposuction, it was processed in the Celution 800 System® to wash and isolate the adipose-derived regenerative cells and produce a fat graft enriched with the regenerative cells. Clinical outcomes measured included improvement in circumferential breast measurement from baseline state. There was improvement in circumferential breast measurement in all patients, and breast measurements were stable.
by 3 months after grafting. At 9 months, the mean breast measurement had increased 3.3 cm from preoperative measurements. The procedure was well-tolerated without any serious adverse events.

Postoperative cyst formation was seen in 2 patients.

In 2008, Yoshimura and colleagues reported on the development of a novel strategy known as cell-assisted lipotransfer (CAL), in which autologous ADSCs are used in combination with lipoinjection. From 2003-2007, the group performed CAL in 70 patients: in the breast in 60 patients (including 8 who had breast reconstruction after mastectomy). They reported outcomes for 40 patients with healthy thoraxes and breasts who underwent CAL for purely cosmetic breast augmentation; patients undergoing breast reconstruction for an inborn anomaly or after mastectomy were not included. Nineteen of the 40 patients had been followed for more than 6 months, with a maximum follow-up of 42 months. The authors observed that the transplanted adipose tissue was gradually absorbed during the first 2 postoperative months, and the breast volume showed a minimal change thereafter. Final breast volume showed augmentation by 100 to 200 mL after a mean fat amount of 270 mL was injected. The difference in breast circumference (defined as the chest circumference at the nipple minus the chest circumference at the inframammary fold) had increased in all cases by 4 to 8 cm at 6 months. Cyst formation or microcalcification was detected in 4 patients. The authors concluded that their preliminary results suggest that CAL is effective and safe for soft tissue augmentation and superior to conventional lipoinjection but that additional study is necessary to further evaluate the efficacy of this technique.

In 2007, Rigotti et al. reported the results of a pilot study on the presence and effectiveness of ADSCs in 20 consecutive patients undergoing therapy for adverse effects of radiation treatment to the breast, chest wall or supraclavicular region, with severe symptoms or irreversible function damage (LENT-SOMA scale grade 3 and 4). LENT-SOMA is one of the most common systems to assess the late effects of radiotherapy. The mean patient age was 51 years (range, 37-71 years). The rationale behind the study was that the ADSCs, which have been shown to secrete angiogenic and antiapoptotic factors and to differentiate into endothelial cells, could promote neovascularization in ischemic tissue such as irradiated tissue. Targeted areas included the supraclavicular region, the anterior chest wall after mastectomy with or without breast prosthesis, and breast after quadrantectomy. A lipoaspirate purification procedure was performed by centrifugation to remove a large part of the triglyceride portion of the tissue and disrupt the cytoplasm of the mature adipocytes to favor their rapid clearance after injection. A stromal-vascular fraction was isolated by enzymatic digestion of extracellular matrix, centrifugation and filtration, and the fractions were cultured for 2 to 3 weeks to obtain a homogenous cell population. To assess the presence of mesenchymal stem cells, the stromal-vascular fraction derived from the adipose tissue was cultured and characterized by flow cytometry. The number of procedures was 1 in 5 patients, 2 in 8, 3 in 6, and 6 in 1 patient. Clinical follow-up varied between 18 and 33 months (mean, 30 months). Clinical results after treatment with lipoaspirates were assessed by LENT-SOMA scoring. The 11 patients initially classified as LENT-SOMA grade 4 (irreversible functional damage) progressed to grade 0 (no symptoms), grade 1 and grade 2 in 4, 5 and 1 cases, respectively. In 1 case, no improvements were observed. In the group of 9 patients classified as LENT-SOMA grade 3, fibrosis, atrophy, and retraction progressed to grade 0 and 1 in 5 and 4 cases, respectively.

**Clinical Practice Guidelines**

National Institute for Health and Clinical Excellence (NICE)
In 2012 NICE published an evidence-based clinical practice guideline that states that current evidence on the efficacy of breast reconstruction using lipomodelling after breast cancer treatment is adequate.\[31\] The guideline noted that there is a safety concern regarding increased recurrence of breast cancer in the long term, although the evidence for this in published clinical studies is lacking. Long-term studies addressing the safety concerns are still needed. In addition, the guideline notes that a degree of fat resorption is common in the first six months and that there are concerns that fat grafting make future mammographic images more difficult to interpret.

American Society of Aesthetic Plastic Surgery and American Society of Plastic Surgeons\[32\]

A joint task force of the American Society for Aesthetic Plastic Surgery (ASAPS) and the American Society of Plastic Surgeons released a position statement on the use of stem cells in aesthetic surgery during the 2011 annual meeting of ASAPS.\[32\] Based on a systematic review of the peer-reviewed literature, the task force concluded that while there is potential for the future use of stem cells in aesthetic surgical procedures, the scientific evidence and other data are very limited in terms of assessing the safety or efficacy of stem cell therapies in aesthetic medicine.

Summary

Fat grafting to the breast has gained popularity with the development of improved harvesting and transplanting techniques. As an adjunct to reconstructive surgery, reported complication rates have been low, however, the clinical effectiveness, interference with screening mammography and the oncologic safety of fat grafting to the breast is still unclear. Because the impact on net health outcomes is unknown, fat grafting in reconstruction of the breast is considered investigational.

The current research on the use of supplemented adipose-derived stem cells in conjunction with fat grafting to the breast has many limitations and is starting to show that the use of these cells does not increase graft survival or decrease resorption rates. Additional research is needed for the long term effectiveness and safety of adipose-derived stem cells in conjunction with fat grafting. Therefore, the use of adipose-derived stem cells in conjunction with fat grafting to the breast is considered investigational.

REFERENCES


CROSS REFERENCES

**Transgendered Services**, Medicine, Policy No. 153

**Endometrial Ablation**, Surgery, Policy No. 01

**Cosmetic and Reconstructive Surgery**, Surgery, Policy No. 12

**Reconstructive Breast Surgery/Mastopexy, and Management of Breast Implants**, Surgery, Policy No. 40
Reduction Mammaplasty, Surgery, Policy No. 60

<table>
<thead>
<tr>
<th>CODES</th>
<th>NUMBER</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>11950</td>
<td>Subcutaneous injection of filling material (eg, collagen); 1 cc or less</td>
</tr>
<tr>
<td></td>
<td>11951</td>
<td>Subcutaneous injection of filling material (eg, collagen); 1.1 to 5.0 cc</td>
</tr>
<tr>
<td></td>
<td>11952</td>
<td>Subcutaneous injection of filling material (eg, collagen); 5.1 to 10.0 cc</td>
</tr>
<tr>
<td></td>
<td>11954</td>
<td>Subcutaneous injection of filling material (eg, collagen); over 10.0 cc</td>
</tr>
<tr>
<td></td>
<td>19366</td>
<td>Breast reconstruction with other technique</td>
</tr>
<tr>
<td></td>
<td>19499</td>
<td>Unlisted procedure, breast</td>
</tr>
<tr>
<td>HCPCS</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

There is no specific CPT code for this procedure. One of the following CPT codes might be used:

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage.

Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
Regence

Medical Policy Manual

Topic: Bariatric Surgery

Section: Surgery

Policy No: 58

Date of Origin: January 1996

Last Reviewed Date: February 2016

Effective Date: February 11, 2017

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Morbid obesity is defined as a body mass index (BMI) >40 kg/m2 (normal BMI range: 19-25 kg/m2)

Note: BMI may be calculated by using a BMI calculator.

Individuals with morbid obesity are at high risk for developing weight-related complications such as diabetes, hypertension, obstructive sleep apnea, and various types of cancers (colon, prostate, breast, uterus, and ovaries). In addition, morbid obesity is associated with a shortened life span.\(^\text{[1]}\)

The first-line treatment of morbid obesity involves dietary and lifestyle changes. Although this strategy may be effective in some patients, a majority of morbidly obese patients do not achieve significant weight loss through lifestyle modifications. In addition, the weight loss may not be durable, as only a small number of patients are able to comply with the changes on a long-term basis. When conservative measures fail, some patients may consider surgery for morbid obesity (bariatric surgery).

Several bariatric procedures have been developed, but based on the underlying mechanism of weight loss, all fall into one or both of the following categories:

Restrictive procedures
• Decrease the size of the stomach and limit food intake

Malabsorptive procedures

• Limit the absorption of calories and nutrients by altering the way food moves through the intestinal track
• Multiple variants exist, differing in the reconfiguration of the small intestines and consequently the extent of malabsorption.
The following table briefly summarizes different bariatric procedures:

<table>
<thead>
<tr>
<th>Procedure</th>
<th>CPT Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gastric Bypass with Roux-en-Y Anastomosis (RYGBP)</strong> AKA: Proximal or Short Limb Gastric Bypass</td>
<td>43846</td>
<td>• Currently considered “gold-standard” for weight loss surgery</td>
</tr>
<tr>
<td></td>
<td>43644</td>
<td>• Involves both restrictive and malabsorptive components:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>o A small gastric pouch is created from the upper part of the stomach by segmentation or resection to restrict the amount of food that can be ingested</td>
</tr>
<tr>
<td></td>
<td></td>
<td>o The mid portion of the jejunum is divided and the cut end of the distal limb (≤ 150 cm) is attached to the gastric pouch outlet (Roux limb). The cut end of the proximal limb (the limb consisting of the duodenum and proximal jejunum) is attached to the side of the Roux limb (the limb connected to the pouch). This creates the Y configuration of the small intestine, allowing food to bypass the duodenum and proximal jejunum, resulting in malabsorption.</td>
</tr>
<tr>
<td><strong>Distal (Long Limb) Gastric Bypass</strong></td>
<td>43847</td>
<td>• The procedure involves both restrictive and malabsorptive components and is a variant of the standard gastric bypass with the longer (&gt;150 cm) Roux limb. The longer the Roux limb, the greater the bypass of the small intestine and consequently the degree of malabsorption.</td>
</tr>
<tr>
<td><strong>Biliopancreatic Diversion (Bypass) Procedure</strong></td>
<td>43847</td>
<td>• Involves both restrictive and malabsorptive components:</td>
</tr>
<tr>
<td>AKA Scopinaro procedure</td>
<td></td>
<td>o Subtotal (distal) gastrectomy creates small gastric pouch at the top of the stomach to limit food intake</td>
</tr>
<tr>
<td></td>
<td></td>
<td>o A long limb Roux-en-Y anastomosis (&gt;150 cm) results in the biliopancreatic juices being diverted into the distal ileum, significantly increasing malabsorption</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Designed to preferentially inhibit the absorption of fat</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Only partially reversible</td>
</tr>
<tr>
<td><strong>Biliopancreatic Diversion (Bypass) with Duodenal Switch (BPD-DS)</strong></td>
<td>43845</td>
<td>• This procedure is an adaptation of the standard biliopancreatic bypass:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>o The restrictive component involves subtotal gastrectomy resulting in a tube or sleeve-like stomach remnant that leaves the pyloric valve and the initial segment of duodenum intact.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>o The long limb Roux-en-Y anastomosis (&gt;150 cm) provides malabsorption in this variant as well, but the distal ileum is connected to the duodenal segment leading from the stomach sleeve, instead of the stomach pouch itself.</td>
</tr>
<tr>
<td><strong>Laparoscopic duodenal switch with single anastomosis</strong> AKA Single loop duodenal switch</td>
<td>No specific CPT code</td>
<td>• Restrictive and malabsorptive procedure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Simplified version of the BPD-DS procedure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Surgery consists of:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>o Creation of a small gastric pouch by section the curvature of the stomach</td>
</tr>
<tr>
<td></td>
<td></td>
<td>o Duodenum is transected while keeping the pylorus intact</td>
</tr>
<tr>
<td></td>
<td></td>
<td>o A 1-loop duodenal switch is performed with creation of a 200-250 cm anastomosis</td>
</tr>
<tr>
<td><strong>Mini-Gastric Bypass</strong></td>
<td>no specific code</td>
<td>• The procedure is a variant of the gastric bypass and involves both restrictive and malabsorptive components:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>o The stomach is segmented to create a small gastric pouch similar to traditional gastric bypass</td>
</tr>
<tr>
<td></td>
<td></td>
<td>o Instead of creating a Roux-en-Y anastomosis, the loop of jejunum is Anastomosed directly to the stomach pouch (similar to a Billroth II procedure)</td>
</tr>
<tr>
<td><strong>Sleeve Gastrectomy</strong></td>
<td>43775</td>
<td>• Greater curvature of the stomach is resected resulting in a gastric remnant shaped like a tube or sleeve.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• The pyloric sphincter is preserved leaving stomach function unaltered.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Not reversible</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Can be performed as:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>o A stand-alone procedure (restrictive)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>o The first part of a two-stage surgical procedure for the very high-risk patients (BMI ≥50 kg/m²) who need to lose some weight before they can proceed with a malabsorptive procedure (most commonly BPD-DS or RYGBP)</td>
</tr>
<tr>
<td><strong>Adjustable Gastric Banding</strong></td>
<td>43770-43774</td>
<td>• Restrictive procedure</td>
</tr>
<tr>
<td>Procedure</td>
<td>CPT Code</td>
<td>Description</td>
</tr>
<tr>
<td>----------------------------------------------------------------</td>
<td>----------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Lap-Band®</strong> (original applicant, Allergan, Inc.; sold to Apollo Endosurgery, Inc.) and the REALIZE™ (Ethicon Endo-Surgery, Inc.) have received approval from the U.S. Food and Drug Administration (FDA).</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Vertical Banded Gastroplasty                                   | 43842          | • Restrictive procedure  
• Surgical stapling is used to create a small, vertical gastric pouch at the top of the stomach  
• The pouch outlet (stoma) is reinforced with an external mesh collar                                                                                                                                 |
| Endoscopic (Endoluminal) Bariatric Procedures                  | No specific CPT code | • The access to the stomach is gained through the mouth, so no incisions are necessary.  
• Endoluminal procedures being developed:  
  o Primary bariatric procedure  
  o Revision (e.g. for treatment of enlarged gastric stoma and/or enlarged gastric pouches that may be associated with weight gain after bariatric surgery)  
• Examples of the endoscopic revision bariatric procedures include:  
  o Gastroplasty using an endoscopically guided stapler (reduces the size of the gastric pouch)  
  o Placement of gastric balloon (soft, silicone balloon inserted into the stomach and filled with sterile saline to induce feeling of satiety)  
  o Placement of duodenal-jejunal sleeve (sleeve placed inside duodenum and upper jejunum to prevent contact between food and the intestine).  
• StomaphyX®, an endoscopically guided system intended for tissue plication and ligation, has received 510(k) FDA approval. The device is also being investigated for endoscopic treatment of gastroesophageal reflux. |
| Laparoscopic Gastric Plication                                | No specific CPT code | • Sutures are laparoscopically placed over the greater curvature (laparoscopic greater curvature plication) or anterior gastric region (laparoscopic anterior curvature plication) to create a tube-like stomach.  
• The procedure involves 2 main steps:  
  o Mobilization of the greater curvature of the stomach, and  
  o Suture plication of the stomach to achieve gastric restriction |
MEDICAL POLICY CRITERIA

Notes: Member contracts for covered services vary. Member contract language takes precedence over medical policy.

I. All of the following general criteria (I.A-D.) must be met for bariatric surgery to be considered for coverage:

A. At the start of the medically supervised, nonsurgical weight reduction program, one of the following must be met:

   1. BMI greater than or equal to 40 kg/(meter squared); or
   2. BMI greater than or equal to 35 kg/(meter squared) with at least one of the following comorbid conditions which have not responded to medical management and which are generally expected to improve as a result of obesity surgical treatment:
      a. Diabetes mellitus
      b. Hypertension
      c. Coronary artery disease
      d. Obstructive sleep apnea

B. Documentation of active participation for at least 6 months in a structured, medically supervised nonsurgical weight reduction program. A comprehensive commercial weight loss program is an acceptable program component, but it must be approved and monitored under the supervision of the healthcare practitioner providing medical oversight. Comprehensive weight loss programs generally address diet, exercise and behavior modification, e.g., Weight Watchers.

   Documentation from the clinical medical records must indicate that the structured medical supervision meets all of the following criteria:

   1. Occur during at least 6 consecutive months within the 24 months prior to the request for surgery; and
   2. Include at least three visits for medical supervision, occurring at intervals of no longer than four months apart, e.g., at the start, middle and end of the 6-month weight loss program; and
   3. Be provided by an MD, DO, NP, PA, or RD under the supervision of an MD, DO, NP, or PA; and
   4. Include assessment and counseling concerning weight, diet, exercise, and behavior modification.

C. Preoperative evaluation to include both of the following:

   1. A licensed psychologist, psychiatrist, LCSW/LICSW, Licensed Masters level counselor, or NP in a behavioral health practice, documents the absence of
significant psychopathology that can limit an individual's understanding of the procedure or ability to comply with medical/surgical recommendations (e.g., active substance abuse, eating disorders, schizophrenia, borderline personality disorder, uncontrolled depression); and

2. Clinical documentation, by either a psychological or surgical evaluation, of willingness to comply with preoperative and postoperative treatment plan.

D. Age greater than or equal to 18 years.

II. Procedures

A. Sleeve gastrectomy as a stand-alone procedure, or adjustable gastric banding, consisting of an adjustable external band placed around the stomach, may be considered medically necessary in the treatment of morbid obesity when all of the following criteria are met:

1. Not currently requiring regular treatment for gastroesophageal reflux disease (GERD); and

2. Procedure is not in combination with takedown of fundoplication; and

3. All of Criteria I. (A-D) above are met.

B. Gastric bypass using a Roux-en-Y anastomosis with an alimentary limb of 150 cm or less may be considered medically necessary in the treatment of morbid obesity when all criteria I. (A-D) are met.

C. Sleeve gastrectomy, adjustable gastric banding, gastric bypass using a Roux-en-Y anastomosis with an alimentary limb of 150 cm or less is not medically necessary in the treatment of morbid obesity when criteria II.A or II.B are not met.

III. The vertical banded gastroplasty is no longer a standard of care and is therefore considered not medically necessary.

IV. Adjustable gastric banding, gastric bypass using a Roux-en-Y anastomosis, and sleeve gastrectomy are considered investigational for the treatment of any condition other than morbid obesity, including but not limited to gastroesophageal reflux disease or gastropareses.

V. The following surgical procedures are considered investigational for the treatment of morbid obesity:

A. Distal (i.e. antrectomy) or partial (other than standard sleeve gastrectomy) gastrectomy performed with or without any of the following:

   1. Gastroduodenostomy

   2. Gastrojejunostomy

   3. Roux-en-Y reconstruction

B. Hiatal hernia repair, including repair of sliding or paraesophageal hernia

October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
C. Gastric restrictive procedure, without gastric bypass, for morbid obesity; other than vertical banded gastroplasty or sleeve gastrectomy

VI. The following surgical procedures are considered investigational for the treatment of any condition, including but not limited to morbid obesity and gastroesophageal reflux disease:

A. Mini-gastric bypass (gastric bypass using a Billroth II type of anastomosis)
B. Distal gastric bypass (long limb gastric bypass, i.e., >150 cm)
C. Biliopancreatic bypass (i.e., the Scopinaro procedure)
D. Biliopancreatic bypass with duodenal switch
E. Laparoscopic duodenal switch with single anastomosis
F. Two-stage bariatric surgery procedures (e.g., sleeve gastrectomy followed by gastric bypass, sleeve gastrectomy followed by biliopancreatic diversion)
G. Adjustable gastric banding with existing gastric bypass or sleeve gastrectomy, or other bariatric surgical procedure.
H. Parietal cell separating gastrojejunostomy
I. Laparoscopic gastric plication

VII. Endoscopic procedures

A. Endoscopic procedures as the primary bariatric procedure are considered investigational.

B. Endoscopic procedures, except for balloon dilatation of anastomotic strictures, are considered investigational to treat complications of primary bariatric surgery, including but not limited to weight gain due to a large gastric stoma or large gastric pouch and dumping syndrome. Examples of endoscopic devices/procedures include but are not limited to the following:

1. StomaphyX (EndoGastric Solutions, Inc)
2. ROSE procedure (Restorative Obesity Surgery, Endoscopic)
3. EndoCinch (Bard)
4. EndoSurgical Operating System (EOS) (USGI Medical, Inc.)
5. Sclerotherapy of stoma
6. Endoscopic gastroplasty
7. Endoscopically placed duodenal-jejunal sleeve
8. Endoscopic stoma revision
9. Gastric balloon systems
10. AspireAssist

VIII. Reoperation may be considered medically necessary when either criteria A. or B. are met:

A. Reoperation with revision of a bariatric procedure (i.e. adjustable gastric band, gastric bypass, or sleeve gastrectomy) or adjustable gastric band removal may be considered medically necessary when one or more of the following documented significant complications is present:

1. Bowel perforation, including band erosion
2. Band migration (slippage), that cannot be corrected with manipulation or adjustment
3. Leak
4. Obstruction
5. Staple-line failure (such as, Gastro-gastric fistula)
6. Weight loss to 80% or less of ideal body weight
7. Band infection

B. Removal of adjustable gastric band and conversion to a gastric bypass using a Roux-en-Y anastomosis with an alimentary limb of 150 cm or less may be considered medically necessary when criteria I. A-D are met. Note that criteria I. A-D must be met during the period after placement of the adjustable gastric band.

IX. Reoperation which does not meet criteria VIII. above, is considered not medically necessary, including but not limited to reoperation for the following indications:

A. Early satiety
B. Nausea
C. Patient dissatisfaction
D. Gastroesophageal reflux disease (GERD)
E. Conversion, which does not meet criteria VIII.A. or VIII.B. above, of a prior procedure to a different procedure (such as, laparoscopic adjustable banding to gastric bypass or sleeve gastrectomy, sleeve gastrectomy to gastric bypass, or a gastric bypass to a sleeve gastrectomy)

SCIENTIFIC EVIDENCE[2]

Background

- Roux-en-Y Gastric Bypass (RYGBP)

The Roux-en-Y gastric bypass is the most commonly performed procedure with the most...
accumulated evidence in the published literature.\[3\] Consequently, in order to determine the safety and efficacy of other bariatric surgical procedures, they need to be compared to RYGBP in well-designed, well-executed randomized controlled trials (RCTs).

- Laparoscopic Adjustable Gastric Banding (LAGB)
  
  RCT data comparing LAGB and RYGBP are limited, however:
  
  o LAGB is reversible and the least invasive of all bariatric procedures.
  o Weight loss following LAGB is less than what is usually seen following RYGBP.
  o LAGB has low perioperative complications; however inadequate weight loss or long term complications of band erosion, slippage, or malfunction may require additional surgery.

- Sleeve Gastrectomy (SG)
  
  o Despite limited evidence, SG has been gaining increased acceptance in clinical practice.
  o SG offers an alternative to adjustable gastric banding with potentially greater weight loss but without the complications associated with malabsorptive procedures, such as RYGBP.

- Other Bariatric Surgical Procedures

  Randomized Controlled Trials
  
  Very few randomized controlled trials compared other bariatric procedures with RYBP. Overall, the trials were of poor quality and the findings unreliable due to at least one of the following design flaws:
  
  o The trials had very small study populations, limiting the ability to rule out the role of chance as an explanation of findings.
  o The randomization scheme was either inadequate or not explained. Inadequate randomization of study participants may result in unequal distribution of potential confounders, such as clinical characteristics, which in turn may affect the outcome.
  o The studies have short follow-up times so there is no long-term (5-10 years or longer) evidence regarding:
    
    - durability of weight loss
    - complications (e.g. metabolic side effects, nutritional deficiencies, anastomotic ulcers, esophagitis, procedure-specific complications such as band erosion)
    - resolution of comorbidities (e.g. diabetes, hypertension, obstructive sleep apnea, increased cholesterol)
    - need for reoperations
  
  o Short-term complications, adverse events, morbidity, resolution of comorbidities, and reoperation rates are inconsistently reported, limiting conclusions and comparisons across studies.
  o There is limited understanding of appropriate patient selection criteria for each of the non-RYGBP bariatric procedures (e.g. superobese patients vs. morbidly obese patients).
Nonrandomized Studies

Although the published, peer-reviewed literature on non-RYGBP bariatric procedures is voluminous, it consists mostly of case series and retrospective, nonrandomized comparisons. Evidence from these studies is unreliable due to design flaws, such as non-random allocation of treatment, lack of adequate comparison groups, and short-term follow-up. In addition, the inconsistent reporting of weight loss, resolution of comorbidities, adverse events, morbidity, and reoperation rates further limit meaningful comparisons across these studies.

- Bariatric Surgery in the Pediatric Population

Overall, there is very little evidence on the role of bariatric surgery in treating morbidly obese pediatric patients. Moreover, the evidence mostly comes from small, nonrandomized and therefore unreliable studies. Specifically:

  o There is limited evidence that bariatric surgery leads to clinically significant, long-term sustained weight loss and resolution of obesity-related comorbidities in the pediatric population.
  o The evidence does not permit conclusions regarding morbidity associated with and safety of any bariatric procedure in the pediatric population.
  o There is no evidence regarding the long-term potential impact of bariatric procedures on growth and development in the pediatric population.

- Bariatric Surgery as a Treatment for Gastroesophageal Reflux Disease (GERD)

In order to determine the safety and efficacy of bariatric surgical procedures as treatments for GERD, they need to be compared to standard medical or surgical treatments of this condition in well-designed, well-executed randomized controlled trials.

- Endoscopic Bariatric Procedures

There is insufficient evidence to determine the safety and efficacy of any endoluminal procedure as either a primary bariatric procedure or a revision procedure. The published evidence is very limited and consists of only a few case series and one unreliable randomized trial.

- Multidisciplinary Approach to the Clinical Management of Bariatric Surgery Patients

The National Institutes of Health/National Heart, Lung, and Blood Institute (NIH/NHLBI) clinical practice guidelines state the importance of a multidisciplinary approach to the clinical management of bariatric surgery patients. Comprehensive programs should address nursing, nutrition, exercise, behavior modification, and psychological support, and they should provide lifelong follow-up for treated patients.\[1\]

- Bariatric Surgery Centers of Excellence

The published evidence indicates that high volume bariatric centers are more likely to be successful in achieving optimal outcomes and lower complication and mortality rates than low volume bariatric centers.\[4-6\] These data have led to national efforts to establish bariatric surgery centers of excellence by the American Society for Metabolic and Bariatric Surgery, the American College of Surgeons,
and the BlueCross BlueShield Association.

Literature Appraisal

The following literature appraisal is based on randomized controlled trials (RCT), Blue Cross Blue Shield Association (BCBSA) Technology Evaluation Center (TEC) Assessments, Cochrane reviews, Agency for Healthcare Research and Quality (AHRQ) comparative effectiveness reviews, Washington State Health Technology Assessment and evidence-based guidelines.

Distal (Long Limb) Gastric Bypass

TEC Assessment

The 2005 Blue Cross Blue Shield Association (BCBSA) Technology Evaluation Center (TEC) Assessment identified six comparative trials of long limb gastric bypass with Roux-en-Y anastomosis (LL-RYGBP) vs. standard RYGBP. However, only two were randomized controlled trials (RCT). The assessment determined that there was not sufficient evidence to reach conclusions on the efficacy and safety of LL-RYGBP compared to standard RYGBP:

- In both RCTs, there was no significant difference in weight loss between the two groups at 1 year.
- The evidence for the super obese (BMI ≥50 kg/m²) population was weak and did not allow conclusions concerning whether LL-GBRY is superior in this subgroup of patients.
- The adverse events were poorly reported in all comparative studies. Some of the reports contradicted one another.
- There was no definite cut-off for “long” vs. “standard” limb, making comparisons even more challenging.

Randomized Controlled Trials

One RCT evaluated the effectiveness of the distal gastric bypass for weight loss and control of comorbidities. The study included only super obese patients (BMI ≥50 kg/m²). There was no significant difference in the control or improvement of hypertension, sleep apnea, or gastroesophageal reflux disorder between the patients who underwent long-limb (Roux limb = 250 cm) and short-limb gastric bypass (Roux limb = 150 cm). In addition, there was no difference in excess weight loss between the groups. Although the study reports better control of lipid disorders and diabetes in patients who underwent the long-limb gastric bypass, several design flaws undermine the reliability of the study findings:

- The small study population (n=105) limits the ability to rule out the role of chance as an explanation of findings.
- The randomization scheme was not explained. Inadequate randomization of study participants may result in unequal distribution of potential confounders, such as clinical characteristics.
- The short-term follow-up limits conclusions regarding the long-term complications and the effectiveness of the distal gastric bypass in controlling weight loss and comorbidities.
- The study included only super obese patients limiting the generalizability of the study findings to other patient populations (i.e. morbidly obese).
- The need for nutritional supplementation after the surgery was reported for the two treatment groups, but there was a failure to include statistical testing for this outcome.

October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
Nonrandomized Studies

A number of nonrandomized studies (retrospective comparisons, case series) describe the experiences of patients undergoing distal gastric bypass.[3,8-10] As noted at the beginning of the evidence section, conclusions cannot be reached from these studies as the evidence is considered unreliable.

Conclusion

Evidence regarding long limb gastric bypass with Roux-en-Y anastomosis (LL-RYGBP) vs. standard RYGBP is limited to three RCTs which showed either no benefit to the LL approach compared to the RYGBP and/or had numerous methodological limitations. In addition, without a standardized cut-off for long vs. standard limb length, comprehensive assessment of the long limb procedure is unlikely. Therefore, current evidence is insufficient to recommend LL-RYGBP over standard RYGBP, including in the super obese.

Biliopancreatic Bypass and Biliopancreatic Bypass with Duodenal Switch

Cochrane Review

In 2013, Colquitt and colleagues updated a 2009 Cochrane review[11] which compared outcomes for a variety of surgical weight loss procedures.[12] Two RCTs were identified which assessed outcomes of biliopancreatic diversion with duodenal switch (BPD-DS) compared to RYGBP. At a mean three year follow-up, data from the two trials were pooled (n= 107) and the following conclusions were reached:

- BPD-DS resulted in significantly greater weight loss than RYGBP.
- Quality of life measures were similar between the two groups.
- Reoperation rates were higher in the BPD-DS group (16.1%-27.6%) compared to the RYGBP group (4.3%-8.3%), with one death reported in the BPD-DS group.

TEC Assessment

The 2005 BCBSA TEC Assessment identified only one comparative trial that compared RYGBP with BPD-DS.[3] Although the trial included 237 RYGBP and 113 BPD-DS patients, it was not a randomized clinical study (the choice of the surgery was determined by surgeon and/or patient) and it followed participants for only one year. The TEC Assessment did not find this data sufficient to determine the risk/benefit ratio for this procedure or that it results in greater weight loss than RYGBP:

- The % estimated weight loss (EWL) at one year was the same for both the RYGBP and BPD-DS groups.
- Data on short-term adverse events was limited, except for the mortality and wound infection rates which were equivalent in both groups.
- More anastomotic leaks were reported in BPD-DS group.
- Long-term complications were not reported.
- Nutritional concerns were not adequately addressed. This is of concern because BPD-DS further reduces fat absorption, affecting the absorption of fat soluble vitamins.

Randomized Controlled Trials
Two prospective randomized trials compared the experiences of obese patients undergoing RYGBP vs. BPD.

The first trial compared weight loss, metabolic deficiencies, and resolution of comorbidities in morbidly obese patients undergoing RYGBP vs. a variant of BPD (BPD with RYGBP).[13] The study reports comparable nutritional deficiencies between the two procedures. Although better weight loss and resolution of diabetes and hypercholesterolemia was reported in the BPD group, several design flaws undermine the reliability of the study findings:

- The study employed an inadequate randomization scheme: the report states that patients were chosen to undergo RYGBP or BPD, but fails to provide any further explanation of how the treatment was assigned. Inadequate randomization of study participants may result in unequal distribution of potential confounders, such as clinical characteristics.
- The RYGBP group had a significantly higher level of preexisting comorbidities (p = 0.01), suggesting a difference between the treatment groups that may have affected the outcome.
- The small study population (65 patients/surgery group) limits the ability to rule out the role of chance as an explanation of findings.
- The short-term follow-up (2 years) limits conclusions regarding the long-term metabolic complications and the long-term effectiveness of the BPD in controlling weight loss and comorbidities.

Another small randomized trial (n=60) compared laparoscopic RYGBP and BPD-DS for superobese patients (BMI 50-60 kg/m²).[14] The study found comparable 30-day perioperative safety and greater weight loss following BPD-DS in the first year. However, several design flaws undermine the reliability of the study findings:

- It is not certain from the data presented whether the study was adequately powered to reliably observe the treatment differences, especially in the stratified sub-analyses.
- The effectiveness of the procedures in controlling comorbidities was not compared in this study.

In 2015, long-term 5-year follow-up results were published on data from 55 patients (92%).[15] Results indicated a mean reduction of body mass index was greater with duodenal switch compared to bypass (mean between-group difference was 8.5 [95% CI, 4.9-12.2; P < .001]); however, duodenal switch was associated with more surgical, nutritional and gastrointestinal adverse effects.

Nonrandomized Studies

A number of non-randomized studies (retrospective comparisons, case series) describe the experiences of patients undergoing biliopancreatic diversion with or without duodenal switch.[16-33] As noted at the beginning of the evidence section, conclusions cannot be reached from these studies as the evidence is considered unreliable.

Conclusion

Studies that compared RYGBP with BPD-DS are limited by methodological limitations, including inadequate power analysis, unequal distribution of preexisting comorbidities between groups, small sample size and short-term follow-up. In addition, a recent Cochrane review reported higher reoperation rates with BPD-DS compared to RYGBP. Given these limitations and high reoperation rates, the efficacy of BPD-DS versus RYGBP as a treatment for obesity cannot be determined.
Sleeve Gastrectomy

There are various types of gastrectomy, which include distal, partial (including sleeve gastrectomy) or complete gastrectomy which may be performed with or without gastroduodenostomy, gastrojejunostomy, or Roux-en-Y reconstruction. There is insufficient evidence regarding the use of gastrectomy, other than sleeve gastrectomy, as a treatment of obesity. Numerous studies were identified which evaluated outcomes of these alternative gastrectomy methods as a treatment of other conditions, including gastric cancer; however, no studies or clinical practice guidelines were identified which evaluated the efficacy of these alternative types of gastrectomy as a treatment of obesity. Therefore, the following evidence review will focus on the use of sleeve gastrectomy as a treatment of obesity:

Systematic Review and Meta-analysis

The 2013 Cochrane review of bariatric surgery identified only one randomized controlled trial that compared sleeve gastrectomy to gastric bypass with Roux-en-Y anastomosis (RYGBP). This very small (n=32) and short trial that followed participants for only 1 year reported that:

- Weight loss and BMI were similar between the two procedures, but % excess weight loss was greater with sleeve gastrectomy.
- Two patients had diabetes at baseline, both in the RYGBP group. The condition was resolved at 1 year in both patients. The outcome of other comorbidities reported at baseline was not reported for the RYGBP or SG groups.
- Although the study reported no conversions to open surgery and no intraoperative and postoperative complications, the other complications and additional operative procedures were not reported.
- The study did not assess a two-stage approach using sleeve gastrectomy prior to another bariatric procedure and consequently no conclusions about the two-stage approach could be made.
- The short duration of the follow-up results in underestimation of the impact of late complications and the need for revision surgery.

In 2013, Trastulli and colleagues published a systematic review of randomized trials that compared sleeve gastrectomy to other bariatric procedures. A total of 15 RCTs with 1191 patients were included. In 6 trials laparoscopic sleeve gastrectomy (LSG) was compared to laparoscopic RYGBP. The authors reported mean complication rates with sleeve gastrectomy of 12.1% (range 10%-13.2) compared with 20.9% with laparoscopic gastric bypass (range 10%-26.4%). Percentage of excess weight loss ranged from 49%-81% with sleeve gastrectomy compared with 62.1%-94.4% with laparoscopic gastric bypass. Included studies which compared LSG to laparoscopic RYGBP were small (n<60) and several contained a risk for bias which included unclear blinding, randomization methods and outcome data.

A 2013 meta-analysis by Li and colleagues pooled data from 5 trials, 4 of which were included in the Trastulli review, to compare the impact of these procedures on type 2 diabetes rates. Laparoscopic Roux-en-Y gastric bypass was associated with higher rates of type 2 diabetes remission and greater estimated weight loss, but higher rates of complications.

In 2015, Zhang and colleagues published a separate review comparing LGS to laparoscopic RYGBP (LRYGBP) which included 21 studies involving 18,766 morbidly obese patients. Data regarding percentage of excess weight loss (%EWL), resolution or improvement of comorbidities, and adverse
events were pooled. Although no difference in %EWL was observed between the two groups in the first 6 months-1.5 year follow-up, LRYGBP achieved higher %EWL compared to LSG (p<0.05). Except for improvements in type 2 diabetes, comorbidities did not differ significantly between the two groups. Adverse events were more frequent following Roux-en-Y bypass (OR for major complication: 1.29; 95% CI 1.22 to 3.22; P<0.01). Results of this review must be interpreted with caution as 13 of the 21 included studies were nonrandomized, limiting the ability to control for confounding factors.

A 2014 review by Zellmer and colleagues compared complication rates of laparoscopic RYGBP to LSG in 61 publications which included 10,906 laparoscopic RYGBP patients and 4,816 LSG patients.[41] Authors reported similar leak and mortality rates in both groups; laparoscopic RYGBP (leak: 1.9%, mortality: 0.4%) vs. LSB (leak: 2.3%, mortality: 0.2%).

Randomized Controlled Trials

Two additional RCTs were identified which were not addressed in the reviews above. These RCTs found SG and RYGBP to be overall comparable, however at least two major design flaws undermine the reliability of the reported study findings:

- The very small study populations (n=23)[42] limit the ability to rule out the role of chance as an explanation of findings.
- The very short follow-up durations (1 year)[42,43] limit conclusions regarding medium- and long-term outcomes (e.g., weight loss, glucose metabolism, resolution of co-morbidities, reoperation rates, and safety).

Nonrandomized Studies

A number of nonrandomized studies (retrospective comparisons, case series) describe the experiences of patients undergoing sleeve gastrectomy.[44-82] As noted at the beginning of the evidence section, conclusions cannot be reached from these studies as the evidence is considered unreliable.

Clinical Practice Guidelines[83]

In 2012, the American Society for Metabolic & Bariatric Surgery (ASMBS)[83,84] updated their position statement on Sleeve Gastrectomy as a Bariatric Procedure. The ASMBS recognizes sleeve gastrectomy as an acceptable option as a primary bariatric procedure and as a first stage procedure in high risk patients as part of a planned staged approach. In addition, the group noted that substantial comparative and long-term data have now been published which demonstrate durable weight loss, improved medical comorbidities, long-term patient satisfaction, and improved quality of life after SG. However, the ASMBS Statement does not include a critical appraisal of the reviewed evidence.

Conclusion

Recent systematic reviews of existing trials indicate sleeve gastrectomy (SG) is a comparable procedure to RYGBP. Although the evidence regarding SG with RYGBP compared to standard RYGBP is limited by short-term follow-up, SG has become a recognized surgical option in clinical practice for the treatment of morbid obesity.

Adjustable Gastric Banding

Systematic Review
The 2013 Cochrane review of bariatric surgery identified three randomized controlled trial that compared laparoscopic adjustable gastric banding (LAGB) to laparoscopic gastric bypass with Roux-en-Y anastomosis (RYGBP). At five-year follow-up, the review reported the following conclusions:

- RYGBP was superior to LAGB on more than one measure of weight loss (% excess weight loss, mean BMI).
- Quality of life measures and comorbidities were not assessed due to the low quality of the evidence.
- RYGBP resulted in a greater duration of hospitalization and a greater number of late major complications.
- One study reported high rates of reoperation for removal of LAGB (9 patients, 40.9%).

**TEC Assessment**

In 2012, TEC conducted an updated Assessment, focusing on LAGB in patients with BMIs less than 35 kg/m². TEC made the following observations and conclusions:

- The evidence on LAGB for patients with lower BMIs is limited both in quantity and quality. There was only one small randomized, controlled trial, which had methodologic limitations, one nonrandomized comparative study based on registry data, and several case series. Using the GRADE evaluation, the quality of evidence on the comorbidity outcomes was judged to be low and the quality of the evidence on the weight loss outcomes was judged to be moderate.
- The evidence was sufficient to determine that weight loss following LAGB was greater than with nonsurgical therapy.
- Direct data on improvement in weight-related comorbidities was lacking. The limited evidence was not sufficient to conclude that the amount of weight loss was large enough that improvements in weight-related comorbidities could be assumed.
- There was very little data on quality of life in this population of patients.
- The frequency and impact of long-term complications following LAGB was uncertain, thus it was not possible to determine whether the benefit of LAGB outweighed the risk for this population. TEC concluded that while the short-term safety of LAGB was well-established, the long-term adverse effects occur at a higher rate and are less well-defined.

**Randomized Controlled Trials**

An updated literature search failed to identify any additional randomized controlled trials that compare LAGB with RYGBP.

**Nonrandomized Studies**

A number of non-randomized studies (retrospective comparisons, case series) describe the experiences of patients undergoing LAGB. As noted at the beginning of the evidence section, conclusions cannot be reached as the evidence from these studies is considered unreliable.

**Conclusion**

Although the evidence regarding the laparoscopic adjustable gastric banding (LAGB) compared to standard RYGBP is limited, there appear to be benefits associated with LAGB in terms of the...
procedures reversibility and laparoscopic approach. Despite limited evidence, the LAGB has been gaining increased acceptance in clinical practice.

Laparoscopic Duodenal Switch with Single Anastomosis

Several nonrandomized studies were identified which describe the experiences of patients undergoing laparoscopic duodenal switch with single anastomosis (LSDSA). As noted at the beginning of the evidence section, conclusions cannot be reached from these studies as the evidence is considered unreliable. Well-designed RCTs which compare LSDSA with RYGBP are needed in order to evaluate the safety and efficacy of this procedure compared to accepted surgical treatments of morbid obesity.

Mini-Gastric Bypass

Randomized Controlled Trials

One small RCT compared the safety and effectiveness of laparoscopic RYGBP and mini-gastric bypass (MGBP). The study found a comparable rate of late complications (>30 days post-op), weight loss, and comorbidity resolution. MGBP was associated with fewer early complications (<30 days post-op). However, the following design flaws undermine reliability of the study findings:

- The small study population (n=80) limits the ability to rule out the role of chance as an explanation of findings.
- Short-term follow-up (2 years) limits comparisons regarding the longer-term complications rates and the effectiveness of the two procedures in controlling weight loss and comorbidities

Nonrandomized Studies

Several nonrandomized studies (retrospective comparisons, case series) and a systematic review of these nonrandomized studies, describe experiences of patients undergoing MGBP. As noted at the beginning of the evidence section, conclusions cannot be reached as this evidence is considered unreliable.

Conclusion

Data regarding the mini-gastric bypass (MGBP) is limited to a small RCT, prohibiting conclusions regarding the efficacy of this procedure compared to RYGBP.

Vertical Banded Gastroplasty (VBG)

VBG has largely been abandoned in the United States due to insufficient weight loss and high reoperation rates (approximately 30%).

Hiatal Hernia Repair

Numerous studies were identified which evaluated outcomes of hiatal hernia repair performed in conjunction with other bariatric surgical procedures; however, no studies or clinical practice guidelines were identified which evaluated the efficacy of hiatal hernia repair and an independent treatment of obesity.

Two-Stage Bariatric Surgery Procedures

October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
Bariatric surgeries that are performed in 2 stages have been proposed as a treatment option, particularly for patients with “super-obesity” defined as a BMI greater than 50. The rationale for a 2-stage procedure is that the risk of an extensive surgery is prohibitive in patients with extreme levels of obesity. Therefore, an initial procedure with low risk, usually a sleeve gastrectomy, is performed first. After a period of time in which the patient loses some weight, thus lowering the surgical risk, a second procedure that is more extensive, such as a biliopancreatic diversion (BD), is performed.

Case series on 2-stage procedures for patients undergoing sleeve gastrectomy (SG) as the initial procedure generally did not report on the second-stage operation, and in those that did, only a minority of patients undergoing the first stage actually proceeded to the second-stage surgery. For example, Cottam et al.[52] reported on 126 patients with a mean BMI of 65 who underwent laparoscopic SG as the first portion of a planned 2-stage procedure. A total of 36 patients (29%) proceeded to the second-stage procedure, which was laparoscopic gastric bypass. In a similar study, Alexandrou et al.[111] reported on 41 patients who underwent SG as the first stage of a planned 2-stage procedure. After 1-year follow-up, 12 patients (29%) achieved a BMI less than 35 and were not eligible for the second-stage procedure. Of the remaining 28 patients, 10 (24% of total) underwent the second-stage procedure. The remaining 18 patients (44% of total) were eligible for, but had not undergone, the second-stage procedure at the last follow-up.

Patients who undergo 2-stage procedures are at risk for complications from both procedures. Silecchia et al.[112] described the complication rates in 87 patients undergoing a stage I SG followed by a BPD in 27 patients. For the first stage of the operation, 16.5% of patients had complications of bleeding, fistula, pulmonary embolism, acute renal failure, and abdominal abscess. For the 27 patients who underwent the second-stage BPD, major complications occurred in 29.6% including bleeding, duodenoileal stenosis, and rhabdomyolysis.

Conclusion

The current evidence does not indicate that a 2-stage bariatric surgery procedure improves outcomes for patients with extreme levels of obesity. There is no evidence to suggest that weight loss is improved or that complications are reduced by this approach. A majority of patients who received SG as the initial procedure lost sufficient weight during the first year such that a second procedure was no longer indicated. In addition, patients undergoing a 2-stage procedure are at risk for complications from both procedures; therefore, it is possible that overall complications are increased by this approach.

Endoscopic (Endoluminal) Bariatric Procedures

Systematic Review

A systematic review of the effect of EndoBarrier® on weight loss and diabetic outcomes was published in 2015.[113] There were five small RCTs included with a total of 235 individuals (range, 18-77) and follow-up ranging from 12 to 24 weeks. The comparators were diet and/or other lifestyle modifications, and 2 studies had sham controls. All studies were judged to be at high risk of bias using the Cochrane risk of bias tool. Combined results demonstrated that the EndoBarrier® group had 12.6% greater EWL (95% CI, 9.0 to 16.2) compared to medical therapy. For diabetic outcomes, there were trends toward greater improvement in the EndoBarrier® group that did not reach statistical significance. The mean difference in HgA1c was -0.8% (95% CI, -1.8 to 0.3) and the relative risk of reducing or discontinuing diabetic medications was 3.28 (95% CI, 0.54 to 10.73).
Randomized Controlled Trials

In June 2016 the AspireAssist (Aspire Bariatrics, King of Prussia, PA) weight loss therapy system was approved by the FDA to assist in weight reduction in adults aged 22 and older with a BMI of 35.0-55.0 kg/m² who have failed to achieve and maintain weight loss with non-surgical weight loss therapy. Feasibility data for the AspireAssist was reported by Sullivan and colleagues in 2013.[114] Preliminary results from the ongoing PATHWAY Pivotal Trial (sponsored by Aspire Bariatrics) are included in the FDA Summary of Safety and Effectiveness Data, though results have not been published in peer-reviewed literature at this point in time.[115]

In 2014, Eid et al. reported results from a single-center RCT of the StomaphX device compared with a sham procedure for revision procedures in patients with prior weight loss after Roux-en-Y gastric bypass at least 2 years earlier.[116] Enrollment was initially planned for 120 patients, but the trial was stopped prematurely after 1-year follow up was completed by 45 patients in the StomaphyX group and 29 patients in the sham control group after preliminary analysis failed to achieve the primary efficacy endpoint in at least 50% of StomaphyX patients. The primary efficacy end point (reduction in pre-Roux-en-Y gastric bypass excess weight by 15% or more, excess BMI loss, and BMI less than 35, at 12 months post-procedure) was achieved by 10/45 (22.2%) of the StomaphyX group and 1/29 (3.4%) of the sham control group (P<0.01). Conclusions regarding the use of the StomaphX device as a primary procedure for the treatment of obesity may not be drawn due to the discontinuation of the trial and the limited use of the device as a revision procedure in patients who had failed a prior bariatric surgery.

In 2014, Koehestanie and colleagues published results from an RCT of duodenal-jejunal bypass liner (DJBL) treatment in comparison with dietary intervention for obesity and type 2 diabetes mellitus (T2DM).[117] a total of 77 patients were included in the trial with 38 patients randomized to 6 months DJBL in combination with dietary intervention and 39 patients were randomized to dietary interventions only. The total study duration for both groups was 12 months, including 6 months of post-DJBL removal follow-up. At 6 months follow-up, prior to DJBL removal, the DJBL group lost a higher percentage of excess weight compared to the dietary only group, 32% (22%-46.7%) vs. 16.4% (4.1%-34.6%) respectively. However, better HbA1c levels improvement was observed in the dietary only group compared to the DJBL at both 6 and 12 month follow-ups. Conclusions are limited in this study as both groups underwent dietary interventions limiting the isolation of the effects of DJBL upon obesity and type 2 diabetes.

In 2013, Sullivan and colleagues reported results from a small feasibility pilot RCT (n=18) comparing the AspireAssist siphon assembly (Aspire Bariatrics, King of Prussia, PA) combined with lifestyle therapy (AT) versus lifestyle therapy (LT) alone.[114] Only fourteen subjects completed the 12-month trial (10 in the AT group and four in the LT group). Although weight loss in the AT group was greater at 52 weeks than the LT group (18.6% ± 2.3% of body weight vs 5.9% ± 5.0%) the study was limited by the very small sample size, and unblinded design. The study was partially funded by the manufacturer. The authors all disclosed having previously performed contracted research for the manufacturer of the device and one author also disclosed having consulted on a pivotal trial for the company.

In 2013, Fuller and colleagues published a small RCT (n=66) which evaluated intragastric balloons (IGB) compared to behavioral modification as a treatment of obesity.[118] Subjects were either randomized to IGB and 12 months behavior modification (BH) and or 12 months BH alone. At six months the IGB treatment group demonstrated superior weight loss compared to the BH group (-14.2 vs. -4.8; P < 0.0001). However at 12 months the difference in weight loss between groups, although still statistically significant, diminished (-9.2 vs. -5.2; P = 0.007). There were numerous adverse events related to IGB placement which typically resolved in 2 weeks. Limitations of this study include a
relatively small population size and short-term follow-up with which to evaluate the lasting effects of weight reduction with IGB. In addition, RCTs which evaluate IGB to other standard surgical treatments of obesity are needed.

Additional, small RCTs assessing IGB were identified\[119-121\]; however, large, long-term data remain lacking with which to evaluate the safety and sustained benefit of IGB in weight reduction compared to conservative measures and accepted bariatric procedures.

**Nonrandomized Studies**

A small number of non-randomized studies, primarily case series, describe experiences of patients undergoing different endoluminal procedures, such as endoscopic gastroplasty and endoscopically placed sleeves, gastric balloons or tissue anchors.\[122-138\] As noted at the beginning of the evidence section, conclusions cannot be reached as this evidence is considered unreliable.

**Laparoscopic Gastric Plication**

**Nonrandomized Studies**

Similar to the data for endoscopic bariatric procedures, the data for laparoscopic gastric plication (also known as laparoscopic gastric imbrication) is limited to case series and case reports and a single small RCT (n=30), which describe patient outcomes after different laparoscopic plication procedures.\[139-143\] As noted at the beginning of the evidence section, conclusions cannot be reached as this evidence is considered unreliable.

**Revision Bariatric Surgical Procedures**

There are a number of reasons why patients who are treated with accepted forms of bariatric surgery may not lose weight or may regain weight that is initially lost. These reasons include issues of adherence (compliance), as well as technical (structural) issues. A number of studies\[144-146\] have evaluated the efficacy of revision procedures after failed bariatric surgery and reported satisfactory weight loss and resolution of co-morbidities with somewhat higher complication rates than for primary surgery. However, criteria for classifying what constitutes a failed, primary bariatric procedure, has not been clearly established.\[147\]

In 2016, Dang et al. reported results from a systematic review and meta-analysis comparing revisional single-step versus two-step bariatric surgery from laparoscopic adjustable gastric banding (LAGB) to Roux-en-Y gastric bypass (RYGB) or sleeve gastrectomy (SG).\[148\] Single-step procedures involved revisional surgery wherein the LAGB was removed and replaced by RYGB or SG in the same operation; two-step procedures allowed a delay before the second bariatric procedure was performed. Although the authors found comparable rates of complications, morbidity and mortality between the one- and two-step procedures, the study was not designed to evaluate differences in patient outcomes between the second bariatric procedure (i.e., RYGB vs SG).

In 2014, Sudan et al. reported safety and efficacy outcomes for reoperative bariatric surgeries using data from a national registry, the Bariatric Outcomes Longitudinal Database.\[149\] The Bariatric Outcomes Longitudinal Database is a large multi-institutional bariatric surgery-specific database to which data was submitted from June 2007 through March 2012 by 1,029 surgeons and 709 hospitals participating in the Bariatric Surgery Centers of Excellence (BSCOE) program. Surgeries were classified as primary or...
Reoperative bariatric surgery. Reoperations were further divided into corrective operations (when complications or incomplete treatment effect of a previous bariatric operation was addressed but the initial operation was not changed) or conversions (when an index bariatric operation was changed to a different type of bariatric operation or a reversal restored original anatomy.) There were a total of 449,473 bariatric operations in the database of which 420,753 (93.6%) operations had no further reoperations (primary operations) while 28,270 (6.3%) underwent reoperations. Of the reoperations, 19,970 (69.5%) were corrective operations and 8,750 (30.5%) were conversions. The primary bariatric operations were Roux-en-Y gastric bypass (N=204,705, 49.1%), adjustable gastric banding (N=153,142, 36.5%), sleeve gastrectomy (N=42,178, 10%), and BPD±DS (N=4,260, 1%), with the rest classified as miscellaneous. Adjustable gastric banding was the most common primary surgery among conversions (57.5% of conversions; most often [63.5%] to Roux-en-Y gastric bypass). Compared with primary operations, mean length of stay was longer for corrections (2.04±6.44 vs 1.8±4.9, P<0.001) and for conversions (2.86±4.58 vs 1.8±4.9, P<0.001). The mean % excess weight loss at 1 year was 43.5% after primary operation, 39.3% after conversions, and 35.9% after corrective operations (statistical comparison not reported). One-year mortality was higher for conversions compared with primary operations (0.31% vs 0.17%, P<0.001), but not for corrections compared with primary operations (0.24% vs 0.17%, P=NS). One-year serious adverse event rates were higher for conversions compared with primary operations (3.61% vs 1.87%, P<0.001), but not for corrections compared with primary operations (1.9% vs 1.87%, P=NS). The authors conclude that reoperation after primary bariatric surgery is relatively uncommon, but generally safe and efficacious when it occurs.

As part of the American Society for Metabolic and Bariatric Surgery Revision Task Force, Brethauer et al. conducted a systematic review of reoperations after primary bariatric surgery that included 175 studies, most of which were single-center retrospective reviews.[150] The review was primarily descriptive, but the authors made the following conclusions:

“The current evidence regarding reoperative bariatric surgery includes a diverse group of patient populations and procedures. The majority of the studies are single institution case series reporting short- and medium-term outcomes after reoperative procedures. The reported outcomes after reoperative bariatric surgery are generally favorable and demonstrate that additional weight loss and co-morbidity reduction is achieved with additional therapy. The risks of reoperative bariatric surgery are higher than with primary bariatric surgery and the evidence highlights the need for careful patient selection and surgeon expertise.”

Revision or Removal of Adjustable Gastric Band

Evidence regarding the indications for band removal or revision procedure is primarily limited to small cohort[151] and case series studies; however, reoperation or removal rates are estimated to range from 4.1%-53%, depending on the time of reported follow-up.[152-155] Several of the largest cohort studies have reported the following complications which resulted in reoperation or band removal:

Arapis et al.[156], reported the following complications in 87 patients who underwent reoperation: chronic dilatation of the proximal gastric pouch (27 patients - 14.5%), acute dilatation (21 patients - 11.3%), intragastric migration of the prosthesis (6 patients - 3.2%), reflux esophagitis (6 patients - 3.2%), infection of the gastric band (1 patient - 0.5%), and Barrett's esophagus (1 patient - 0.5%).

Perathoner and colleagues reported on 108 patients who underwent laparoscopic conversion of gastric banding to gastric bypass due to the following complications: band migration, inadequate weight loss, pouch dilation, band leakage, band intolerance, band infection and esophageal dilation.[157]
Other reported complications included: band erosion, gastric obstruction, and gastric slippage.

Avriel and colleagues reported major respiratory complications and chronic disease development in 30 patients who underwent LAGB. Reported complications included aspiration pneumonia (19 patients) including pulmonary abscess (4 patients) and empyema (2 patients), exacerbation of asthma (3 patients), hemoptysis (1 patient), interstitial lung disease (5 patients) and bronchiectasis (3 patients). However, the impact of LAGB upon the development of these conditions is unclear given that 83% of the patients smoked or had a smoking history (mean pack years 34).

Studies which evaluated band conversion to a second bariatric surgery primarily indicated that bypass was the preferred revision surgery due to better long-term outcomes compared to sleeve gastrectomy. In one large retrospective study published in 2014, bypass was compared to sleeve gastrectomy after band removal and conversion. National Surgical Quality Improvement Project data from 2005-2011 were analyzed and included 495 patients who converted from LAGB to bypass and 130 patients who converted to sleeve gastrectomy. Conversion to bypass was not associated with higher morbidity or mortality compared to primary RYGB; however, conversion to sleeve gastrectomy was independently associated with a higher rate of major complications and mortality compared to primary sleeve gastrectomy (OR 8.02, 95% CI 1.08-59.34, p = 0.04).

Conclusion

For surgical revision of bariatric surgery after failed treatment, evidence from nonrandomized studies suggests that revisions are associated with improvements in weight similar to those seen in primary surgery. However, evidence from large long-term studies is required to determine the appropriate clinical indications for band removal or reoperation.

Bariatric Surgery in Patients with Diabetes with BMI < 35kg/m²

Systematic Review

In 2015 Muller-Stich published a systematic review comparing surgical versus medical treatment of type II diabetes in patients with a BMI less than 35 kg/m². The analysis included data from five RCTs and six observational studies for a total of 702 patients. The follow-up of included studies ranged from 12-36 months. Authors concluded that surgery was associated with higher diabetes remission rate (OR: 14.1, 95% CI: 6.7–29.9, P < 0.001), higher rate of glycemic control (OR: 8.0, 95% CI: 4.2–15.2, P < 0.001) and lower HbA1c level (MD: −1.4%, 95% CI −1.9% to −0.9%, P < 0.001) compared to medical treatment. However results are limited by inclusion of studies in which the BMI of some patients was greater than 35 kg/m² and short-term follow-up, limiting conclusion regarding the long-term benefits of bariatric surgery upon glycemic control.

In 2013, the Agency for Healthcare Research and Quality (AHRQ) published a comparative effectiveness review of bariatric surgery and nonsurgical therapy in adults with metabolic conditions, including diabetes, and a BMI of 30.0-34.9 kg/m². The report evaluated key issues which included the effectiveness of bariatric surgery compared to nonsurgical therapies, short and long-term effects in symptom control and racial and demographic disparities regarding benefits and harms of surgery in patients with metabolic conditions and a BMI of 30.0-34.9 kg/m². Evidence was gathered from global literature searches, reference mining and titles identified from external sources. A total of 24 studies reported bariatric surgery results, with a majority of studies evaluating RYGBP or LAGB...
procedures in diabetic patients with a BMI of 30-35 kg/m².[167] The AHRQ report concluded that there was moderate strength evidence of efficacy for certain bariatric procedures as a treatment for diabetes in the short term. However, the report noted that the evidence contained many limitations, “(m)ost importantly, very few studies of this target population have long-term follow-up. Only two studies followed patients for more than 2 years; one has a followup rate of only 13.8 percent and the other includes only seven patients. Thus, we have almost no data on long-term efficacy and safety.” In addition the AHRQ report noted the lack of evidence on major clinical outcomes such as all-cause mortality, cardiovascular risks, or peripheral arterial disease. Although short-term studies suggest an improvement in glucose control, the AHRQ report pointed out that, “…the available evidence from the diabetes literature indicates it may be premature to assume that controlling glucose to normal or near normal levels completely mitigates the risk of microvascular and macrovascular events. Thus, claims of a “cure” for diabetes based on glucose control within 1 or 2 years require longer term data before they can be substantiated.”

**Randomized Controlled Trials**

Since the publication of the AHRQ report, two RCTs have been reported on bariatric surgery compared to medical therapy in diabetic patients with a BMI between 30-40 kg/m².

Ikramuddin et al. performed an unblinded RCT of gastric bypass versus intensive medical therapy on 120 patients with type II diabetes for at least 6 months and an HgbA1C of at least 8.0%.[169] Patients were followed for 12 months with the primary endpoint being a composite of HgbA1C less than 7.0%, low-density lipoprotein (LDL) cholesterol less than 100 mg/dl and systolic blood pressure less than 130 mm Hg. A total of 28 patients in the surgery group achieved the primary outcome compared to 11 patients in the medical therapy group (odds ratio [OR]: 4.8, 95% CI: 1.9-11.7). The percent of patients achieving HgbA1C of less than 7.0% was 75% in the surgery group compared to 32% of patients in the medical therapy group (OR: 6.0, 95% CI: 2.6-13.9). There were 22 serious complications in the surgery group, including 4 perioperative complications, compared to 15 serious complications in the medical group. A limitation of this study was that results were not provided separately for patients who were above and below a BMI of 35 kg/m², thus restricting conclusions regarding the benefits of bariatric surgery compared to medical management in diabetic patients with a BMI < 35 kg/m².

In 2014, Prikh and colleagues published a small (n=57), short-term (6 month follow-up) RCT which compared intensive medical weight management to bariatric surgery in patients with a BMI of 30-35 kg/m² and type 2 diabetes.[170] Significant improvements in primary outcome measures of homeostatic model of insulin resistance and higher diabetes remission rates were observed in the surgical group compared to the MWM group. Additional small RCTs have been identified,[171] however, larger, long-term RCTs are needed to confirm these findings.

In 2015, Mingrone and colleagues published results of a small (n=60) RCT comparing long-term outcomes of either medical treatment or surgery by Roux-en-Y gastric bypass or biliopancreatic diversion in patients with type II diabetes.[172] A total of 53 patients were included in the 5-year follow-up assessment. Primary outcome measures included the rate of diabetes remission at 2 years which was defined as glycated HbA1c concentration of 6.5% or less (≤47.5 mmol/mol) and a fasting glucose concentration of 5.6 mmol/L or less without active pharmacological treatment for 1 year. At 5-year follow-up 19 (50%) of the 38 surgical patients (7 of 19 [37%] in the gastric bypass group and 12 of 19 in the [63%] biliopancreatic diversion group) maintained diabetes remission at 5 years, compared with none of the 15 medically treated patients (p=0.0007). Fifteen incidents of hyperglycemic relapse occurred in 34 surgical of the patients who achieved 2 year remission, suggesting continued monitoring of glycemic control may be necessary. Authors also reported that both surgical procedures were associated with
significantly lower plasma lipids, cardiovascular risk, and medication use and no late complications or deaths.

Clinical Practice Guideline

American College of Cardiology, American Heart Association, and the Obesity Society

In 2013, the American College of Cardiology (ACC), American Heart Association (AHA), and the Obesity Society published guidelines on the management of obesity and overweight in adults.\textsuperscript{[173]} The guidelines were based upon a high-quality systematic review of the evidence which included transparent methods for grading the strength of the evidence and subsequent recommendations. The guidelines make the following recommendations related to bariatric surgery:

“For adults with a BMI >40kg/m\textsuperscript{2} or BMI >35 kg/m\textsuperscript{2} with obesity-related comorbid conditions who are motivated to lose weight and who have not responded to behavioral treatment (with or without pharmacotherapy) with sufficient weight loss to achieve targeted health outcome goals, advise that bariatric surgery may be an appropriate option to improve health and offer referral to an experienced bariatric surgeon for consultation and evaluation.” (Grade A: Indicating a strong recommendation, indicating there is a high certainty based on the evidence that the net benefit is substantial).

“For individuals with a BMI <35 kg/m\textsuperscript{2}, there is insufficient evidence to recommend for or against undergoing bariatric surgical procedures.” (No recommendation given, indicating there is insufficient evidence or evidence is unclear or conflicting)

American Association of Clinical Endocrinologists, the Obesity Society, and American Society for Metabolic & Bariatric Surgery\textsuperscript{[174]}

In 2013, joint guidelines were published by the American Association of Clinical Endocrinologists, the Obesity Society, and American Society for Metabolic & Bariatric Surgery (AACE/ASM/Obesity Society) regarding the perioperative nutritional, metabolic and nonsurgical support of the bariatric surgery patient. Recommendations regarding which patients should be offered bariatric surgery indicated the following:

“Patients with BMI of 30–34.9kg/m\textsuperscript{2} with diabetes or metabolic syndrome may also be offered a bariatric procedure although current evidence is limited by the number of subjects studied and lack of long-term data demonstrating net benefit.

There is insufficient evidence for recommending a bariatric surgical procedure specifically for glycemic control alone, lipid lowering alone, or cardiovascular disease risk reduction alone, independent of BMI criteria.”

Institute for Clinical Systems Improvement\textsuperscript{[175]}

In 2012, the Institute for Clinical Systems Improvement (ICSI) published guidelines regarding the diagnosis and management of type 2 diabetes mellitus in adults and indicated:

“Bariatric surgery may be considered for adults with BMI >35 if diabetes or comorbidities are difficult to control with lifestyle and pharmacologic therapy.”

Conclusion
Evidence regarding the efficacy of bariatric surgery as a treatment for diabetes in patients with a BMI < 35 kg/m² primarily consists of small cases series with short-term follow-up as noted in the AHRQ report. Since the publication of these reports a single RCT was identified which was limited by the inclusion of obese (BMI 35-40 kg/m²) and non-obese (BMI 30-34.9 kg/m²) patients, precluding conclusions regarding the clinically non-obese population. Only one clinical practice guideline was identified which recommended bariatric surgery in diabetic patients who do not meet the clinical definition of obesity; however, a lack of long-term data was noted. Overall, the current evidence does not demonstrate the safety and efficacy of bariatric surgery as a treatment for diabetes in patients with a BMI < 35 kg/m².

Adolescent and Pediatric Bariatric Surgery

Systematic Reviews and Meta-analysis

The 2007 Washington State Health Technology Assessment evaluated the published, peer reviewed scientific literature describing bariatric surgery in the pediatric population.[176] Data from 17 studies that enrolled a total of 553 pediatric patients were included. Only one study was clearly prospective. Eight studies reported outcomes after LAGB, six after RYGBP, two after VBG, and one after banded bypass. The report concluded that:

- The evidence that LAGB for morbidly obese pediatric patients leads to sustained and clinically significant weight loss compared to non-operative approaches was weak at the longest follow-up after surgery (1.7 to 3.3 years).
- The evidence that RYGBP for morbidly obese pediatric patients leads to sustained and clinically significant weight loss compared to non-operative approaches was weak at the longest follow-up after surgery (1 to 6.3 years).
- The evidence was insufficient to permit quantitative estimates of the precise amount of weight loss after any bariatric surgical procedure for pediatric patients.
- The evidence was insufficient to permit any conclusions about weight loss after other bariatric surgical procedures for pediatric patients.
- The evidence was insufficient to permit any conclusions about weight loss in specific age subgroups (18-21, 13-17, 12 or less) within the pediatric population.
- The evidence that LAGB for morbidly obese pediatric patients does resolve comorbid conditions linked to obesity (diabetes, hypertension) compared to non-operative approaches was weak.
- The evidence that RYGBP for morbidly obese pediatric patients does resolve comorbid conditions linked to obesity (diabetes, hypertension) compared to non-operative approaches was weak.
- The evidence was insufficient to permit quantitative estimates of the likelihood of comorbidity resolution, quality of life improvement, or survival after any bariatric surgical procedure for pediatric patients.
- The evidence was insufficient to permit any conclusions about comorbidity resolution in specific age subgroups (18-21, 13-17, 12 or less) within the pediatric population.
- The LAGB studies reported no in-hospital or postoperative death. However, the most commonly reported complication was band slippage. Reoperations were performed on 7.9% of the LAGB patients to correct various complications (band slippage, intragastric migration, port/tubing problems).
- The RYGBP studies reported one postoperative death. The most frequently reported complication was related to malnutrition and micronutrient deficiency. In addition, potentially
life threatening complications (shock, pulmonary embolism, severe malnutrition, bleeding, gastrointestinal obstructions) were reported.

- The evidence was insufficient to permit any conclusions on potential impacts of bariatric surgery on growth and development of pediatric patients.
- The evidence was insufficient to permit any conclusions on potential harms in specific age groups (18-21, 13-17, 12 or less).

In summary, the assessment found that longer term, prospective collection of data on physical growth, quality of life, weight loss, persistence or resolution of comorbid conditions, and long-term survival are needed in order to fully understand the role of bariatric surgical procedures in treating morbidly obese pediatric patients.

In 2013, Black and colleagues published a systematic review and meta-analysis of 23 studies (22 nonrandomized) that included 637 young patients (age 6-18 years) who underwent bariatric surgery.\[177\] Although significant weight loss was reported at the 1-year follow-up, limitations of the evidence were similar to those reported in the Washington State Health Technology Assessment. Included studies were limited by small sample size with a median number of 24 patients per study (range: 10-108) and short term follow-up (range: 6-12 months). Authors reported that complications were inconsistently reported and indicated that, “long-term, prospectively designed studies, with clear reporting of complications and comorbidity resolution, alongside measures of [health-related quality of life], are needed to firmly establish the harms and benefits of bariatric surgery in children and adolescents.”

In 2015, the Washington State Health Technology Assessment compared various bariatric procedures and also re-examined the role of bariatric surgery in children and adolescents upon obesity related comorbidities.\[178\] The group concluded that there was, “a lack of both short- and long-term data demonstrating effectiveness for any bariatric surgery procedure in both children and adolescents.” Only two studies were identified which were deemed to be of sufficient quality and only one of those was a RCT. In addition, no comparative studies were identified which evaluated any bariatric procedure exclusively in children (under 13 years).

Additional reviews were identified;\[179\] however, conclusions were limited due to a lack of long-term follow-up.\[180\]

**Randomized Controlled Trials**

One small randomized trial compared the outcomes of gastric banding with an optimal lifestyle program in adolescents 14-18 years of age with a BMI >35.\[181\] Although the study reports that gastric banding resulted in greater percentage achieving a loss of 50% of excess weight, several flaws undermine the reliability of the study findings:

- The small study population (n=50) limits the ability to rule out the role of chance as an explanation of findings.
- The study had significant loss to follow-up suggesting a difference that may affect the outcome.
- Short-term follow-up (2 years) limits comparisons regarding the longer-term complications rates and the effectiveness of the procedure in controlling weight loss and comorbidities.

**Nonrandomized Studies**

Studies with short follow-up time
A small number of nonrandomized comparative studies reported significant weight loss and resolution of some of the comorbidities in pediatric patients undergoing bariatric surgery. However, the studies were small and had a very short follow up time.

In 2014, Inge et al reported results from Teen-Longitudinal Assessment of Bariatric Surgery (Teen-LABS) study, a prospective, multicenter observational study of bariatric surgery in patients aged 19 or under. The study enrolled 242 participants, with mean age 17.1 and median BMI 50.5 (IQR 45.2-58.2) at the time of operation. All patients had at least 1 obesity-related comorbidity, most commonly dyslipidemia (74%), followed by sleep apnea (57%), back and joint pain (46%), hypertension (45%), and fatty liver disease (37%). Roux-en-Y gastric bypass, adjustable gastric banding, and vertical sleeve gastrectomy were performed in 66.5%, 5.8%, and 27.7%, respectively. Within 30 days of surgery, 20 major complications occurred in 19 patients (7.9%), most of which were perioperative complications. The cohort will be followed to assess longer-term outcomes.

Studies with mid-term follow-up time

Two observational studies with mid-term follow-up times (≤10 and ≤8 years) reported experiences of pediatric patients undergoing LAGB (sample size 41 and 107 respectively). The first study found that weight loss was initially successful and resulted in resolution of some comorbidities, but it slowly increased over the time and ultimately was unsatisfactory in many patients. The second study reported 65.5% excess weight loss at eight years. Both studies reported high complication and reoperation rates (Lanthaler: 46% patients had complications that required reoperation; Mittermaier: 46% patients had complications and 29% required reoperation).

However, as noted at the beginning of the evidence section, conclusions cannot be reached as this evidence is considered unreliable.

Clinical Practice Guidelines for Pediatric Bariatric Surgery

American College of Physicians

The 2005 American College of Physicians (ACP) evidence-based guideline on use of bariatric surgery in adolescents and children states that the current evidence on surgical treatment of pediatric populations is limited to a few case series which do not permit quantitative analysis. Further, the guideline states that it is unclear whether extrapolation of adult data for bariatric surgery to the pediatric population is appropriate and that RCTs are needed (and feasible) to establish the role of bariatric surgery in this population.

American Academy of Pediatrics

In 2007, the American Academy of Pediatrics (AAP) published, “Recommendations for Treatment of Child and Adolescent Overweight and Obesity,” which stated that although there is increased use of bariatric surgery in adults:

“There is limited research on the safety, efficacy, and long-term outcomes of bariatric surgery for adolescents; therefore, data from adult studies must be considered as surrogate evidence.”

Ultimately, the AAP noted that additional trials are needed to determine whether bariatric surgery is acceptable in adolescents.
American Heart Association

In 2013, the American Heart Association (AHA)\(^{[190]}\) published a statement regarding severe obesity in children and adolescents which concluded:

“Current treatment approaches using lifestyle modification and medications to reduce BMI and improve chronic disease risk factors are insufficient for most patients and significant residual risk (unacceptably high BMI and risk factor levels) remains. Although experts recommend stepped intensification of interventions, the “step” after behavior-based and pharmaceutical interventions to the next established alternative, bariatric surgery, is unacceptably large because of its limited applicability and availability.”

The AHA indicated that the following evidence was needed before bariatric surgery could be widely recommended in children and adolescents:

“Generation of additional safety and efficacy data (especially long-term) on bariatric surgery, including studies describing improvements in vascular structure and function, insulin resistance, and \(\beta\) -cell function.”

Society of American Gastrointestinal and Endoscopic Surgeons

The 2008 the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES)\(^{[191]}\) evidence-based guidelines state:

“RGB is well tolerated and produces excellent weight loss in patients younger than 18 years with 10-year follow-up… Well-designed prospective studies are just emerging to better define the place for adolescent bariatric surgery.”

This statement is based on eight publications of which six are retrospective studies, each with less than 35 participants and most with limited follow-up. Two of the supporting articles are opinion papers.

Endocrine Society

In 2008 the Endocrine Society\(^{[192]}\) published clinical guidelines on the, “Prevention and Treatment of Pediatric Obesity”, which utilized the GRADE\(^{[193]}\) system to describe the quality of evidence and the strength of recommendations. The term ‘recommend’ was used for strong recommendations and the term ‘suggest’ for weak recommendations. Ultimately, the Endocrine Society’s guidelines are based upon expert opinion. The Endocrine Society suggests that bariatric surgery be considered for adolescents, but only after the following criteria have been met:

- The child has attained Tanner 4 or 5 pubertal development and final or near-final adult height.
- Psychological evaluation confirms the stability and competence of the family unit.
- The patient demonstrates the ability to adhere to the principles of healthy dietary and activity habits.

Institute for Clinical Systems Improvement

October 1, 2017  

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage.  
Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
In 2011, the Institute for Clinical Systems Improvement (ICSI)\footnote{194} published an information guideline for health professionals addressing the prevention and management of obesity in mature and adolescent adults. The group notes a limited number of randomized trials with long-term follow-up regarding the various bariatric procedures in adolescents. ICSI concluded that bariatric surgery in adolescents is highly controversial and should be carried out on a case-by-case basis at a high volume center. This statement, however, is based upon evidence from a randomized controlled trial of 80 adults.

In 2013, ICSI published updated guidelines regarding the prevention and management of obesity for children and adolescents.\footnote{195} The group noted that, “there is limited information on the long-term efficacy and safety of bariatric surgery in children and adolescents.” However, ICSI concluded that bariatric surgery may be considered at centers of excellence when specific criteria where met and should not be considered in preadolescent children. These guidelines are primarily based upon review articles and consensus opinion.

National Heart, Lung and Blood Institute

In 2011, National Heart, Lung and Blood Institute (NHLBI)\footnote{196} published guidelines regarding cardiovascular health and risk reduction in overweight and obese children and adolescents which indicated bariatric surgery may be considered:

“For adolescents with BMI far above 35 kg/m² and associated comorbidities, bariatric surgery on a research protocol, in conjunction with a comprehensive lifestyle weight loss program, improved weight loss, BMI, and other outcomes—such as IR, glucose tolerance, and cardiovascular (CV) measures—in a small case series.”

This guideline is based on a Grade D recommendation which is defined as, “Expert opinion, case reports, or reasoning from first principles (bench research or animal studies).”

**Conclusion**

Despite evidence which suggest bariatric surgery may provide the benefits of weight reduction and improved comorbidities compared to non-surgical treatments in the obese children and adolescents, long-term data regarding the life-long impact of bariatric surgery on physical growth, nutrition status, weight loss, resolution of obesity-related comorbidities and long-term survival is lacking. Therefore, the efficacy of bariatric surgery in patients younger than 18 years of age is undetermined.

**Gastroesophageal Reflux Disease (GERD)**

**Systematic Review**

In 2016, Oor and colleagues reported results from a systematic review and meta-analysis of studies reporting prevalence of GERD symptoms, the use of anti-reflux medication, and/or outcome of esophageal function tests before and after laparoscopic sleeve gastrectomy (LSG) in patients with a BMI of more than 35.\footnote{197} Pooled data from seven studies using validated symptom questionnaires for new-onset of GERD symptoms resulted in a 20% incidence following LSG (follow-up time ranging from one- to 60-months). There was heterogeneity amongst these studies ($I^2=68\%$). For difference in prevalence of GERD before and after LSG, the pooled risk difference was found to be 4.3%; with heterogeneity present ($I^2=89\%$). Of the 24 studies reviewed, the authors found new-onset GERD symptom incidence to range from zero to 34.9%. The authors therefore concluded that LSG could
induce serious GERD symptoms in patients with no preoperative GERD complaints. The heterogeneity found in analyses may be due to a lack of a standardized approach to LSG, as well has the variability in follow-up length. The authors also noted that range in prevalence of GERD symptoms may be in part due to the variability in reported preoperative BMI, as the LSG will be a more technically challenging procedure in those with a BMI of 60 kg/m² versus those with a BMI of 40 kg/m².

Li and colleagues (2016) conducted a systematic review and meta-analysis comparing Roux-en-Y gastric bypass (LRYGB) with LSG for treating morbid obesity.[198] Randomized controlled trials and nonrandomized studies were included. Amongst five studies that reported GERD resolution post-operation (147 in the LRYGB group and 93 in the LSG group), symptoms resolved significantly more after LRYGB as compared to LSG (OR = 8.99, 95% CI 4.77-16.95). Heterogeneity was not detected between these groups ($I^2 = 48\%$ $P=0.12$).

Nonrandomized Studies

Several nonrandomized studies have retrospectively reviewed weight reduction and GERD symptoms following Roux-en-Y gastric bypass surgery for treatment of morbid obesity.[199-204] Authors have reported reduction in self-reported GERD symptoms, prescribed medications, and weight loss. As demonstrated in small case series, in combination with takedown of fundoplication, Roux-en-Y gastric bypass for morbid obesity has been effective in weight reduction as well as self-reported GERD symptom improvement.[202,203] Evidence regarding high incidence of GERD following laparoscopic adjustable gastric banding and laparoscopic sleeve gastrectomy makes Roux-en-Y gastric bypass the ideal procedure in the presence of already existing reflux symptoms.[43,75,205]

Clinical Practice Guidelines

The Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) clinical practice guidelines for the surgical treatment of GERD (2010) state the following:[206]

Due to concerns for higher failure rates after fundoplication in the morbidly obese patient (BMI >35 kg/m²) and the inability of fundoplication to address the underlying problem (obesity) and its associated comorbidities, gastric bypass should be the procedure of choice when treating GERD in this patient group (Grade B). The benefits in patients with BMI > 30 is less clear and needs further study.

Conclusion

Systematic review of GERD symptoms following laparoscopic sleeve gastrectomy (LSG) as a treatment for morbid obesity is limited by heterogeneity in the technical approach to the procedure, therefore presenting statistical challenges to analyzing pooled results. In comparing LSG with Roux-en-Y gastric bypass (RYGB) directly, GERD symptoms resolve significantly more post-RYGB as compared to LSG. In the presence of GERD, the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) clinical practice guidelines state that gastric bypass is the procedure of choice in patients who are morbidly obese. In those who are not morbidly obese, evidence does not indicate that bariatric surgery is an appropriate treatment for GERD, and SAGES states this is an area in need of further study.

Safety of Bariatric Surgery

General Surgical Risks
Bariatric procedures are associated with all the potential risks of any major abdominal surgical procedure including but not limited to:

- Bleeding
- Death
- Infection
- Injury to internal organs or gastrointestinal tract
- Thromboembolic complications

**Procedure-Specific Surgical Risks**

The following table summarizes the most common procedure-specific risks. However, other adverse events are also possible.
<table>
<thead>
<tr>
<th>Procedure</th>
<th>Complications</th>
</tr>
</thead>
</table>
| RYGBP[3,207,208] | - Cholecystitis  
- Depression  
- Dilated stomach pouch  
- Dumping syndrome†  
- Gastritis  
- Leaks or obstructions at the anastomotic site  
- Marginal ulcer  
- Reoperations†††  
- Staple line failure  
- Vitamin/mineral deficiencies (iron, folate, B₁₂)  
- Kidney stones |
| LL-RYGBP[3] | - All RYGBP risks  
- Additional unknown risks associated with the greater bypass of the small intestine and consequent increase in malabsorption†† |
| BPD/BPD-DS[3,11,207] | - Dilated stomach pouch  
- Gastric obstruction  
- GERD  
- Leaks or stenoses at anastomotic sites  
- Malnutrition and/or vitamin deficiencies  
- Nausea/vomiting  
- Wound dehiscence  
- Abscesses  
- Frequent vomiting  
- Gastric fistulas  
- GERD  
- Leaking from the stomach pouch  
- Reoperations††† |
- Dilated stomach pouch  
- Marginal ulcer  
- Reoperations†††  
- Vitamin/mineral deficiency |
| LAGB[87,207] | - Bile reflux  
- Gastrojejunostomy leak  
- Marginal ulcer  
- Reoperations†††  
- Vitamin/mineral deficiency |
| MGB[99] | - Bile reflux  
- Gastrojejunostomy leak  
- Marginal ulcer  
- Reoperations†††  
- Vitamin/mineral deficiency |

* The safety concerns are specific to the endoluminal procedure performed:  
  - Transoral circular stapler (SurgASSIST®)[212]:  
    - Bowel obstruction  
    - Intra-abdominal adhesions  
  - Duedenal-jejunal bypass sleeve (DJBS)[125]:  
    - Abdominal pain  
    - Implant site inflammation  
    - Nausea and vomiting  
  - TOGa system endoscopic stapling:[126]:  
    - Nausea  
    - Vomiting  
    - Pain  
    - Transient dysphagia

† Abdominal pain, diarrhea, and/or vomiting shortly after eating due to reduced transit time in the intestine;  
††The evidence, especially from the studies with long-term follow-up, is limited and not much is known about the long-term complications of LL-RYGBP;  
†††Due to insufficient weight loss or technical issues;
**Summary**

Roux-en-Y Gastric Bypass (RYGBP), Adjustable Gastric Banding (AGB), and Sleeve Gastrectomy (SG)

Roux-en-Y gastric bypass is well established in clinical practice, is the most studied bariatric procedure in the published literature, and is used as the gold standard against which other procedures are measured. Adjustable gastric banding is reversible, the least invasive of all bariatric procedures, and has minimal complications. Sleeve gastrectomy as a stand-alone procedure gained acceptance in clinical practice despite the lack of research. Sleeve gastrectomy offers an alternative to adjustable gastric banding with potentially greater weight loss and fewer complications. Sleeve gastrectomy and adjustable gastric banding are associated with significantly more gastroesophageal reflux than Roux-en-Y gastric bypass. Neither procedure should be performed in the presence of gastroesophageal reflux disease, or in combination with takedown of fundoplication. Therefore, Roux-en-Y gastric bypass, adjustable gastric banding, and Sleeve gastrectomy may be considered medically necessary in the treatment of morbid obesity when policy criteria are met.

There is not enough research to show that any of the following procedures improves health outcomes. Therefore, Roux-en-Y gastric bypass, adjustable gastric banding, and sleeve gastrectomy are considered investigational for the treatment of any condition other than morbid obesity, including, but not limited to gastroesophageal reflux disease.

There is not enough research to show that any of the following procedures improves health outcomes. Therefore, the use of distal, partial (not including sleeve gastrectomy) or complete gastrectomy with or without gastroduodenostomy, gastrojejunostomy, or Roux-en-Y reconstruction, are considered investigational as a treatment of obesity.

Mini-gastric bypass, distal gastric bypass, biliopancreatic bypass, biliopancreatic bypass with duodenal switch, and laparoscopic duodenal switch with single anastomosis

There is not enough research for these procedures on health outcomes. Therefore, mini-gastric bypass, distal gastric bypass, biliopancreatic bypass, biliopancreatic bypass with duodenal switch, and laparoscopic duodenal switch with single anastomosis are considered investigational for the treatment of morbid obesity, gastroesophageal reflux disease or any other condition.

**Hiatal Hernia Repair**

There is not enough research regarding the use of hiatal hernia repair as an independent treatment of obesity. In addition, no evidence-based clinical practice guidelines were identified which addressed the use of hiatal hernia repair as a treatment of obesity. Therefore hiatal hernia repair is considered investigational as an independent treatment of obesity.

**Vertical Banded Gastroplasty**

Due to insufficient weight loss and high reoperation rates, vertical banded gastroplasty is no longer considered a standard of care and is therefore considered not medically necessary.

**Endoscopic Bariatric Procedures**

There is not enough evidence to establish the safety and efficacy of any endoscopic bariatric procedure.
Therefore, endoscopic bariatric procedures are considered investigational for all indications.

**Laparoscopic Gastric Plication**

There is not enough evidence to establish the safety and efficacy of any laparoscopic gastric plication bariatric procedure. Therefore, laparoscopic gastric plication procedures are considered investigational for all indications.

**Revision Bariatric Surgical Procedures**

Research regarding reoperation of a primary bariatric surgery is limited to noncomparative studies without long-term outcome data. In addition, current research shows that the complication and mortality rate is slightly higher in cases of reoperation. However, reoperation appears to be beneficial for patients with serious complications related to the primary bariatric surgery and may be considered medically necessary when criteria are met.

Research regarding the revision or removal of an adjustable gastric band is limited to noncomparative studies with short-term follow-up. These studies suggest band removal or revision is associated with improvement in band related complications. In addition, studies indicate gastric bypass is the preferred secondary procedure in cases of adjustable band conversion as bypass is associated with fewer complications and lower mortality rates compared to sleeve gastrectomy. Therefore, adjustable gastric band removal and/or conversion to gastric bypass may be considered medically necessary when criteria are met.

The research is insufficient to determine the safety or efficacy of all other bariatric surgery reoperations or revisions; therefore, reoperations or revisions are considered not medically necessary when criteria are not met.

**Two-staged Bariatric Procedures**

There is not enough research to establish the safety and efficacy of any two-stage bariatric procedure. Therefore, two-stage bariatric procedures are considered investigational for all indications.

**Adolescent and Pediatric Bariatric Surgery**

Research for the safety and effectiveness of bariatric surgery as a treatment for obesity in patients younger than 18 years of age is of limited quality. Studies mostly report short-term outcomes, and though there are few studies with longer follow-up, researchers and clinical practice guidelines state there is still a need for additional high-quality studies. Such trials would evaluate the life-long impact of bariatric surgery on physical growth, nutrition status, weight loss, resolution of obesity-related comorbidities and overall survival in this population. Therefore, bariatric procedures in patients younger than 18 years of age are considered not medically necessary.

**Bariatric Surgery in Patients with Diabetes with BMI < 35kg/m²**

Research for the safety and effectiveness of bariatric procedures as a treatment for diabetes in patients with a BMI < 35 kg/m² is limited by small study sizes and short-term follow-up. High-quality studies that include long-term follow-up are needed in order to evaluate the impact of bariatric surgery on health outcomes in this population. In addition, the majority of evidence-based clinical practice guidelines do
not recommended bariatric surgery in diabetic patients with a BMI < 35 kg/m². Therefore, bariatric procedures in diabetic patients with a BMI < 35 kg/m² are considered not medically necessary.

REFERENCES


44. Moon Han, S, Kim, WW, Oh, JH. Results of laparoscopic sleeve gastrectomy (LSG) at 1 year in morbidly obese Korean patients. *Obes Surg.* 2005 Nov-Dec;15(10):1469-75. PMID: 16354529


86. TEC Assessment 2012. "Laparoscopic Adjustable Gastric Banding In Patients With Body Mass Index Less Than 35 kg/m2 With Weight-Related Comorbidity." BlueCross BlueShield Association Technology Evaluation Center, Vol. 27 Tab TBA.


143. Ahluwalia, JS, Kuo, HC, Chang, PC, Sun, PL, Hung, KC, Huang, CK. Standardized Technique of Laparoscopic Adjustable Gastric Banded Plication with 4-Year Results. *Obes Surg.* 2015 Sep;25(9):1756-7. PMID: 26130177


CROSS REFERENCES

Gastric Electrical Stimulation, Surgery, Policy No. 111

Gastric Reflux Surgery, Surgery, Policy No. 186
<table>
<thead>
<tr>
<th>CODES</th>
<th>NUMBER</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>43631</td>
<td>Gastrectomy, partial, distal; with gastroduodenostomy</td>
</tr>
<tr>
<td></td>
<td>43632</td>
<td>;with gastrojejunostomy</td>
</tr>
<tr>
<td></td>
<td>43633</td>
<td>;with roux-en-Y reconstruction</td>
</tr>
<tr>
<td></td>
<td>43634</td>
<td>;with formation of intestinal pouch</td>
</tr>
<tr>
<td></td>
<td>43644</td>
<td>Laparoscopy, surgical, gastric restrictive procedure; with gastric bypass and Roux-en-Y gastroenterostomy (roux limb 150 cm or less)</td>
</tr>
<tr>
<td></td>
<td>43645</td>
<td>Laparoscopy, surgical, gastric restrictive procedure; with gastric bypass and small intestine reconstruction to limit absorption</td>
</tr>
<tr>
<td></td>
<td>43649</td>
<td>Unlisted laparoscopy procedure, stomach</td>
</tr>
<tr>
<td></td>
<td>43770</td>
<td>Laparoscopy, surgical, gastric restrictive procedure; placement of adjustable gastric restrictive device (gastric band and subcutaneous port components)</td>
</tr>
<tr>
<td></td>
<td>43771</td>
<td>Laparoscopy, surgical, gastric restrictive procedure; revision of adjustable gastric restrictive device component only</td>
</tr>
<tr>
<td></td>
<td>43772</td>
<td>Laparoscopy, surgical, gastric restrictive procedure; removal of adjustable gastric restrictive device component only</td>
</tr>
<tr>
<td></td>
<td>43773</td>
<td>Laparoscopy, surgical, gastric restrictive procedure; removal and replacement of adjustable gastric restrictive device component only</td>
</tr>
<tr>
<td></td>
<td>43774</td>
<td>Laparoscopy, surgical, gastric restrictive procedure; removal of adjustable gastric restrictive device and subcutaneous port components</td>
</tr>
<tr>
<td></td>
<td>43775</td>
<td>Laparoscopy, surgical, gastric restrictive procedure; longitudinal gastrectomy (ie, sleeve gastrectomy)</td>
</tr>
<tr>
<td></td>
<td>43842</td>
<td>Gastric restrictive procedure, without gastric bypass, for morbid obesity; vertical banded gastroplasty</td>
</tr>
<tr>
<td></td>
<td>43843</td>
<td>Gastric restrictive procedure, without gastric bypass, for morbid obesity; other than vertical banded gastroplasty</td>
</tr>
<tr>
<td></td>
<td>43845</td>
<td>Gastric restrictive procedure with partial gastrectomy, pylorus-preserving duodenoileostomy and ileoileostomy (50 to 100 cm common channel) to limit absorption (biliopancreatic diversion with duodenal switch)</td>
</tr>
<tr>
<td></td>
<td>43846</td>
<td>Gastric restrictive procedure, with gastric bypass for morbid obesity; with short limb (150 cm or less) Roux-en-Y gastroenterostomy</td>
</tr>
<tr>
<td>CODES</td>
<td>NUMBER</td>
<td>DESCRIPTION</td>
</tr>
<tr>
<td>-------</td>
<td>--------</td>
<td>-------------</td>
</tr>
<tr>
<td></td>
<td>43847</td>
<td>Gastric restrictive procedure, with gastric bypass for morbid obesity; with small intestine reconstruction to limit absorption</td>
</tr>
<tr>
<td></td>
<td>43848</td>
<td>Revision, open, of gastric restrictive procedure for morbid obesity, other than adjustable gastric restrictive device (separate procedure)</td>
</tr>
<tr>
<td></td>
<td>43860</td>
<td>Revision of gastrojejunostomy with reconstruction, with or without partial gastrectomy or intestine resection; without vagotomy</td>
</tr>
<tr>
<td></td>
<td>43865</td>
<td>; with vagotomy</td>
</tr>
<tr>
<td></td>
<td>43866</td>
<td>Gastric restrictive procedure, open; revision of subcutaneous port component only</td>
</tr>
<tr>
<td></td>
<td>43867</td>
<td>Gastric restrictive procedure, open; removal of subcutaneous port component only</td>
</tr>
<tr>
<td></td>
<td>43868</td>
<td>Gastric restrictive procedure, open; removal and replacement of subcutaneous port component only</td>
</tr>
<tr>
<td>HCPCS</td>
<td>S2083</td>
<td>Adjustment of gastric band diameter via subcutaneous port by injection or aspiration of saline</td>
</tr>
</tbody>
</table>
**Cochlear Implant**

**Effective:** October 1, 2017

**Next Review:** September 2018  
**Last Review:** September 2017

---

**IMPORTANT REMINDER**

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

---

**DESCRIPTION**

A cochlear implant is a device for treatment of severe-to-profound hearing loss in individuals who only receive limited benefit from amplification with hearing aids.

---

**MEDICAL POLICY CRITERIA**

**Notes:**

- This policy does not apply to surgically anchored bone conduction hearing aids or externally worn air conduction hearing aids. Cochlear implants are not hearing aids. While hearing aids function by amplifying sound, cochlear implants replace the functions of an absent or nonfunctioning cochlea.
- This policy does not address the use of the Nucleus® 24 Auditory Brain Stem Implant, which is designed to restore hearing in patients with neurofibromatosis who are deaf secondary to removal of bilateral acoustic neuromas.
- Hybrid cochlear implant/hearing aid systems are devices that include a hearing aid integrated into the external sound processor of the cochlear implant. If hearing aid components of such systems are billed separately, there may be specific member benefit language addressing coverage of hearing aids that would be applicable. Contract language takes precedence over medical policy.
- Repeat hearing tests or trials of hearing aids are not necessary for patients who have previously met criteria I. and II. as it is unlikely that natural hearing or the benefit from...
hearing aids will improve significantly over time.

I. **Unilateral or bilateral implantation of FDA approved (i.e., PMA or 510k only) cochlear implants, other than cochlear implant/hearing aid hybrid devices, and associated aural rehabilitation may be considered medically necessary when both of the following criteria (A. and B.) are met:

   A. Patients 12 months or older that meet either of the following criteria:
      1. Patients diagnosed with enlarged vestibular aqueduct (EVA) (greater than 1mm at the midpoint), as evidenced by MRI or CT imaging; or
      2. Patients with both of the following (a. and b.):
         a. Bilateral severe to profound pre- or postlingual (sensorineural) hearing loss, defined as a hearing threshold of pure-tone average of 70 decibels (dB) or greater hearing loss at 500 Hz (hertz), 1000 Hz and 2000 Hz; and
         b. Limited or no benefit from hearing aids (defined below) unless hearing aids are unreasonable.
            i. Adults: Scores less than or equal to 50 percent correct on tape recorded sets of open-set sentence recognition in the ear to be implanted
            ii. Children: Failure to develop basic auditory skills, and in older children, less than or equal to 30 percent correct on open-set tests

   B. Patients do not have any of the following contraindications:
      1. Deafness due to lesions of the acoustic nerve (eighth cranial nerve), central auditory pathways, or brain stem in the implanted ear
      2. Active or chronic infections of the external or middle ear and mastoid cavity in the implanted ear, including but not limited to otitis media.
      3. Tympanic membrane perforation
      4. Radiographic evidence of absent cochlear development in the implanted ear
      5. Inability or lack of willingness to participate in post-implantation aural rehabilitation.

II. **Unilateral implantation of FDA approved (i.e., PMA or 510k only) hybrid cochlear implant/hearing aid systems that include the hearing aid integrated into the external sound processor of the cochlear implant, may be considered medically necessary when all of the following criteria are met (A. – E.):

   A. Age 18 years or older; and
   B. Bilateral severe to profound pre- or postlingual (sensorineural) hearing loss, defined as a hearing threshold of pure-tone average of 70 decibels (dB) or greater hearing loss at 500 Hz (hertz), 1000 Hz and 2000 Hz; and
   C. Limited or no benefit from hearing aids unless hearing aids are unreasonable, defined as scores less than 50 percent correct on tape recorded sets of open-set sentence recognition in the ear selected for implantation; and
   D. Meets all of the following hearing thresholds:

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage.

Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
1. Low frequency hearing thresholds no poorer than 60 dB hearing level up to and including 500 Hz (averaged over 125, 250, and 500 Hz) in the ear selected for implantation; and

2. Severe to profound mid-to-high frequency hearing loss (threshold average of 2000, 3000, and 4000 Hz greater than or equal to 75 dB hearing level) in the ear selected for implantation; and

3. Moderately severe to profound mid-to-high frequency hearing loss (threshold average of 2000, 3000, and 4000 Hz less than or equal to 60 dB hearing level) in the contralateral ear; and

4. Aided consonant-nucleus-consonant word recognition score from 10 percent to 60 percent in the ear selected for implantation in the preoperative aided condition and in the contralateral ear will be equal to or better than that of the ear selected for implantation but not more than 80 percent correct.

E. Does not have any of the following contraindications:
   1. Deafness due to lesions of the acoustic nerve (eighth cranial nerve), central auditory pathways, or brain stem in the implanted ear
   2. Active or chronic infections of the external or middle ear and mastoid cavity in the implanted ear, including but not limited to otitis media.
   3. Tympanic membrane perforation
   4. Radiographic evidence of absent cochlear development in the implanted ear
   5. Inability or lack of willingness to participate in post-implantation aural rehabilitation.
   6. A duration of severe to profound hearing loss of 30 years or greater.

III. Implant replacement with a next-generation device may be considered medically necessary only in the small subset of patients whose response to existing components is inadequate to the point of interfering with activities of daily living, which would include school and work.

IV. Implant replacement with a next-generation device is considered not medically necessary when criterion III. is not met.

V. Implantation of cochlear implants is considered not medically necessary when criteria I. or II. above is not met.

VI. Upgrades of an existing, functioning external system to achieve aesthetic improvement, such as smaller profile components, or a switch from a body-worn external sound processor to a behind-the-ear (BTE) model are considered not medically necessary.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

CROSS REFERENCES
1. Implantable Bone Conduction and Bone-Anchored Hearing Aids, Surgery, Policy No. 121

BACKGROUND

Back to Top
A cochlear implant provides direct electrical stimulation to the auditory nerve, bypassing the usual transducer cells that are absent or nonfunctional in deaf cochlea. The basic components of a cochlear implant include both external and internal components. The external components include a microphone, an external sound processor, and an external transmitter. The internal components are implanted surgically and include an internal receiver implanted within the temporal bone, and an electrode array that extends from the receiver into the cochlea through a surgically created opening in the round window of the middle ear.

Sounds that are picked up by the microphone are carried to the external signal processor, which transforms sound into coded signals that are then transmitted transcutaneously to the implanted internal receiver. The receiver converts the incoming signals to electrical impulses that are then conveyed to the electrode array, ultimately resulting in stimulation of the auditory nerve.

Hearing loss is rated on a scale based on the threshold of hearing. Severe hearing loss is defined as a bilateral hearing threshold of 70-90 decibels (dB) and profound hearing loss is defined as a hearing threshold of 90 dB and above.

A post-cochlear implant rehabilitation program is necessary to achieve benefit from the cochlear implant. The rehabilitation program includes development of skills in understanding running speech, recognition of consonants and vowels, and tests of speech perception ability.

**REGULATORY STATUS**

Note: Full FDA approval includes only Premarket Approval (PMA) and 510k approval. Devices with Investigational Device Exemption (IDE) or Humanitarian Device Exemption (HDE) are not considered fully FDA approved.

Several cochlear implants are commercially available in the United States. The FDA-labeled indications for currently marketed electrode arrays are summarized in the table below. Over the years, subsequent generations of the various components of the devices have been FDA approved, focusing on improved electrode design and speech-processing capabilities. Furthermore, smaller devices and the accumulating experience in children have resulted in broadening of the selection criteria to include children as young as 12 months.

<table>
<thead>
<tr>
<th>Manufacturer and FDA approved Cochlear Implants</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Advanced Bionics®</strong></td>
<td></td>
</tr>
<tr>
<td>• HiResolution Bionic Ear System (HiRes 90K*)</td>
<td>Adults:</td>
</tr>
<tr>
<td>• Predecessors:</td>
<td></td>
</tr>
<tr>
<td>o Clarion Multi-Strategy</td>
<td>• ≥ 18 years of age</td>
</tr>
<tr>
<td>o HiFocus CII Bionic Ear</td>
<td>• Post-lingual onset of severe to profound bilateral sensorineural hearing loss [≥70 decibels (dBs)]</td>
</tr>
<tr>
<td></td>
<td>• Limited benefit from appropriately fitted hearing aids, defined as scoring ≤ 50% on a test of open-set Hearing in Noise Test (HINT) sentence recognition</td>
</tr>
<tr>
<td></td>
<td>Children:</td>
</tr>
<tr>
<td></td>
<td>• 12 months to 17 years of age</td>
</tr>
<tr>
<td></td>
<td>• Profound bilateral sensorineural deafness (&gt;90dB)</td>
</tr>
<tr>
<td></td>
<td>• Use of appropriately fitted hearing aids for at least 6 months in children 2 to 17 years of age or at least 3 months in children 12 to 23 months of age.</td>
</tr>
</tbody>
</table>
Lack of benefit in children <4 years of age is defined as a failure to reach developmentally-appropriate auditory milestones (e.g., spontaneous response to name in quiet or to environmental sounds) measured using the Infant-Toddler Meaningful Auditory Integration Scale or Meaningful Auditory Integration Scale or < 20% correct on a simple open-set word recognition test (Multisyllabic Lexical Neighborhood Test) administered using monitored live voice [70 dB SPL (sound pressure level)]

Lack of hearing aid benefit in children >4 years of age is defined as scoring < 12% on a difficult open-set word recognition test (Phonetically Balanced-Kindergarten Test) or < 30% on an open-set sentence test (HINT for Children) administered using recorded materials in the soundfield (70 dB SPL)

<table>
<thead>
<tr>
<th>Cochlear®</th>
<th>Adults:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Kanso™</td>
<td>≥ 18 years old</td>
</tr>
<tr>
<td>• Nucleus® 6</td>
<td>Pre- or post-lingual onset of moderate to profound bilateral sensorineural hearing loss</td>
</tr>
<tr>
<td>• Nucleus® 5*</td>
<td>≤50% sentence recognition in the ear to be implanted</td>
</tr>
<tr>
<td>• Nucleus Freedom</td>
<td>≤60% sentence recognition in the opposite ear or binaurally</td>
</tr>
<tr>
<td>• Predecessors:</td>
<td>Children 12 months to 24 months:</td>
</tr>
<tr>
<td>o Nucleus 22, 24</td>
<td>Profound sensorineural hearing loss bilaterally</td>
</tr>
<tr>
<td></td>
<td>Limited benefit from appropriate binaural hearing aids</td>
</tr>
<tr>
<td></td>
<td>Lack of progress in the development of auditory skills</td>
</tr>
<tr>
<td></td>
<td>Children 25 months to 17 years 11 months:</td>
</tr>
<tr>
<td></td>
<td>Severe to profound bilateral sensorineural hearing loss</td>
</tr>
<tr>
<td></td>
<td>Multi-syllabic Lexical Neighborhood Test (MLNT) scores of ≤30% in best-aided condition in children 25 months to 4 years 11 months</td>
</tr>
<tr>
<td></td>
<td>Lexical Neighborhood Test (LNT) scores of ≤30% in best-aided condition in children 5 years to 17 years and 11 months</td>
</tr>
<tr>
<td></td>
<td>Lack of progress in the development of auditory skills</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Med El®</th>
<th>Adults:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Maestro (Concerto, Sonata or Pulsar)</td>
<td>≥ 18 years old</td>
</tr>
<tr>
<td>• Predecessor:</td>
<td>Severe to profound bilateral sensorineural hearing loss (≥70dB)</td>
</tr>
<tr>
<td>o Combi 40+</td>
<td>≤40% correct Hearing in Noise test (HINT) sentences with best-sided listening condition</td>
</tr>
<tr>
<td></td>
<td>Children:</td>
</tr>
<tr>
<td></td>
<td>12 months to 18 years with profound sensorineural hearing loss (≥90dB)</td>
</tr>
<tr>
<td></td>
<td>In younger children, little or no benefit is defined by lack of progress in the development of simple auditory skills with hearing aids over a 3-6 month period</td>
</tr>
<tr>
<td></td>
<td>In older children, lack of aided benefit is defined as &lt;20% correct on the MLNT or LNT depending upon the child's cognitive ability and linguistic skills</td>
</tr>
</tbody>
</table>

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. 
Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
A 3-6 month trial with hearing aids is required if not previously experienced

<table>
<thead>
<tr>
<th>Cochlear®</th>
<th>Adults:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Nucleus® Hybrid™ L24 Cochlear Implant (Nucleus 6)</td>
<td>• ≥ 18 years old</td>
</tr>
<tr>
<td></td>
<td>• Residual low-frequency hearing sensitivity</td>
</tr>
<tr>
<td></td>
<td>• Severe to profound high-frequency sensorineural hearing loss</td>
</tr>
<tr>
<td></td>
<td>• Limited benefit from appropriately fit bilateral hearing aids</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Med El®</th>
<th>Adults:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Med EL EAS™</td>
<td>• ≥ 18 years old</td>
</tr>
<tr>
<td></td>
<td>• Residual low-frequency hearing sensitivity</td>
</tr>
<tr>
<td></td>
<td>• Severe to profound high-frequency sensorineural hearing loss</td>
</tr>
<tr>
<td></td>
<td>• Candidates should go through a suitable hearing aid trial, unless already appropriately fit with hearing aids</td>
</tr>
</tbody>
</table>

*Note: Cochlear, Ltd. voluntarily recalled the Nucleus CI500 range in September 2011 for device malfunction in the CI512 implant. The external Nucleus 5 sound processor is not a part of the recall. Advanced Bionics HiRes90K was voluntarily recalled in November 2010 and given FDA-approval for re-entry to market the device in September 2011.

While cochlear implants have typically been used mono laterally, in recent years, interest in bilateral cochlear implantation has arisen. The proposed benefits of bilateral cochlear implants are to improve understanding of speech in noise and localization of sounds. Improvements in speech intelligibility may occur with bilateral cochlear implants through binaural summation; i.e., signal processing of sound input from two sides may provide a better representation of sound and allow one to separate out noise from speech. Speech intelligibility and localization of sound or spatial hearing may also be improved with head shadow and squelch effects, i.e., the ear that is closest to the noise will be received at a different frequency and with different intensity, allowing one to sort out noise and identify the direction of sound. Bilateral cochlear implantation may be performed independently with separate implants and speech processors in each ear or with a single processor. However, no single processor for bilateral cochlear implantation has been FDA approved for use in the United States. In addition, single processors do not provide binaural benefit and may impair localization and increase the signal to noise ratio received by the cochlear implant.

In March 2014, FDA approved the Nucleus® Hybrid™ L24 Cochlear Implant System (Cochlear Corporation) through the premarket approval process.[1] This system is a hybrid cochlear implant and hearing aid, with the hearing aid integrated into the external sound processor of the cochlear implant. It is indicated for unilateral use in patients aged 18 years and older who have residual low-frequency hearing sensitivity and severe to profound high-frequency sensorineural hearing loss, and who obtain limited benefit from appropriately fit bilateral hearing aid. The electrode array inserted into the cochlea is shorter than conventional cochlear implants. According to the FDA’s premarket approval notification, labeled indications for the device include:

- Preoperative hearing in the range from normal to moderate hearing loss (HL) in the low frequencies (thresholds no poorer than 60 dB HL up to and including 500 Hz).
- Preoperative hearing with severe to profound mid- to high-frequency hearing loss (threshold average of 2000, 3000, and 4000 Hz ≥75 dB HL) in the ear to be implanted.
- Preoperative hearing with moderately severe to profound mid- to high-frequency hearing loss (threshold average of 2000, 3000, and 4000 Hz ≥60 dB HL) in the contralateral ear.
- Consonant-Nucleus-Consonant (CNC) word recognition score between 10% to 60% ( inclusively) in the ear to be implanted in the preoperative aided condition and in the contralateral ear equal to or better than that of the ear to be implanted but not more than 80% correct.

In September 2016, FDA approved the Med EL EAS™ (Electric Acoustic Stimulation) Hearing Implant System (Med EL Corp.).[2] This system is a hybrid cochlear implant and hearing aid, with the hearing aid integrated into the external sound processor of the cochlear implant. It is the combination of the SYNCHRONY cochlear implant and the SONNET EAS audio processor. According to the FDA’s premarket approval notification:[3]

The MED-EL EAS System is indicated for partially deaf individuals aged 18 years and older who have residual hearing sensitivity in the low frequencies sloping to a severe/profound sensorineural hearing loss in the mid to high frequencies, and who obtain minimal benefit from conventional acoustic amplification. Typical preoperative hearing of candidates ranges from normal hearing to moderate sensorineural hearing loss in the low frequencies (thresholds no poorer than 65 dB HL up to and including 500 Hz) with severe to profound mid- to high-frequency hearing loss (no better than 70 dB HL at 2000 Hz and above) in the ear to be implanted. For the non-implanted ear, thresholds may be worse than the criteria for the implanted ear, but may not be better. The CNC word recognition score in quiet in the best-aided condition will be 60% or less, in the ear to be implanted and in the contralateral ear. Prospective candidates should go through a suitable hearing aid trial, unless already appropriately fit with hearing aids.

**EVIDENCE SUMMARY**

Cochlear implants (CI) are recognized effective treatment of sensorineural deafness in select patient, as noted in a 1995 National Institutes of Health Consensus Development conference, which offered the following conclusions:[4]

- Cochlear implantation has a profound impact on hearing and speech reception in postlingually deafened adults with positive impacts on psychological and social functioning.
- The results are more variable in children. Benefits are not realized immediately but rather are manifested over time, with some children continuing to show improvement over several years.
- Prelingually deafened adults may also benefit, although to a lesser extent than postlingually deafened adults. These individuals achieve minimal improvement in speech recognition skills. However, other basic benefits, such as improved sound awareness, may meet safety needs.
- Training and educational intervention are fundamental for optimal post implant benefit.
- Cochlear implants in children under two years old are complicated by the inability to perform detailed assessment of hearing and functional communication. However, a younger age of implantation may limit the negative consequences of auditory deprivation and may allow more efficient acquisition of speech and language. Some children with postmeningitis hearing loss have been implanted under the age of two years due to the risk of...
new bone formation associated with meningitis, which may preclude a cochlear implant at a later date.

ENLARGED VESTIBULAR AQUEDUCTS (EVA)

Enlarged vestibular aqueduct (also known as enlarged vestibular aqueduct syndrome (EVAS), large vestibular aqueduct, large vestibular aqueduct syndrome (LVAS), or dilated vestibular aqueduct) is a condition which is associated with childhood hearing loss. According to the NIH National Institute on Deafness and other Communication Disorders (NIDCD), most children with enlarged vestibular aqueducts (EVA) will develop some amount of hearing loss, and approximately 5-15% of children with sensorineural hearing loss (hearing loss caused by damage to sensory cells inside the cochlea) have EVA.

Systematic Reviews

In 2014, Xu conducted a systematic review in Chinese to assess the efficacy and safety of cochlear implantation in deaf patients with inner ear malformations compared to deaf patients with normal inner ear structure, including 11 RTCs (N=655 patients). In terms of postoperative complications, electrode impedance, behavior T-level, hearing abilities and speech discrimination; patients with mixed inner ear malformations, Mondini syndrome or EVA were not significantly different than controls. However, the reviewers concluded that additional larger controlled studies with longer follow-up may help to evaluate the efficacy of cochlear implantation for deaf patients with inner ear malformation more reliably.

In 2012, Pakdaman conducted a systematic review to determine if abnormal cochleovestibular anatomy influences surgical and audiologic outcomes following cochlear implant (CI) surgery in children, including 22 studies. Out of the 311 children included, 89 (29%) were diagnosed with EVA, considered to be a mild/moderate anomaly. Outcomes of CI surgery were analyzed based on the severity of the ear malformation (mild/moderate anomaly versus severe), and subgroup analyses were not performed based on the different malformations observed. The reviewers reported that severe inner ear dysplasia was associated with increased surgical difficulty and lower speech perception.

Nonrandomized Studies

There have been a number of case series and retrospective analyses published on the efficacy of cochlear implants in patients with EVA, all generally reporting an improvement of outcomes including various clinical scores for hearing improvement and scores measuring quality of life. These studies range in size from three to 47 cases. Some of these studies have focused on pediatric patients, while others have included mixed patient populations and have not analyzed pediatric patients from adults in terms of outcomes. Overall, these studies report that outcomes in EVA patients are comparable to cochlear implant patients with no malformations, including similar risk of cerebrospinal fluid (CSF) gusher during cochlear implantation.

There is research indicating that the age of cochlear implantation for patients with EVA affects health outcomes. In 2013, Ko conducted a study to assess health outcomes of Mandarin-speaking patients with EVA after cochlear implantation (CI); to compare their performance with a group of CI users without EVA; to understand the effects of age at implantation and duration of implant use on the CI outcomes. Forty-two patients with EVA participating in this study were divided into two groups: the early group received CI before five years of age and the late group after five years of age. The patients with EVA with more than five years of age...
Implant use (18 cases) achieved a mean score higher than 80% on the most recent speech perception tests and reached the highest level on the CAP/SIR scales. The early group developed speech perception and intelligibility steadily over time, while the late group had a rapid improvement during the first year after implantation. The two groups, regardless of their age at implantation, reached a similar performance level. These patients do not necessarily need to wait until their hearing thresholds are higher than 90 dB HL or PB word score lower than 40% to receive CI. Similar results have been reported in small pediatric case series, indicating that if patients receive cochlear implants prior to becoming severely to profoundly deaf, that residual hearing is preserved.\(^{[8,20]}\)

In contrast to studies reporting favorable outcomes, one small retrospective study performed by Bichy in 2002 that reported better hearing outcomes in patients with EVA using hearing aid than those who had undergone cochlear implantation.\(^{[21]}\) The analysis in this study included 16 children and adults with EVA that had undergone cochlear implantation and 10 children and adults undergoing treatment of progressive or fluctuant sensorineural hearing loss with the use of a hearing aid alone. Although the hearing aid group had a better mean pure-tone average (70.8 dB; SD 24.4) versus (107.0 dB; SD 21.7) for the cochlear implant group, the use of health utility indexes determined that greater net health benefit (including quality of life) was derived from cochlear implantation over hearing aids.

**INFANTS UNDER AGE 12 MONTHS**

Note: FDA approval of cochlear implants (CI) includes patients over 12 months of age; therefore, implantation in infants who are under the age of 12 months is an off-label use of these devices.

The literature review focused on studies comparing the impact on hearing, speech development and recognition, and complication rates of implantation in infants younger than 12 months with those of older age groups. This includes the question of whether any early benefits that may occur in these very young patients later converge with those in older patients.

**Systematic Reviews**

Two systematic reviews were identified that addressed CI in children under 12 months of age. The reviews, summarized below, reported few studies of CI in this age group compared with CI in children over one year of age. Both systematic reviews ranked the available studies as poor to fair due to heterogeneity in study participants and study designs, and high risk for potential bias. In addition, differences in outcomes between the age groups did not reach statistical significance. Therefore, it remains unclear whether the benefits of early cochlear implantation outweigh the risk of surgery and anesthesia in these very young patients.

In 2011 Forli reported similar findings in seven studies comparing CI implanted prior to one year of age with implantations performed after one year of age.\(^{[22]}\) The studies precluded meta-analysis due to heterogeneity of age ranges analyzed and outcomes evaluated. While studies suggested improvements in hearing and communicative outcomes in children receiving implants prior to one year of age, between-group differences did not reach statistical significance. In addition, it is not certain whether any improvements were related to duration of cochlear implant usage rather than age of implantation. Nor is it clear whether any advantages of early implantation are retained over time.
In 2010, Vlastarakos conducted a systematic review of studies on bilateral cochlear implants in a total of 125 children implanted before one year of age.\textsuperscript{[23]} The authors noted that follow-up times ranged from a median duration of 6 to 12 months and, while results seemed to indicate accelerated rates of improvement in implanted infants, the evidence available was limited and of lower quality. Additionally, the lack of reliable outcome measures for infants demonstrated the need for further research before cochlear implantation prior to one year of age becomes widespread.

**Nonrandomized Studies**

A 2017 retrospective study by Kalejaiye assessed surgical complications, operative times, and reoperation rates in 73 patients under one year of age.\textsuperscript{[24]} They compared these patients, identified from the American College of Surgeons National Surgical Quality Improvement Program Pediatric database (2012-2013), with pediatric patients in the database above the age of one. They found that the patients under one year had higher readmission rates (6.9\% vs. 2.7\%) and longer mean operative times (191 minutes vs. 160 minutes), but no significant differences were noted in complication rate, postoperative length of stay, or reoperation rate.

In 2015, Guerzoni conducted a prospective study of 28 children with profound sensorineural hearing loss who were implanted early with cochlear implants (mean age at device activation: 13.3 months).\textsuperscript{[25]} The investigators reported that at one-year follow-up, assertiveness and responsiveness scores were within the normal range of normal-hearing age-matched peers. Age at cochlear implant activation exerted a significant impact, with the highest scores associated to the youngest patients.

In 2011, Colletti reported on the 10-year results comparing 19 children with cochlear implants received between the ages of 2 to 11 months to 21 children implanted between 12-23 months and 33 children implanted between 24-35 months.\textsuperscript{[26]} Within the first six months post-implantation, there was no significant difference among groups in Category of Auditory Performance testing but differences became significantly better in the infant group (early implantation) at the 12 and 36 month testing. Previously, Colletti reported on findings from 13 infants who had implants placed before 12 months.\textsuperscript{[27]} The procedures were performed between 1998 and 2004. In this small study, the rate of receptive language growth for these early implant infants overlapped scores of normal-hearing children. This overlap was not detected for those implanted at 12–23 or 24–36 months.

In 2009 Ching and colleagues published an interim report on early language outcomes of children with cochlear implants.\textsuperscript{[28]} This study evaluated 16 children who had implants before 12 months of age compared to 23 who had implants after 12 months (specific time of implantation was not provided). The preliminary results demonstrated that children who received an implant before 12 months of age developed normal language skills at a rate comparable to normal-hearing children, while those with later implants performed at two standard deviations below normal. The authors noted that these results are preliminary, as there is a need to examine the effect of multiple factors on language outcomes and the rate of language development.

Johr (2008) highlighted the surgical and anesthetic considerations when performing cochlear implant surgery in very young infants.\textsuperscript{[29]} This was an observational study and literature review by pediatricians at a tertiary children’s hospital in Switzerland. Surgical techniques and anesthetic management aspects of elective surgeries in small infants were analyzed in patients younger than one year of age undergoing cochlear implant surgeries. The results
demonstrated that the age of the patient and the pediatric experience of the anesthesiologist, but not the duration of the surgery, are relevant risk factors. The authors concluded, “Further research is needed to provide more conclusive evidence that the performance outcome for children implanted before 12 months of age does not converge with the results of children implanted between 12 and 18 months.”

ADULTS AND CHILDREN OVER AGE 12 MONTHS

Since there is sufficient evidence that bilateral and unilateral cochlear implants are safe and lead to improvements in health outcomes in adults and children over the age of twelve months with bilateral severe to profound pre- or postlingual (sensorineural) hearing loss, the evidence reviewed below will be focused on systematic reviews and randomized studies. Nonrandomized studies will not be described in detail.

Systematic Reviews

The following is a summary of the most recent systematic reviews related to CI. These reviews included a critical analysis of the quality of the included studies. While noting the heterogeneity of the studies, and the potential for bias, these reviews found that the studies consistently reported beneficial outcomes for both bilateral and unilateral CI in select children and adults compared with no hearing devices or with conventional hearing aids.

Adults

In 2013, the authors of the 2011 AHRQ technology assessment reported the following findings of an updated systematic review of studies published through May 2012:[30]

- **Unilateral cochlear implants**

  Sixteen (of 42) studies were of unilateral cochlear implants. Most unilateral implant studies showed a statistically significant improvement in mean speech scores as measured by open-set sentence or multi-syllable word tests. A meta-analysis of four studies revealed a significant improvement in cochlear-implant relevant quality of life (QOL) after unilateral implantation. However, these studies varied in design and there was considerable heterogeneity observed across studies, making it difficult to compare outcomes across studies.

- **Bilateral cochlear implants**

  Thirteen studies reported improvement in communication-related outcomes with bilateral implantation compared with unilateral implantation and additional improvements in sound localization compared with unilateral device use or implantation only. The risk of bias varied from medium to high across studies. Based on results from at least two studies, the QOL outcomes varied across tests after bilateral implantation. A meta-analysis was not performed because of heterogeneity in design between the studies.

In 2012 and 2013 Crathorne and van Schoonhoven, respectively, published updated systematic reviews for the National Institute for Health and Care Excellence (NICE). Included studies were from the U.S. and Europe and compared bilateral with unilateral cochlear implants. In two studies the unilateral implant group also had an acoustic hearing aid for the contralateral ear. Neither systematic review was able to conduct a meta-analysis due to the
heterogeneity of the studies and the level of evidence of the studies which was rated as moderate-to-poor.

In October 2011, Berrettini published results of a systematic review of unilateral and bilateral cochlear implant effectiveness in adults.[31]

- **Unilateral cochlear implants**

  Eight articles on unilateral cochlear implants in advanced age patients were included. All of the studies reported benefits with cochlear implantation despite advanced age at time of implant (age 70 years or older). In six studies, results were not significantly different between younger and older patients. However, two studies reported statistically significant inferior perceptive results (e.g., hearing in noise test and consonant nucleus consonant test) in older patients. This systematic review also examined three studies totaling 56 adults with pre-lingual deafness who received unilateral cochlear implants. The authors concluded unilateral cochlear implants provided hearing and quality-of-life benefits in prelingually deaf patients, but results were variable.

- **Bilateral cochlear implants**

  Thirteen articles on bilateral cochlear implants were reviewed. Sound localization improved with bilateral cochlear implants compared with monaural hearing in six studies. Significant improvements in hearing in noise and in quiet environments with bilateral implants compared with unilateral implants were reported in ten studies and seven studies, respectively. Five of the studies reviewed addressed simultaneous implantation, five studies reviewed sequential implantation, and three studies included a mix of simultaneous and sequential implantation. However, no studies compared simultaneous to sequential bilateral implantation results, and no conclusions could be made on the timing of bilateral cochlear implantation.

In June 2011 the most recent technology assessment, by the Tufts Evidence-based Practice Center for the Agency for Health Care Research and Quality (AHRQ), reported the following findings on the effectiveness of unilateral and bilateral cochlear implants (CIs) in adults:[32]

- **Unilateral cochlear implants**

  The assessment examined 22 studies with 30 or more patients and concluded that, while the studies reviewed were rated as poor to fair quality, unilateral cochlear implants are effective in adults with sensorineural hearing loss. Pre- and post-cochlear implant scores on multi-syllable tests and open-set sentence tests demonstrated significant gains in speech perception regardless of whether a contralateral hearing aid was used along with the cochlear implant. Additionally, the assessment found generic and disease-specific health-related quality of life improved with unilateral cochlear implants. However, the available evidence was insufficient to draw conclusions on improvements in open-set sentence test scores (i.e., >40% and ≤50% or >50% and ≤60%), and any relationship between pre-implantation patient characteristics and outcomes [e.g., age, duration of hearing impairment, Hearing in Noise Test (HINT) scores and pre- or post-linguistic deafness.]
Bilateral cochlear implants

The technology assessment examined 16 studies published since 2004 which were determined to be of fair to moderate quality. The assessment concluded that bilateral cochlear implants provided greater benefits in speech perception test scores, especially in noise, when compared with unilateral cochlear implants with or without contralateral hearing aids. Significant binaural head shadow benefits were noted along with some benefit in binaural summation, binaural squelch effects, and sound localization with bilateral cochlear implants. However, it was unclear if these benefits were experienced under quiet conditions, although benefits increased with longer bilateral cochlear implant usage indicating a need for longer term studies. Hearing-specific quality of life could not be assessed because only one study evaluated this outcome. Additionally, although gains were experienced in speech perception using open-set sentences or multi-syllable tests compared with unilateral cochlear implants or unilateral listening conditions, the evidence available on simultaneous bilateral implantation was found to be insufficient. The assessment noted longer term studies are needed to further understand the benefits with bilateral cochlear implantation and identify candidacy criteria given the risks of a second surgery and the destruction of the cochlea preventing future medical intervention.

Children

In a 2015 systematic review, Fernandes evaluated 18 published studies and two dissertations that reported hearing performance outcomes for children with ANSD and cochlear implants. Studies included four nonrandomized controlled studies considered high quality, five RCTs considered low quality, and 10 clinical outcome studies. Most studies (n=14) compared the speech perception in children with ANSD and cochlear implants with the speech perception in children with sensorineural hearing loss and cochlear implants. Most of these studies concluded that children with ANSD and cochlear implants developed hearing skills similar to those with sensorineural hearing loss and cochlear implants; however, these types of studies do not allow comparisons of outcomes between ANSD patients treated with cochlear implants and those treated with usual care.

In a 2014 systematic review, Lammers summarized the evidence on the effectiveness of bilateral cochlear implantation compared with unilateral implantation among children with sensorineural hearing loss. The authors identified 21 studies that evaluated bilateral cochlear implantation in children, with no RCTs identified. Due to the limited number of studies, heterogeneity in outcomes and comparison groups, and high risk for bias in the studies, the authors were unable to perform pooled statistical analyses, so a best-evidence synthesis was performed. The best-evidence synthesis demonstrated that there was consistent evidence indicating the benefit of bilateral implantation for sound localization. One study demonstrated improvements in language development, although other studies found no significant improvements. The authors noted that the currently available evidence consisted solely of cohort studies that compared a bilaterally implanted group with a unilaterally implanted control group, with only one study providing a clear description of matching techniques to reduce bias.

In 2013, Eze published a systematic review comparing outcomes for cochlear implantation for children with developmental disability with those without developmental disability. The authors noted that while approximately 30% to 40% of children who receive cochlear implants have developmental disability and that evidence about outcomes in this group was limited. Their review included 13 studies that compared receptive or expressive language outcomes in
children with cochlear implants with and without developmental disability. The included studies were heterogeneous in terms of comparator groups and outcome measures, precluding data pooling and meta-analysis. In a structured systematic review, the authors reported that seven of the eligible studies demonstrated a significantly poor cochlear implant outcome in children with developmental disability, while the remaining studies reported no significant difference in outcomes between the groups.

Humphriss (2013) published a systematic review evaluating outcomes after cochlear implantation among pediatric patients with auditory neuropathy spectrum disorder (ANSD), a sensorineural hearing disorder characterized by abnormal auditory brainstem response with preserved cochlear hair cell function as measured by otoacoustic emissions testing. The authors identified 27 studies that included an evaluation of cochlear implantation in patients with ANSD, including 15 noncomparative studies, one that compared children with ANSD who received a cochlear implant with children with ANSD with hearing aids, and 12 that compared children with ANSD who received a cochlear implant with children with severe sensorineural hearing loss who received a cochlear implant. Noncomparative studies were limited in that most (11/15) did not include a measure of speech recognition before cochlear implantation. Among the comparative studies, those comparing cochlear implantation to “usual care”, typically a hearing aid, provided the most information about effectiveness of cochlear implantation among patients with ANSD; the one small study that used this design found no significant differences between the groups. Overall, the authors suggested that further RCT evidence is needed.

The 2011 Forli systematic review noted above also addressed the effect of bilateral versus unilateral cochlear implants on verbal perception in children. Bilateral CI improved verbal perception in noise, and sound localization compared with unilateral implants in 19 of 20 studies reviewed. However, none of the studies compared learning development and language in bilateral versus unilateral cochlear implant recipients. Simultaneous versus sequential bilateral cochlear implantation results were not examined in any of the studies reviewed. Seven studies were reviewed that examined cochlear implant outcomes in children with associated disabilities. In this population, cochlear implant outcomes were inferior and occurred more slowly but were considered to be beneficial.

In a 2011 systematic review of 38 studies, Black sought to identify prognostic factors for cochlear implantation in pediatric patients. A quantitative meta-analysis was not able to be performed due to study heterogeneity. However, four prognostic factors: age at implantation, inner ear malformations, meningitis, and Connexin 26 (a genetic cause of hearing loss), consistently influenced hearing outcomes.

Pakdaman conducted a systematic review of cochlear implants in children with cochleovestibular anomalies in 2011. Anomalies included inner ear dysplasia such as large vestibular aqueduct and anomalous facial nerve anatomy. Twenty-two studies were reviewed totaling 311 patients. The authors found implantation surgery was more difficult and speech perception was lower in patients with severe inner ear dysplasia. However, heterogeneity in the studies limited interpretation of these findings.

In another 2011 systematic review, Roush examined the audiologic management of children with auditory neuropathy spectrum disorder. The review included 15 studies that addressed cochlear implantation in these patients. All of the studies reported auditory benefit with cochlear implantation in children with auditory neuropathy spectrum disorder. However, the
studies were noted to be limited methodologically and further research is needed in this population.

Adults and Children

Smulders (2011) examined the timing of cochlear implantation in a systematic review of 11 studies; five studies addressed postlingually deafened adults and seven studies addressed prelingually deafened children (discussed below). One study on adults showed a delay in the timing of the second implantation resulted in poorer outcomes in quiet environments. Nevertheless, all studies reported benefits with bilateral implants, but all studies were considered to be of poor quality and with a high risk of bias.

Randomized Trials

In 2016, Smulder conducted a small prospective multi-center randomized trial to evaluate the benefits of bilateral implants compared to unilateral implants in adults with postlingual deafness, including 38 patients. At one-year follow-up, there were no significant differences between groups on the speech-in-noise or the consonant-vowel-consonant test. The bilaterally implanted group performed significantly better when noise came from different directions (p <0.001) and was better able to localize sounds (p <0.001) compared to the unilaterally implanted group. These results were consistent with the patients' self-reported hearing capabilities. The results were consistent at a two year follow up, reported in 2017.

Nonrandomized Studies

Adults

Numerous case series have been published on adult patients with bilateral cochlear implants. Most but not all studies report slight to modest improvements in sound localization and speech intelligibility with bilateral cochlear implants especially with noisy backgrounds but not necessarily in quiet environments. In addition, depression scores improved in cochlear implant patients from pre-implantation to 12 months post-treatment (geriatric depression scale improvement: 31%, 95% CI 10% to 47%) in a prospective observational study including 113 patients with postlingual hearing loss, of whom 50 were treated with cochlear implants and 63 with hearing aids.

When reported, the combined use of binaural stimulation improved hearing in the range of one to four decibels or 1%–2%. While this improvement seems slight, any improvement in hearing can be considered beneficial in the deaf. However, this improvement may not outweigh the significant risks of a second implantation. In addition, similar binaural results can be achieved with a contralateral hearing aid, assuming the contralateral ear has speech recognition ability. A number of studies have reported benefits for patients with a unilateral cochlear implant with hearing aid (HA) in the opposite ear.

Children

Several recent publications have evaluated bilateral cochlear implants in children. These studies, ranging in size from 91 to 961 patients, generally report improved speech outcomes with bilateral implantation, compared with unilateral implantation. In a retrospective case series of 73 children and adolescents who underwent sequential bilateral cochlear implantation with a long (>five year) interval between implants, performance on the second implanted side was
worse than the primary implanted side, with outcomes significantly associated with the interimplant interval.\cite{46,50,56-61}

**Adults and Children**

Ching (2006) subsequently reported on 29 children and 21 adults with unilateral cochlear implant and a contralateral hearing aid.\cite{44} They noted that both children and adults localized sound better with bilateral inputs.

**UNILATERAL HEARING LOSS WITH OR WITHOUT TINNITUS**

The use of cochlear implants in patients with unilateral hearing loss is an off-label use of these devices. As noted in the 2011 AHRQ technology assessment, a number of narrative literature reviews\cite{62-64} and small (n<30) observational studies (described below) conducted primarily in adult patients have been published. However, these studies have included small numbers of patients (n<30) and had risk of reporting bias.

**Systematic Reviews**

In 2015, van Zon published a systematic review of studies evaluating cochlear implantation for single-sided deafness or asymmetric hearing loss.\cite{65} The authors reviewed 15 studies, nine of which (n=112 patients) were considered high enough quality to be included in data review. The authors identified no high-quality studies of cochlear implantation in this population. Data were not able to be pooled for metaanalysis due to high between-study heterogeneity, but the authors conclude that studies generally report improvements in sound localization, quality of life scores, and tinnitus after cochlear implantation, with varying results for speech perception in noise.

In 2014, Vlastarakos published a systematic review of the evidence related to cochlear implantation for single-sided deafness.\cite{66} The authors included 17 studies, including prospective and retrospective comparative studies, case series and case reports that included 108 patients. The authors report that sound localization is improved after cochlear implantation, although statistical analysis was not included in some of the relevant studies. In most patients (95%), unilateral tinnitus improved. The authors note that most of the studies included had short follow-up times, and evaluation protocols and outcome measurements were heterogeneous.

In 2014, Blasco and Redleaf published a systematic review and meta-analysis of studies evaluating cochlear implantation for unilateral sudden deafness.\cite{67} The review included nine studies with a total of 36 patients. In pooled analysis, subjective improvement in tinnitus occurred in 96% of patients (of 27 assessed), subjective improvement in speech understanding occurred in 100% of patients (of 16 assessed), and subjective improvement in sound localization occurred in 87% of patients (of 16 assessed). However, the small number of patients in which each outcome was assessed limits any conclusions that may be drawn.

**Nonrandomized Studies**

In a 2017 prospective study, Sladen examined speech recognition and self-perceived health-related quality of life in a cohort of 20 adults and children with unilateral hearing loss.\cite{68} Improvements were observed in speech recognition, both in quiet and noise, and self-perceived benefit with disease-specific instruments. Pure tone audiometry improved with air conduction in the implanted ear. CNC scores in quite improved from 4.8% (SD 9.0%) in the
preoperative period to 42.3% (SD 14.8%) at the 6-month post-activation check in the patients who reached that follow-up.

A 2016 study also from Sladen reported on a retrospective review of prospectively-collected data of short-term (six-month) follow-up for 23 adults and children with single-sided deafness from a variety of mechanisms who received a cochlear implant.[69] In the implanted ear, CNC word recognition improved significantly from pre-implantation to three months post-activation (P=0.001). However, for AzBio sentence understanding in noise (+5 dB signal-to-noise [SNR]), there was no significant improvement from pre-implantation to six months post-activation.

Also in 2016, Rahne reported on a retrospective review of four children and 17 adults with single-sided deafness treated with cochlear implants and followed for 12 months.[70] Sound localization with aided hearing improved from pre-implantation to aided hearing for all individuals. The Speech recognition threshold in noise (signal-to-noise) ratio improved from -1.95 dB (CI off, SD: 2.7 dB) to -4.0 dB after three months (SD 1.3 dB, P<0.05), with continued improvements through six months.

In 2016, Mertens reported a case series including 23 individuals who received cochlear implants for single-sided deafness with tinnitus.[71] Eligible patients had either single-sided deafness or asymmetric hearing loss and ipsilateral tinnitus. Subjects had a mean eight years of experience with their cochlear implant (range, 3-10 years). Patients demonstrated improvements in VAS from baseline (mean score, 8) to one month (mean score: 4; p<0.01 vs baseline) and three months (mean score: 3; p<0.01 vs baseline) after the first fitting. Tinnitus scores improved from baseline to three months post fitting (55 vs 31, p<0.05) and were stable for the remainder of follow-up.

In 2015, Ramos Macias reported results of a prospective multicenter study with repeated measures related to tinnitus, hearing, and quality of life, among 16 individuals with unilateral hearing loss and severe tinnitus who underwent cochlear implantation.[72] All patients had a severe tinnitus handicap (THI score ≥ 58%). Eight (62%) of the 13 patients who completed the six-month follow-up visit reported a lower tinnitus handicap on the THI score. Perceived loudness/annoyingness of the tinnitus was evaluated with a 10-point VAS. When the CI was on, tinnitus loudness decreased from 8.4 preoperatively to 2.6 at the six-month follow-up; 11 of 13 patients reported a change in score of three or more.

In 2015, Arndt reported outcomes for 20 children who underwent cochlear implantation for single-sided deafness, which represented a portion of their center’s cohort of 32 pediatric patients with single-sided deafness who qualified for cochlear implants.[73] Repeated-measure analyses of hearing data sets were available for 13 implanted children, excluding five who had undergone surgery too recently to be evaluated and two children who were too young to be evaluated for binaural hearing benefit. There was variability in the change in localization ability across the tested children. Self- (or child-) reported hearing benefit was measured with the Speech, Spatial and Qualities of Hearing Scale (SSQ). Significant improvements were reported on the child and parent evaluations for the scale’s three subcategories: speech hearing, spatial hearing, hearing quality, and total hearing.

In 2013, Hansen reported results of a prospective study of cochlear implantation for severe-to-profound single-sided sensorineural hearing loss in 29 patients, 10 of whom had single-sided deafness due to Meniere’s disease.[74] Performance was compared pre- to post-implant within each subject; outcomes were measured at three-, six-, and 12-months postoperatively. Patients showed significant improvements in CNC word and AzBio sentence scores showed...
improvement in the implanted ear pre- and post-implant. For the 19 patients with pre- and post-
operative data available, the average improvement on CNC word score was 28% (range: -26% 
to 64%). The average AzBio score improvement was 40% (range: -57% to 92%).

Tavora-Vieira (2013) reported results of a prospective case series that included nine post-
lingually deaf subjects with unilateral hearing loss, with or without tinnitus in the ipsilateral ear,
with functional hearing in the contralateral ear, who underwent cochlear implantation.[75]
Speech perception was improved for all subjects in the "cochlear implant on" state compared
with the "cochlear implant off" state, and subjects with tinnitus generally reported improvement.

Arndt published a pilot study in 2010 of 11 adult patients with unilateral hearing loss of various
causes.[76] The aim was to evaluate the use of unilateral electrical stimulation with normal
hearing on the contralateral side and after a period of six months compared with the
preoperative unaided situation, conventional contralateral routing of signal or bone-anchored
hearing aid hearing aids. Ten patients also suffered from tinnitus. Two tests were used to
assess speech comprehension, localization was assessed using an array of multiple speakers,
and QOL was evaluated using three questionnaires. The study results were presented as p-
values without adjustment for multiple testing. The authors reported that cochlear implantation
improved hearing abilities in these study patients and was superior to the above alternative
treatment options. The use of the cochlear implant did not interfere with speech understanding
in the normal-hearing ear.

The application of cochlear implants for tinnitus relief in patients with unilateral deafness has
also been described in previous studies. For example, van de Heyning published a study in
2008 of 21 patients with unilateral hearing loss accompanied by severe tinnitus for at least two
years who underwent cochlear implants at a university center in Belgium.[77] The majority of
patients demonstrated a significant reduction in tinnitus loudness based on a visual analogue
scale (two years after implantation, 2.5 ± 1.9; before implantation, 8.5 ± 1.3). Three patients
showed complete tinnitus relief.

COCHLEAR RESTORATION

The optimal timing of cochlear implantation in children is of particular interest given the strong
associations between hearing and language development. While there is current research
investigating the ability to restore hearing by stimulating cochlear hair cell regrowth, cochlear
implantation damages the cochlea and eliminates the possibility of cochlear restoration.
However, the potential to restore cochlear function is not foreseeable in the near future;
therefore, if implantation of cochlear implants is felt to be most beneficial at a younger age
when the nervous system is "plastic", this potential development seems too far in the future to
benefit young children who are current candidates for a cochlear implant.

HYBRID COCHLEAR IMPLANTATION

Systematic Review

Santa Maria (2014) conducted a systematic review and meta-analysis of hearing outcomes
after various types of hearing-preservation cochlear implantation, including implantation hybrid
devices, cochlear implantation with surgical techniques designed to preserve hearing, and the
use of post-operative systemic steroids.[78] The study included 24 studies, but only two studies
focused specifically on a hybrid cochlear implant system, and no specific benefit from a hybrid
system was reported.
Nonrandomized Studies

The pivotal trial for the Med-EL EAS system was a prospective, multi-center, non-randomized, non-blinded, repeated measures clinical study of 73 subjects at 14 U.S. sites, implanted with either SONATA FLEX24 or a PULSAR FLEX24.\(^3\) The score was compared across two conditions: the acoustic-only condition (baseline) and the 12-month post-activation EAS condition (ipsilateral electric + ipsilateral acoustic). Performance was compared pre- to post-implant within each subject; outcomes were measured at three-, six-, and 12-months postoperatively. Patients’ hearing was evaluating in three states: preoperative acoustic-only (acoustic stimulation to the ear to be implanted), postoperative electric-only (electric stimulation to the ear to be implanted), and postoperative EAS (simultaneous electric and acoustic stimulation in the implanted ear via the MED-EL EAS system. The primary effectiveness endpoint of improvement of CUNY sentence-in-noise scores from baseline to 12-months post-implant was 42.4% (95% confidence interval [CI]: 33.6%, 51.2%) in 66 of the 73 total enrolled patients. CUNY sentence in noise scores between the postoperative EAS condition and the postoperative electric-only condition (CUNY post EAS – post E) showed a mean improvement of 18.4% (95% CI: -19%, 77%, \(p = 0.003\)). Thirty five adverse events were reported to be related to the device or procedure, eight of which (11%) were profound/total residual hearing loss. At 12-months post-insertion, two subjects had undergone device explantation, one due to migration of the electrode and one due to device failure.

The pivotal trial for the Nucleus® Hybrid™ L24 Cochlear Implant System, published by Roland in 2016, was a prospective, multi-center, one-arm, non-randomized, non-blinded, repeated-measures clinical study of 50 subjects at 10 U.S. sites.\(^79\) Performance was compared pre- to post-implant within each subject; outcomes were measured at three-, six-, and 12-months postoperatively. Post-operatively, patients’ hearing was evaluated in three states: Hybrid (simultaneous electric and acoustic stimulation in the implanted ear via the Hybrid L24 including the acoustic component), Bimodal (electric stimulation only using the Hybrid L24 minus the acoustic component with contralateral acoustic stimulation), and Combined (electric and acoustic stimulation via the Hybrid L24 and contralateral acoustic stimulation). Results from the Bimodal and Combined conditions were grouped into an “Everyday Listening” category, which was not prospectively defined by the manufacturer. All 50 subjects enrolled underwent device implantation and activation. One subject had the device explanted and replaced with a standard cochlear implant between the three- and six-month follow up visit due to profound loss of low frequency hearing; an additional subject was explanted before the 12-month follow up visit and two additional subjects were explanted after 12 months. For the two primary effectiveness endpoints, CNC word-recognition score and AzBio sentence-in-noise score, a measure of sentence understanding in noisy environments, there were significant within-subject improvements from baseline to six-month follow up. The mean improvement in CNC word score was 35.7% (95% confidence interval [CI] 27.8% to 43.6%); for AzBio score, the mean improvement was 32.0% (95% CI 23.6% to 40.4%) For safety outcomes, 71 adverse events were reported, most commonly profound/total loss of hearing (occurring in 44% of subjects) with at least one adverse event occurring in 34 subjects (68%).

In 2015, Friedmann conducted a retrospective review that included 22 subjects implanted with a cochlear implant with either a standard electrode (n=12) or the Nucleus Hybrid L24 electrode (n=10).\(^80\) At one year post-implant, 30% patients with the Hybrid-L and 58% patients with the standard electrode lost residual acoustic hearing resulting in a profound hearing loss in the implanted ear. The authors reported that while hearing preservation rates with the hybrid...
electrode tended to be better, among recipients who lost residual hearing, speech perception was better in those with the longer standard electrode.

Lenarz (2013) reported results of a prospective multi-center European study evaluating the Nucleus Hybrid™ L24 system. The study enrolled 66 adults with bilateral severe-to-profound high frequency hearing loss. At one year post-operatively, 65% of subjects had significant gains in speech recognition in quiet and 73% had significant gains in noisy environments. Compared with the cochlear implant hearing alone, residual hearing significantly increased speech recognition scores.

Gifford (2013) compared hearing outcomes pre- and post-implantation for 44 adult cochlear implant recipients with preserved low-frequency hearing in two test conditions: cochlear implant plus low-frequency hearing in the contralateral plus low-frequency hearing in the contralateral ear (bimodal condition) and cochlear implant plus low-frequency hearing in both ears (best-aided condition). The authors reported that there were small but statistically significant differences in improvements in adaptive sentence recognition and speech recognition in a noisy “restaurant” environment, suggesting that the presence of residual hearing is beneficial.

A small number of studies in a small number of patients suggest that a hybrid cochlear implant system is associated with improvements in hearing of speech in quiet and noise. However, there are currently no available studies that compare the use of a standard hearing aid with a hybrid cochlear implant, which would be an appropriate comparison to determine if a hybrid device improves outcomes for patients who currently have hearing loss, but might not be a candidate for a cochlear implant. In addition, there is only limited data to suggest that the preservation of residual hearing associated with a hybrid device is associated with improved outcomes compared with a standard cochlear implant.

Section Summary

Current evidence is insufficient to determine the effectiveness of hybrid cochlear implant/hearing aid systems compared with conventional cochlear implants. Nor is there sufficient evidence to determine the rates of adverse events and reoperations associated with these devices.

PRACTICE GUIDELINE SUMMARY

AMERICAN ACADEMY OF OTOLARYNGOLOGY- HEAD AND NECK SURGERY FOUNDATION (AAO-HNS)

In 2014, the AAO-HNS published a revised position statement on cochlear implants. The Academy considers unilateral and bilateral cochlear implantation as appropriate treatment for adults and children with severe to profound hearing loss. Based on extensive literature demonstrating that clinically selected adults and children can significantly perform better with two cochlear implants rather than one, bilateral cochlear implantation is accepted medical practice.

SUMMARY

There is enough research to show that cochlear implants improve health outcomes, specifically, speech reception (especially in noise) and sound localization, for patients aged...
12 months or older who have severe to profound bilateral sensorineural hearing loss. Therefore, cochlear implants may be considered medically necessary in specific patients with bilateral hearing loss who meet the policy criteria. Cochlear implants are considered not medically necessary when the policy criteria are not met, including but not limited to unilateral hearing loss with or without tinnitus.

There are currently no cochlear implants that have approval from the U.S. Food and Drug Administration (FDA) for use in patients who are younger than 12 months of age. There is not enough research to show that cochlear implants improve health outcomes in patients younger than 12 months of age and it is unclear that the benefits of early cochlear implantation outweigh the risk of surgery and anesthesia in these very young patients. In addition, there are no clinical practice guidelines from U.S. professional societies that recommend cochlear implantation in these very young patients. Therefore, cochlear implantation in patients younger than 12 months of age is considered not medically necessary.

The current research on cochlear implantation in patients diagnosed with enlarged vestibular aqueducts (EVA) has limitations. Despite these limitations, there is enough research to show that cochlear implants improve health outcomes, specifically, speech recognition, for patients with EVA. In addition, early placement of cochlear implants avoids atrophy and preserves hearing patients with EVA with moderate hearing loss. Therefore, cochlear implants may be considered medically necessary in patients with EVA when policy criteria are met.

The current research on hybrid cochlear implant/hearing aid systems has limitations. Despite these limitations, there is enough research to show that hybrid cochlear implant/hearing aid systems improve health outcomes, specifically, speech recognition, for patients aged 18 years or older who have high frequency sensorineural hearing loss with preserved low frequency hearing. Therefore, hybrid cochlear implant/hearing aid systems may be considered medically necessary in specific patients with high frequency sensorineural hearing loss with preserved low frequency hearing who meet the policy criteria. Hybrid cochlear implant/hearing aid systems are considered not medically necessary when the policy criteria are not met, including but not limited to unilateral hearing loss with or without tinnitus.

Replacement of an existing cochlear implant with a next-generation device may be considered medically necessary only in those patients whose response to the existing device is inadequate to the point of interfering with activities of daily living, including school or work.

An upgrade of a functioning external system to improve appearance is considered not medically necessary. Examples include components with a smaller profile, or to switch from a body-worn external sound processor to a behind-the-ear model.

REFERENCES


11. Powell, HR, Birman, CS. Large vestibular aqueduct syndrome: Impedance changes over time with different cochlear implant electrode arrays. Cochlear Implants Int. 2015;16(6):326-30. PMID: 26098963


33. Fernandes, NF, Morettin, M, Yamaguti, EH, Costa, OA, Bevilacqua, MC. Performance of hearing skills in children with auditory neuropathy spectrum disorder using cochlear


84. BlueCross BlueShield Association Medical Policy Reference Manual "Cochlear Implant." Policy No. 7.01.05

### CODES

<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>69930</td>
<td>Cochlear device implantation, with or without mastoidectomy</td>
</tr>
<tr>
<td></td>
<td>92601</td>
<td>Diagnostic analysis of cochlear implant, patient younger than 7 years of age; with programming</td>
</tr>
<tr>
<td></td>
<td>92602</td>
<td>;subsequent reprogramming</td>
</tr>
<tr>
<td></td>
<td>92603</td>
<td>Diagnostic analysis of cochlear implant, age 7 years or older; with programming</td>
</tr>
<tr>
<td></td>
<td>92604</td>
<td>;subsequent reprogramming</td>
</tr>
<tr>
<td></td>
<td>92630</td>
<td>Auditory rehabilitation; pre-lingual hearing loss</td>
</tr>
<tr>
<td></td>
<td>92633</td>
<td>Auditory rehabilitation; post-lingual hearing loss</td>
</tr>
<tr>
<td>HCPCS</td>
<td>L8614</td>
<td>Cochlear device, includes all internal and external components</td>
</tr>
<tr>
<td></td>
<td>L8615</td>
<td>Headset/headpiece for use with cochlear implant device, replacement</td>
</tr>
<tr>
<td></td>
<td>L8616</td>
<td>Microphone for use with cochlear implant device, replacement</td>
</tr>
<tr>
<td></td>
<td>L8617</td>
<td>Transmitting coil for use with cochlear implant device, replacement</td>
</tr>
<tr>
<td></td>
<td>L8618</td>
<td>Transmitter cable for use with cochlear implant device, replacement</td>
</tr>
<tr>
<td></td>
<td>L8619</td>
<td>Cochlear implant external speech processor and controller, integrated system, replacement</td>
</tr>
<tr>
<td></td>
<td>L8621</td>
<td>Zinc air battery for use with cochlear implant device and auditory osseointegrated sound processors, replacement, each</td>
</tr>
<tr>
<td></td>
<td>L8622</td>
<td>Alkaline battery for use with cochlear implant device, any size, replacement, each</td>
</tr>
<tr>
<td></td>
<td>L8623</td>
<td>Lithium ion battery for use with cochlear implant device speech processor</td>
</tr>
<tr>
<td></td>
<td>L8624</td>
<td>Lithium ion battery for use with cochlear implant device speech processor, ear</td>
</tr>
<tr>
<td></td>
<td>L8627</td>
<td>Cochlear implant, external speech processor, component, replacement</td>
</tr>
<tr>
<td></td>
<td>L8628</td>
<td>Cochlear implant, external controller component, replacement</td>
</tr>
<tr>
<td></td>
<td>L8629</td>
<td>Transmitting coil and cable, integrated, for use with cochlear implant device, replacement</td>
</tr>
</tbody>
</table>

*Date of Origin: January 1996*
Regence

Medical Policy Manual

**Topic:** Cosmetic and Reconstructive Surgery

**Section:** Surgery

**Policy No:** 12

**Date of Origin:** January 1996

**Last Reviewed Date:** March 2017

**Effective Date:** July 1, 2017

**IMPORTANT REMINDER**

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

**DESCRIPTION**

Cosmetic surgery is performed to reshape normal body structures in order to improve appearance.

Reconstructive surgery is primarily performed to improve or correct a functional impairment.

**NOTE:** This policy is not intended to address treatment of gender dysphoria which is addressed in the Transgender Services medical policy, Medicine, Policy No. 153, which may be applicable.

**MEDICAL POLICY CRITERIA**

Many member contracts have very specific language regarding covered reconstructive services and excluded cosmetic procedures. Specific member contract language has precedence over medical policy, and requests for coverage of potentially cosmetic services should be reviewed by applicable member contract language.

1. Medical necessity criteria for specific procedures:
   - **Blepharoplasty and Brow Ptosis Repair**
   - **Chemical Peels**
   - **Dermabrasion and Microdermabrasion**

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
Laser Treatment for Port Wine Stain
Mastectomy for Gynecomastia
Orthognathic Surgery
Panniculectomy
Pectus Excavatum
Reconstructive Breast Surgery/Mastopexy, and Management of Breast Implants
Reduction Mammaplasty
Varicose Vein Treatment
Ventral Hernia Repair

II. The following criteria may be applied when member contract language is not specific:

A. If the intervention is intended to treat a functional impairment and if no other contract exclusions apply, it may be considered **medically necessary**.

B. If the intervention is not intended to treat a functional impairment, the cause of the condition must be determined, for example, accident/injury/trauma, post-treatment, congenital anomaly, disease. If the cause is included in the definition of reconstructive services in the benefits contract language, then the treatment may be covered.

The following flow chart may be used as a guide to interpreting benefits language.
Blepharoplasty and Brow Ptosis Repair

Description

Blepharoplasty is a surgical procedure performed on the upper and/or lower eyelids to remove or repair excess tissue that obstructs the field of vision. These procedures may also be performed for cosmetic purposes in the absence of visual field obstruction.

Functional visual impairment occurs when excess upper eyelid tissue overhangs the upper eyelid margin and results in significant superior visual field obstruction. Visual field studies are used to determine the degree of obstruction. Visual field studies should be measured both with and without elevation of the excess tissue to determine the extent of visual field defect at rest and the amount of improvement that may be obtained from blepharoplasty.

Medical Policy Criteria

I. Blepharoplasty may be considered medically necessary when either of the following criteria (A. or B.) is met:
   
   A. Trichiasis, ectropion or entropion for an affected upper or lower lid when documented by lateral and full face photographs clearly showing the affected lid(s); or
   
   B. Anophthalmia when there is clinical documentation that the upper eyelid position interferes with the fit of a prosthesis in the socket.

II. Unilateral or bilateral upper lid blepharoplasty or levator resection may be considered medically necessary for reconstructive purposes when all of the following criteria are met:

   A. Any related disease process, such as myasthenia gravis or a thyroid condition, is documented as stable; and

   B. Documentation of clinically decreased vision (e.g., functional impairment due to visual field loss); and

   C. The visual field of at least one eye is limited to 20 degrees or less superiorly, or limited to 15 degrees or less laterally, based on results of complete bilateral visual field examinations, including visual points seen. Examinations may include either automated or hand drawn demarcation line(s), but need to clearly document the edges of visual fields with specific visual points seen at those edges; and

   D. Frontal and lateral facial photographs demonstrate visual field limitation consistent with the visual field examination.

III. Brow ptosis repair including open and endoscopic procedures may be considered medically necessary for reconstructive purposes when at least one eye meets the blepharoplasty Criterion I. or II above AND photographs demonstrate the eyebrow is below the supraorbital rim.

IV. Surgical session

   A. One surgical session for either unilateral or bilateral blepharoplasty and/or brow ptosis may be medically necessary, when criteria I. II. and/or III. are met.

October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage.
Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
B. Surgical session(s) in excess of one, for unilateral or bilateral blepharoplasty and/or brow ptosis is considered **not medically necessary**.

V. Unilateral or bilateral upper lid blepharoplasty, levator resection and brow ptosis repair is considered **not medically necessary** when the Criteria in I., or II., or III above is not met.

VI. Blepharoplasty of the lower lids for excessive skin is considered **not medically necessary**.

---

**Chemical Peels**

**Description**

A chemical peel refers to a controlled removal of varying layers of the epidermis and superficial dermis with the use of a ‘wounding’ agent, such as phenol or trichloroacetic acid (TCA). The most common indication for chemical peeling is as a treatment of photoaged skin, correcting pigmentation abnormalities, solar elastosis, and wrinkles. However, chemical peeling has also been used as a treatment for various stages of acne and multiple actinic keratoses when treatment of individual lesions is not feasible.

An epidermal peel may be used to remove fine, subtle lines, soften the appearance of enlarged pores, improve the skin texture and lighten hyper-pigmentary disorders. Multiple epidermal peels (also referred to as chemical exfoliation) may also be used in patients with active acne.

Dermal peels may be used to treat deep wrinkling, actinic damage, or actinic keratoses. Acne scarring has also been treated with dermal peels.

---

**Medical Policy Criteria**

**Epidermal Chemical Peels**

I. Epidermal chemical peels with 50 - 70% alpha hydroxy acids may be considered **medically necessary** as a treatment of active acne that has failed to respond to a trial of topical and/or oral antibiotic acne therapy.

II. Epidermal chemical peels with 50 - 70% alpha hydroxy acids is considered **not medically necessary** as a first-line treatment of active acne.

III. Epidermal chemical peels for the treatment of photoaged skin, wrinkles, or acne scarring are considered **cosmetic**.

**Dermal Chemical Peels**

I. Dermal chemical peels may be considered **medically necessary** to treat numerous (>10) actinic keratoses or other premalignant skin lesions, when treatment of the individual lesions becomes impractical.

II. Dermal chemical peels are considered **not medically necessary** to treat less than 10 actinic keratoses or other premalignant skin lesions.

---

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
III. Dermal chemical peels as treatments of end-stage acne scarring are considered **cosmetic**.

**Dermabrasion and Microdermabrasion**

*Description*

Dermabrasion uses a rapidly moving brush to remove skin and activate new skin growth. It is commonly used for the treatment of facial scars and wrinkles.

Microdermabrasion uses small microcrystals to abrade the superficial epidermal layer of the skin; suction is then used to remove any skin debris. Microdermabrasion is often performed by estheticians for facial rejuvenation.

**Medical Policy Criteria**

I. Dermabrasion to treat photoaged skin, wrinkles, or acne scarring is considered **cosmetic**.

II. Microdermabrasion for the treatment of any indication is considered **cosmetic**.

**Laser Treatment of Port Wine Stains**

*Description*

Port wine stain (PWS) is a capillary malformation that begins as a pale pink flat area (macular lesion) in childhood and grows as the patient ages. Common areas for PWS to appear are on the face over the areas of the first and second trigeminal nerves and the eyes or mouth. It is common to see a PWS overlying an arteriovenous, arterial or venous malformation. The abnormal blood vessels within the PWS become progressively more dilated in size, which results in the lesion becoming dark purple and elevated in some instances. Nodules and hypertrophy may develop in the soft tissue underlying the PWS. Nodules may continue to grow and can bleed easily if traumatized. PWS persists into adult life and is associated with systemic abnormalities such as glaucoma.

Treatment of a PWS in its macular stage will prevent the development of the hypertrophic component of the lesion. Laser treatment of a PWS diminishes the existing blood vessels making them smaller, fewer in number, and less likely to progress in size.

**Medical Policy Criteria**

I. Laser treatment may be considered **medically necessary** for port wine stains.

II. Destruction of cutaneous vascular lesions for removal of telangiectasias (spider veins) is considered **cosmetic**.

**Mastectomy for Gynecomastia**

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
Description

Gynecomastia refers to the benign enlargement of the male breast, either due to increased adipose tissue, fibrous tissue, glandular tissue, or a combination of all three. In some instances, adolescent gynecomastia may be reported as tender or painful; however, this pain is normally self-limiting or responds to analgesic therapy. Typically no functional impairment is associated with gynecomastia.

Medical Policy Criteria

Mastectomy as a treatment of gynecomastia is considered cosmetic.

Panniculectomy

Description

Panniculectomy refers to the removal of excess skin and subcutaneous tissue typically from the abdominal area. This procedure is often performed after substantial weight loss as a result of bariatric surgery or diet. According to the American Society of Plastic Surgeons, “[a]bdominoplasty and panniculectomy are typically performed for purely cosmetic indications such as unacceptable appearance due to fat maldistribution or contour deformities caused by pregnancy, stretch marks, contracted scars and loose hanging skin after weight loss.”[1] Similar to abdominoplasty, panniculectomy involves the removal of skin in a transverse or vertical wedge, but does not include muscle plication, neoumbilicoplasty or flap elevation.[1] There is limited evidence and clinical practice guidelines which indicate when panniculectomy may be appropriate due to functional impairment.[2,3] Typically no functional impairment is associated with pannus development.

Medical Policy Criteria

NOTE: Member contract language takes precedent over medical policy. Member contracts for covered services vary and may exclude weight loss surgery and all associated, services, supplies, and/or complications.

1. Panniculectomy may be considered medically necessary when ALL of the following are met:
   A. Submission of photographs documenting significant pannus which hangs below the level of the pubis; AND
   B. The pannus causes a chronic and persistent skin condition (e.g., intertriginous dermatitis, panniculitis, cellulitis or skin ulcerations) that is refractory to at least 3 months of medical treatment and associated with at least one episode of cellulitis requiring systemic antibiotics (oral and/or intravenous). In addition to good hygiene practices, treatment should also include topical antifungals, topical and/or systemic corticosteroids, AND
   C. The pannus causes functional physical impairment documented to interfere with activities of daily living (see Policy Guidelines), AND

October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
D. Stable weight for at least 6 months and if following bariatric surgery, at least 18 months after the surgery.

II. Panniculectomy which does not meet the above criteria I. is considered cosmetic

III. Abdominoplasty with or without panniculectomy is considered cosmetic.

POLICY GUIDELINES

It is critical that the list of information below is submitted for review to determine whether the policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome.

- The specific functional physical impairment caused by the pannus
- Front and lateral view photographs demonstrating redundant/excessive skin and the size of the pannus
- Clinical documentation about the nature and extent of the chronic and persistent skin condition that is refractory to at least three months of medical treatment [at least one episode of cellulitis requiring systemic antibiotics (oral and/or intravenous) and good hygiene practices including topical antifungals, topical and/or systemic corticosteroids]
- Any bariatric surgery procedure performed within the past three years, including date of procedure
- Clinical documentation of stable weight for at least six months

Activities of Daily Living (ADLs) Definition: Instrumental ADLs are defined as feeding, bathing, dressing, grooming, meal preparation, household chores, and occupational tasks that are required as a daily part of job functioning.

Pectus Excavatum Repair

Description

Pectus excavatum, commonly referred to as "funnel chest," is a chest wall malformation in which the sternum is depressed inward, causing midline narrowing of the thoracic cavity. Although pectus excavatum may be visually prominent, in most cases the loss of volume is not significant and does not interfere with ventilation. Pectus excavatum is occasionally associated with upper or lower airway obstruction; however, when this condition is successfully treated or resolves spontaneously, the pectus deformity may lessen or disappear. Pectus excavatum may also be associated with segmental bronchomalacia, and in some patients, cardiac function may be adversely affected. In many children, the heart is shifted leftward, and in the rare patient, cardiac function may be adversely affected.

Surgical correction of pectus excavatum is not physiologically beneficial for the vast majority of patients; surgery is most often sought due to psychological and cosmetic concerns. However, for some patients with extreme deformity, operative interventions may be indicated for functional reasons.

Medical Policy Criteria
I. Surgical repair of pectus excavatum may be considered **medically necessary** in children or adults when at least two of the following medical necessity criteria are met:

A. Documented progression of the deformity with associated symptoms.

B. Pulmonary function studies indicate components of restrictive airway disease.

C. Haller Computerized Tomography (CT) scan index greater than 3.25. This Haller CT index is the ratio derived from a chest CT scan by dividing the transverse diameter by the anterior-posterior diameter.

D. Cardiac evaluation (electrocardiogram [EKG], chest CT, and/or echocardiogram) demonstrates compression-caused mitral valve prolapse, abnormal rhythm, conduction abnormalities, or significant cardiac deformity.

II. Surgical repair of pectus excavatum that does not meet at least two of the criteria in I.A. – I. D. above is considered **not medically necessary**.

### Ventral Hernia Repair

#### Description

Ventral hernias occur in the abdomen and develop when a portion of the lining of the peritoneum pushes through a weak area of the abdominal wall fascia. This results in a protrusion which can be filled with intra-abdominal fat or intestine. Ventral hernias are usually acquired when pressure is applied to an area of the abdomen which is weakened. They can occur spontaneously, known as a primary hernia, or at the site of a previous surgical incision, known as an incisional hernia.

Abdominal wall hernias (Epigastric, Umbilical, Lumbar and Spigelian) are defined by their anatomical location. Patients who are obese, older, under-weight, pregnant, have ascites or other factors which increase intra-abdominal pressure may be predisposed to developing abdominal hernias. Most hernias are acquired; however, the occurrence of umbilical hernias in infants is considered a congenital defect which usually resolves before the age of 2. Children with persistent symptoms may require surgical repair.

Diastasis recti is defined as increased distance between the right and left rectus abdominis muscles that is created by the stretching of the collagen sheath (the linea alba) connecting the two rectus abdominis muscles. Diastasis recti is not considered a hernia as there is no fascial defect.

In general small, asymptomatic hernias do not require surgical repair. Adults with larger, symptomatic hernias should be considered for ventral hernia repair. Over time, hernia symptoms may develop and include pain, bowel obstruction, incarceration, thinning of the overlying skin, strangulation and displacement of abdominal contents into the hernia itself, known as loss of abdominal domain.

#### Component Separation Technique

The component separation technique (CST) is a surgical method that may be used to repair large, complicated ventral hernias using a rectus abdominis muscle advancement flap. Mesh reinforcement is often used in recurrent repairs where the abdominal defect is too large and there is a large amount of...
tension on the CST repair. CST is not typically used as an initial surgical approach for primary ventral hernia repairs.

Note:
- CPT states, “select the name of the procedure or service that accurately identifies the service performed”; therefore, an abdominal wall hernia with a specific CPT code (i.e. epigastric, umbilical, spigelian, or lumbar hernia repair) should not be coded as a ventral hernia repair.
- A ventral hernia at the site of a prior surgery is considered an incisional hernia.

Medical Policy Criteria

I. Surgical repair of a ventral hernia may be considered medically necessary in symptomatic patients when there is documentation of any one of the following criteria:
   A. Hernia associated pain
   B. Bowel obstruction
   C. Incarceration
   D. Strangulation
   E. Thinning of the overlying skin
   F. Loss of abdominal domain

II. Surgical repair of recurrent ventral hernias using the component separation technique (CST) may be considered medically necessary.

III. Surgical repair of initial ventral hernias using the component separation technique (CST) is considered not medically necessary.

IV. Surgical repair of asymptomatic ventral hernias, or ventral hernias found incidentally during surgery, is considered not medically necessary.

V. Surgical repair of diastasis recti is considered cosmetic.

VI. Abdominoplasty, and related procedures, including but not limited to fascial plication, surgical imbrication, and tightening of lax fascia, are considered cosmetic.

REFERENCES


CROSS REFERENCES

Transgender Services, Medicine, Policy No. 153
Endometrial Ablation, Surgery, Policy No. 01
Reconstructive Breast Surgery/Management of Breast Implants, Surgery, Policy No. 40
Reduction Mammaplasty, Surgery, Policy No. 60
Varicose Vein Treatment, Surgery, Policy No. 104
Orthognathic Surgery, Surgery, Policy No. 137
Autologous Fat Grafting to the Breast and Adipose-derived Stem Cells, Surgery, Policy No. 182

<table>
<thead>
<tr>
<th>CODES</th>
<th>NUMBER</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>11920</td>
<td>Tattooing, intradermal introduction of insoluble opaque pigments to correct color defects of skin, including micropigmentation; 6.0 sq cm or less</td>
</tr>
<tr>
<td></td>
<td>11921</td>
<td>Tattooing, intradermal introduction of insoluble opaque pigments to correct color defects of skin, including micropigmentation; 6.1 to 20.0 sq cm</td>
</tr>
<tr>
<td></td>
<td>11922</td>
<td>Tattooing, intradermal introduction of insoluble opaque pigments to correct color defects of skin, including micropigmentation; each additional 20.0 sq cm, or part thereof</td>
</tr>
<tr>
<td></td>
<td>15775</td>
<td>Punch graft for hair transplant; 1 to 15 punch grafts</td>
</tr>
<tr>
<td></td>
<td>15776</td>
<td>Punch graft for hair transplant; more than 15 punch grafts</td>
</tr>
<tr>
<td></td>
<td>15780</td>
<td>Dermabrasion; total face (eg, for acne scarring, fine wrinkling, rhytids, general keratosis)</td>
</tr>
</tbody>
</table>

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
<table>
<thead>
<tr>
<th>CODES</th>
<th>NUMBER</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>15781</td>
<td>15782</td>
<td>Dermabrasion; segmental, face</td>
</tr>
<tr>
<td></td>
<td>15783</td>
<td>Dermabrasion; regional, other than face</td>
</tr>
<tr>
<td></td>
<td>15786</td>
<td>Dermabrasion; superficial, any site (eg, tattoo removal)</td>
</tr>
<tr>
<td></td>
<td>15787</td>
<td>Abrasion; single lesion (eg, keratosis, scar)</td>
</tr>
<tr>
<td></td>
<td>15788</td>
<td>Abrasion; each additional four lesions or less</td>
</tr>
<tr>
<td></td>
<td>15789</td>
<td>Chemical peel, facial; epidermal</td>
</tr>
<tr>
<td></td>
<td>15792</td>
<td>Chemical peel; facial; dermal</td>
</tr>
<tr>
<td></td>
<td>15793</td>
<td>Chemical peel; nonfacial; epidermal</td>
</tr>
<tr>
<td></td>
<td>15793</td>
<td>Chemical peel; nonfacial; dermal</td>
</tr>
<tr>
<td></td>
<td>15819</td>
<td>Cervicoplasty</td>
</tr>
<tr>
<td></td>
<td>15820</td>
<td>Blepharoplasty, lower eyelid</td>
</tr>
<tr>
<td></td>
<td>15821</td>
<td>Blepharoplasty with extensive herniated fat pad</td>
</tr>
<tr>
<td></td>
<td>15822</td>
<td>Blepharoplasty, upper eyelid</td>
</tr>
<tr>
<td></td>
<td>15823</td>
<td>Blepharoplasty, upper eyelid; with excessive skin weighting down lid</td>
</tr>
<tr>
<td></td>
<td>15824</td>
<td>Rhytidectomy; forehead</td>
</tr>
<tr>
<td></td>
<td>15825</td>
<td>Rhytidectomy; neck with platysmal tightening (platysmal flap, P-flap)</td>
</tr>
<tr>
<td></td>
<td>15826</td>
<td>Rhytidectomy; glabellar frown lines</td>
</tr>
<tr>
<td></td>
<td>15828</td>
<td>Rhytidectomy; cheek, chin and neck</td>
</tr>
<tr>
<td></td>
<td>15829</td>
<td>Rhytidectomy; superficial musculoaponeurotic system (SMAS) flap</td>
</tr>
<tr>
<td></td>
<td>15830</td>
<td>Excision, excessive skin and subcutaneous tissue (includes lipectomy); abdomen, infraumbilical panniculectomy</td>
</tr>
<tr>
<td></td>
<td>15832</td>
<td>Excision, excessive skin and subcutaneous tissue (includes lipectomy); thigh</td>
</tr>
<tr>
<td></td>
<td>15833</td>
<td>Excision, excessive skin and subcutaneous tissue (includes lipectomy); leg</td>
</tr>
<tr>
<td></td>
<td>15834</td>
<td>Excision, excessive skin and subcutaneous tissue (includes lipectomy); hip</td>
</tr>
<tr>
<td></td>
<td>15835</td>
<td>Excision, excessive skin and subcutaneous tissue (includes lipectomy); buttock</td>
</tr>
</tbody>
</table>

October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
<table>
<thead>
<tr>
<th>CODES</th>
<th>NUMBER</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>15836</td>
<td>Excision, excessive skin and subcutaneous tissue (includes lipectomy); arm</td>
<td></td>
</tr>
<tr>
<td>15837</td>
<td>Excision, excessive skin and subcutaneous tissue (includes lipectomy); forearm or hand</td>
<td></td>
</tr>
<tr>
<td>15838</td>
<td>Excision, excessive skin and subcutaneous tissue (includes lipectomy); submental fat pad</td>
<td></td>
</tr>
<tr>
<td>15839</td>
<td>Excision, excessive skin and subcutaneous tissue (includes lipectomy); other area</td>
<td></td>
</tr>
<tr>
<td>15847</td>
<td>Excision, excessive skin and subcutaneous tissue (includes lipectomy); abdomen (e.g., abdominoplasty) (includes umbilical transposition and fascial plication)</td>
<td></td>
</tr>
<tr>
<td>15876</td>
<td>Suction assisted lipectomy; head and neck</td>
<td></td>
</tr>
<tr>
<td>15877</td>
<td>Suction assisted lipectomy; trunk</td>
<td></td>
</tr>
<tr>
<td>15878</td>
<td>Suction assisted lipectomy; upper extremity</td>
<td></td>
</tr>
<tr>
<td>15879</td>
<td>Suction assisted lipectomy; lower extremity</td>
<td></td>
</tr>
<tr>
<td>17106</td>
<td>Destruction of cutaneous vascular proliferative lesions (e.g., laser technique); less than 10 sq cm</td>
<td></td>
</tr>
<tr>
<td>17107</td>
<td>Destruction of cutaneous vascular proliferative lesions (e.g., laser technique); 10.0 to 50.0 sq cm</td>
<td></td>
</tr>
<tr>
<td>17108</td>
<td>Destruction of cutaneous vascular proliferative lesions (e.g., laser technique); over 50 sq cm</td>
<td></td>
</tr>
<tr>
<td>17360</td>
<td>Chemical exfoliation for acne (eg, acne paste, acid)</td>
<td></td>
</tr>
<tr>
<td>17380</td>
<td>Electrolysis epilation, each 30 minutes</td>
<td></td>
</tr>
<tr>
<td>17999</td>
<td>Unlisted procedure, skin, mucous membrane and subcutaneous tissue</td>
<td></td>
</tr>
<tr>
<td>19300</td>
<td>Mastectomy for gynecomastia</td>
<td></td>
</tr>
<tr>
<td>19355</td>
<td>Correction of inverted nipples</td>
<td></td>
</tr>
<tr>
<td>21137</td>
<td>Reduction forehead; contouring only</td>
<td></td>
</tr>
<tr>
<td>21138</td>
<td>Reduction forehead; contouring and application of contouring material or bone graft (includes obtaining autograft)</td>
<td></td>
</tr>
<tr>
<td>21139</td>
<td>Reduction forehead; contouring and setback of anterior frontal sinus wall</td>
<td></td>
</tr>
</tbody>
</table>

October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
<table>
<thead>
<tr>
<th>CODES</th>
<th>NUMBER</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>21244</td>
<td>21244</td>
<td>Reconstruction of mandible, extraoral, with transosteal bone plate (eg, mandibular staple bone plate)</td>
</tr>
<tr>
<td>21245</td>
<td>21245</td>
<td>Reconstruction of mandible, or maxilla, subperiosteal implant; partial</td>
</tr>
<tr>
<td>21246</td>
<td>21246</td>
<td>Reconstruction of mandible, or maxilla, subperiosteal implant; complete</td>
</tr>
<tr>
<td>21248</td>
<td>21248</td>
<td>Reconstruction of mandible or maxilla, endosteal implant (eg, blade, cylinder); partial</td>
</tr>
<tr>
<td>21249</td>
<td>21249</td>
<td>Reconstruction of mandible or maxilla, endosteal implant (eg, blade, cylinder); complete</td>
</tr>
<tr>
<td>21270</td>
<td>21270</td>
<td>Malar augmentation, prosthetic material</td>
</tr>
<tr>
<td>21280</td>
<td>21280</td>
<td>Medial canthopexy</td>
</tr>
<tr>
<td>21282</td>
<td>21282</td>
<td>Lateral canthopexy</td>
</tr>
<tr>
<td>21295</td>
<td>21295</td>
<td>Reduction of masseter muscle and bone (eg, for treatment of benign masseteric hypertrophy); extraoral approach</td>
</tr>
<tr>
<td>21296</td>
<td>21296</td>
<td>Reduction of masseter muscle and bone (eg, for treatment of benign masseteric hypertrophy); intraoral approach</td>
</tr>
<tr>
<td>21740</td>
<td>21740</td>
<td>Reconstructive repair of pectus excavatum or carinatum; open</td>
</tr>
<tr>
<td>21742</td>
<td>21742</td>
<td>Reconstructive repair of pectus excavatum or carinatum; minimally invasive approach (Nuss procedure), without thoracoscopy</td>
</tr>
<tr>
<td>21743</td>
<td>21743</td>
<td>Reconstructive repair of pectus excavatum or carinatum; minimally invasive approach (Nuss procedure), with thoracoscopy</td>
</tr>
<tr>
<td>26590</td>
<td>26590</td>
<td>Repair macrodactylyia, each digit</td>
</tr>
<tr>
<td>30120</td>
<td>30120</td>
<td>Excision or surgical planing of skin of nose for rhinophyma</td>
</tr>
<tr>
<td>30400</td>
<td>30400</td>
<td>Rhinoplasty, primary; lateral and alar cartilages and/or elevation of nasal tip</td>
</tr>
<tr>
<td>30410</td>
<td>30410</td>
<td>Rhinoplasty, primary; complete, external parts including bony pyramid, lateral and alar cartilages, and/or elevation of nasal tip</td>
</tr>
<tr>
<td>30420</td>
<td>30420</td>
<td>Rhinoplasty, primary; including major septal repair</td>
</tr>
<tr>
<td>30430</td>
<td>30430</td>
<td>Rhinoplasty secondary; minor revision (small amount of nasal tip work)</td>
</tr>
<tr>
<td>30435</td>
<td>30435</td>
<td>Rhinoplasty secondary; intermediate revision (bony work with osteotomies)</td>
</tr>
<tr>
<td>30450</td>
<td>30450</td>
<td>Rhinoplasty secondary; major revision (nasal tip work and osteotomies)</td>
</tr>
</tbody>
</table>

October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage.
Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
<table>
<thead>
<tr>
<th>CODES</th>
<th>NUMBER</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>31830</td>
<td></td>
<td>Revision of tracheostomy scar</td>
</tr>
<tr>
<td>41510</td>
<td></td>
<td>Suture of tongue to lip for micrognathia (Douglas type procedure)</td>
</tr>
<tr>
<td>49250</td>
<td></td>
<td>Umbilectomy, omphalectomy, excision of umbilicus</td>
</tr>
<tr>
<td>49560</td>
<td></td>
<td>Repair initial incisional or ventral hernia, reducible</td>
</tr>
<tr>
<td>49565</td>
<td></td>
<td>Repair recurrent incisional or ventral hernia, reducible</td>
</tr>
<tr>
<td>49654</td>
<td></td>
<td>Laparoscopy, surgical, repair, incisional hernia (includes mesh insertion, when performed); reducible</td>
</tr>
<tr>
<td>49656</td>
<td></td>
<td>Laparoscopy, surgical, repair, recurrent incisional hernia (includes mesh insertion, when performed); reducible</td>
</tr>
<tr>
<td>54360</td>
<td></td>
<td>Plastic operation on penis to correct angulation</td>
</tr>
<tr>
<td>57291</td>
<td></td>
<td>Construction of artificial vagina; without graft</td>
</tr>
<tr>
<td>57292</td>
<td></td>
<td>Construction of artificial vagina; with graft</td>
</tr>
<tr>
<td>57295</td>
<td></td>
<td>Revision (including removal) of prosthetic vaginal graft; vaginal approach</td>
</tr>
<tr>
<td>57296</td>
<td></td>
<td>Revision (including removal) of prosthetic vaginal graft; open abdominal approach</td>
</tr>
<tr>
<td>57426</td>
<td></td>
<td>Revision (including removal) of prosthetic vaginal graft, laparoscopic approach</td>
</tr>
<tr>
<td>67900</td>
<td></td>
<td>Repair or brow ptosis (supraciliary, mid-forehead or coronal approach)</td>
</tr>
<tr>
<td>67901</td>
<td></td>
<td>Repair of blepharoptosis; frontalis muscle technique with suture or other material (eg, banked fascia)</td>
</tr>
<tr>
<td>67902</td>
<td></td>
<td>Repair of blepharoptosis; frontalis muscle technique with autologous fascial sling (includes obtaining fascia)</td>
</tr>
<tr>
<td>67903</td>
<td></td>
<td>Repair of blepharoptosis; (tarso) levator resection or advancement, internal approach</td>
</tr>
<tr>
<td>67904</td>
<td></td>
<td>Repair of blepharoptosis; (tarso) levator resection or advancement, external approach</td>
</tr>
<tr>
<td>67906</td>
<td></td>
<td>Repair of blepharoptosis; superior rectus technique with fascial sling (includes obtaining fascia)</td>
</tr>
<tr>
<td>67908</td>
<td></td>
<td>Repair of blepharoptosis; conjunctivo-tarso-Muller’s muscle-levator resection (e.g., Fasanella-Servat type)</td>
</tr>
</tbody>
</table>

October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
<table>
<thead>
<tr>
<th>CODES</th>
<th>NUMBER</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>67909</td>
<td>Reconstruction of overcorrection of ptosis</td>
</tr>
<tr>
<td></td>
<td>67911</td>
<td>Correction of lid retraction</td>
</tr>
<tr>
<td></td>
<td>67916</td>
<td>Repair of ectropion; excision tarsal wedge</td>
</tr>
<tr>
<td></td>
<td>67917</td>
<td>Repair of ectropion; extensive (eg, tarsal strip operations)</td>
</tr>
<tr>
<td></td>
<td>67923</td>
<td>Repair of entropion; excision tarsal wedge</td>
</tr>
<tr>
<td></td>
<td>67924</td>
<td>Repair of entropion; extensive (eg, tarsal strip or capsulopalpebral fascia repairs operations)</td>
</tr>
<tr>
<td></td>
<td>67950</td>
<td>Canthoplasty (reconstruction of canthus)</td>
</tr>
<tr>
<td></td>
<td>69090</td>
<td>Ear piercing</td>
</tr>
<tr>
<td></td>
<td>69300</td>
<td>Otoplasty, protruding ear, with or without size reduction</td>
</tr>
<tr>
<td>HCPCS</td>
<td>C9800</td>
<td>Dermal injection procedure(s) for facial lipodystrophy syndrome (LDS) and provision of Radiesse or Sculptra dermal filler, including all items and supplies (Deleted 1/1/2017)</td>
</tr>
<tr>
<td></td>
<td>G0429</td>
<td>Dermal filler injection(s) for the treatment of facial lipodystrophy syndrome (LDS) (e.g., as a result of highly active antiretroviral therapy)</td>
</tr>
<tr>
<td></td>
<td>Q2026</td>
<td>Injection, Radiesse, 0.1 ML</td>
</tr>
<tr>
<td></td>
<td>Q2028</td>
<td>Injection, Sculptra, 0.5 mg</td>
</tr>
</tbody>
</table>

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
Cryosurgical Ablation of Miscellaneous Solid Organ, Pulmonary, and Breast Tumors

Effective: October 1, 2017

Next Review: November 2017
Last Review: June 2017

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Cryoablation kills cells freezing the tissue using a coolant that is circulated via a probe inserted into the tumor.

MEDICAL POLICY CRITERIA

Notes:

- This policy is limited to cryosurgery for the treatment of solid organ tumors, as well as breast and pulmonary tumors.
- This policy does not address liver tumors (primary or metastatic). See Cross References.

I. Cryosurgical ablation for the treatment of kidney and prostate tumors may be considered medically necessary.
II. Cryosurgical ablation is considered **investigational** as a treatment of malignant or benign (fibroadenoma) breast tumors, pulmonary tumors, and all other solid organ tumors including but not limited to bone and pancreatic cancer.

*NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.*

**POLICY GUIDELINES**

It is critical that the list of information below is submitted for review to determine if the policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome.

- History and Physical
- Treatment plan including treatment area.

**CROSS REFERENCES**

1. Radioembolization for Primary and Metastatic Tumors of the Liver, Medicine, Policy No. 140
2. Radiofrequency Ablation of Tumors (RFA), Surgery, Policy No. 92
3. Magnetic Resonance (MR) Guided Focused Ultrasound (MRgFUS) and High Intensity Focused Ultrasound (HIFU) Ablation, Surgery, Policy No. 139
4. Microwave Tumor Ablation, Surgery, Policy No. 189
5. Ablation of Primary and Metastatic Liver Tumors, Surgery, Policy No. 204

**BACKGROUND**

Cryosurgical ablation (also called cryosurgery, cryotherapy, or cryoablation) kills cells (cancerous and normal) by freezing target tissues, most often by inserting a probe into the tumor through which coolant is circulated. Cryosurgery may be performed as an open surgical technique or as a closed procedure under laparoscopic or ultrasound guidance.

The goals of cryosurgery may include the following:

- Destruction or shrinkage of tumor tissue
- Controlling local tumor growth and preventing recurrence
- Palliating symptoms
- Extending survival duration for patients with certain tumors.

Potential complications associated with cryosurgery in any organ include the following:

- Hypothermic damage to normal tissue adjacent to the tumor (e.g., nerve damage)
- Structural damage along the probe track
- Secondary tumors if cancerous cells are seeded during probe removal.

**REGULATORY STATUS**

There are several cryoablation devices cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process for use in open, minimally invasive or endoscopic surgical procedures in the areas of general surgery, urology, gynecology, oncology, neurology, dermatology, proctology, thoracic surgery and ear, nose and throat. Examples include:
• Cryocare® Surgical System by Endocare;
• CryoGen Cryosurgical System by Cryosurgical, Inc.;
• CryoHit® by Galil Medical;
• IceRod® CX, IcePearl® 2.1 CX and IceFORCE® 2.1 CX Cryoablation Needles by Galil Medical;
• SeedNet™ System by Galil Medical;
• Visica® System by Sanarus Medical;
• Visual-ICE® Cryoablation System by Galil;
• ERBECRYO 2® Cryosurgical Unit, ERBE USA Incorporated

EVIDENCE SUMMARY

In order to understand the impact of cryosurgical ablation on local or distant tumor recurrence and disease-free and overall survival in patients with solid tumors, randomized trials are needed that compare this technique with current standard treatments. The standard treatment for most solid tumors is surgical resection. For unresectable solid tumors, alternatives to resection depend on the tumor type and location, and may include thermal ablation, percutaneous ethanol injection, chemoembolization, chemotherapy, and radiation therapy.

Despite the weaknesses in the published clinical evidence, cryosurgical ablation has become a recognized standard of care for tumors of the kidney, liver (addressed in Ablation of Primary and Metastatic Liver Tumors, Surgery, Policy No. 204), and prostate.\[1^{-48}\]

The following literature appraisal focuses on the investigational indications noted in medical policy criterion II above.

BREAST TUMORS

The standard treatment for breast cancer is surgical excision by lumpectomy or mastectomy, with or without adjuvant radiation therapy, chemotherapy, and/or hormone therapy. Fibroadenomas, benign tumors of the breast, generally do not require treatment. If treated, they are typically surgically excised.

SYSTEMATIC REVIEWS

One systematic review was found that included cryoablation along with other minimally-invasive thermal ablation techniques (i.e., radiofrequency, microwave, cryoablation and high-intensity focused ultrasound) for treatment of early-stage breast cancer.\[49\] Zhao et al. reported that studies on cryoablation for breast cancer were primarily limited to pilot and feasibility studies conducted in the research setting. A wide range of 36-83% was reported for complete ablation of tumors. The authors concluded that, while promising, large randomized controlled trials are needed to further evaluate patient selection criteria, techniques to ensure complete tumor ablation, and long-term outcomes compared with surgical excision of breast tumors.

RANDOMIZED CONTROLLED TRIALS (RCTS)

There are no prospective, randomized controlled trials comparing survival and recurrence rates following cryoablation of breast tumors with surgical excision or, for unresectable tumors, with nonoperative therapies.

NONRANDOMIZED STUDIES
The remaining nonrandomized evidence does not permit reliable conclusions concerning the impact of cryosurgical ablation on breast cancer survival or recurrence due to a number of methodological limitations, including: heterogeneous or unreported patient selection criteria, the use of varied cryoablation techniques, nonrandomized allocation of treatment, lack of an appropriate surgical excision control group for comparison, small subject population, and limited data on long-term outcomes.\textsuperscript{[50-63]}

**PULMONARY TUMORS**

**SYSTEMATIC REVIEWS**

Ratko et al. conducted a systematic review for the Agency for Healthcare Research and Quality (AHRQ) on the comparative effectiveness and harms of nonsurgical therapies for non-small cell lung cancer (NSCLC).\textsuperscript{[64]} Patients were divided into the following 3 populations: 1) patients with stage I NSCLC who were not surgical candidates, 2) patients with stage I NSCLC who were surgical candidates but declined surgery, and 3) patients with inoperable endoluminal NSCLC causing obstruction. Only group 3 received therapies other than conformal radiotherapy or radiofrequency ablation including brachytherapy, laser and mechanical debridement, cryoablation, endoluminal stents, and photodynamic therapy. Five of the 17 studies related to group 3 were randomized controlled trials (RCTs), 1 was a nonrandomized comparative study, and 11 were single-arm studies. All five RCTs were rated as poor in quality. The authors concluded that the evidence was insufficient to permit conclusions on the comparative effectiveness of local nonsurgical therapies for any patients with inoperable endoluminal NSCLC causing obstruction.

Lee et al (2011) conducted a systematic review of endoscopic cryoablation of lung and bronchial tumors.\textsuperscript{[65]} Included in the review were 15 case studies and 1 comparative observational study. Cryoablation was performed for inoperable, advanced lung and bronchial cancers in most studies. Some studies included patients with comorbid conditions and poor general health who would not be considered surgical candidates. Complications occurred in 11.1\% of patients (10 studies) and consisted of hemorrhage, mediastinal emphysema, atrial fibrillation, and dyspnea. Within 30 days of the procedure, death from hemoptysis and respiratory failure, considered to be most likely related to disease progression, occurred in 7.1\% of patients. Improvements in pulmonary function and clinical symptoms occurred in studies reporting these outcomes. One published review reported the outcomes of 15 case series and one comparative observational study for endoscopic cryotherapy of endobronchial tumors. Most studies were for inoperable, advanced lung and bronchial cancers. A critical analysis of the studies was not provided. However, the authors noted the significant limitations in the available evidence due to lack of control groups, lack of random treatment allocation, and heterogeneity in study methodologies, participants' characteristics (e.g., comorbid conditions, general health, cancer grade), treatment protocols, operative techniques, and outcome measures. Complications occurred in 11.1\% of patients from ten studies and consisted of hemorrhage, mediastinal emphysema, atrial fibrillation, and dyspnea. Within 30 days of the procedure, death from hemoptysis and respiratory failure, considered to be most likely related to disease progression, occurred in 7.1\% of patients. Improvements in pulmonary function and clinical symptoms occurred in studies reporting these outcomes. Because the studies in the review did not include control groups or compare outcomes of cryosurgery to alternative strategies for managing similar patients, no conclusions can be made on the net health outcomes of cryosurgery for lung cancer.
NONRANDOMIZED STUDIES

The ECLIPSE trial is prospective, multicenter trial of cryoablation for metastatic disease in the lungs, interim results at 1-year follow-up were published in 2015.[66] The trial enrolled 40 patients with 60 metastatic lung lesions who were treated with cryoablation and had at least 12 months of follow-up. Outcomes included survival, local tumor control, quality of life, and complications. Local tumor control was achieved in 94.2% (49/52) of treated lesions, and 1-year OS was 97.5% (39/40). There were no significant changes in quality of life over the 12-month study. The most common adverse event was pneumothorax requiring chest tube insertion in 18.8% (9/48 procedures).

OTHER TUMORS

Cryoablation for the treatment of other solid tumors has not been well-studied.

SYSTEMATIC REVIEWS

In 2014, Keane et al. reported on a systematic review of ablation therapies, including cryoablation, for locally advanced pancreatic cancer.[67] The review noted studies have demonstrated ablative therapies, including cryoablation, are feasible but larger studies are needed. No conclusions could be made on whether ablation resulted in better oncologic outcomes than best supportive care.

In 2012, Tao and colleagues reported on a systematic review of cryoablation for pancreatic cancer.[68] The authors identified 29 studies from the literature search and included 5 of these studies in the review. The 5 studies were all case series and considered to be of low quality. Adverse events, when mentioned in the studies, included delayed gastric emptying (0% to 40.9% in 3 studies), pancreatic leak (0% to 6.8% in 4 studies), biliary leak (0% to 6.8% in 3 studies), and one instance of upper gastrointestinal hemorrhage. Pain relief was reported in 3 studies and ranged from 66.7% to 100%. Median survival times reported in 3 studies ranged from 13.4 to 16 months. One-year total survival rates reported in 2 studies were 57.5% and 63.6%.

RANDOMIZED CONTROLLED TRIALS

One preliminary randomized trial studied 36 female patients with NSCLC who also had epidermal growth factor receptor gene mutations.[69] All patients received 6 months treatment with molecular target therapy gefitinib, an epidermal growth factor receptor-tyrosine kinase inhibitor. Patients were randomized to either an experimental group and underwent cryoablation prior to receiving gefitinib, or to a control group in which cryoablation was not performed. At 1-year follow-up, the survival rate in the cryoablation group was significantly higher than that of the control group. The findings of this preliminary study suggest that cryoablation may improve the effects of gefitinib in this patient population. Additional larger, long-term randomized trials are needed to validate these findings.

NONRANDOMIZED STUDIES

The remaining published literature is limited to case series and retrospective reviews.[70-79] As discussed above, these studies do not permit reliable conclusions concerning the impact of cryoablation on health outcomes.
Clinical practice guidelines from U.S. professional associations consistently list cryoablation as a treatment option for tumors of the kidney or prostate.\textsuperscript{[80-84]}

No clinical practice guidelines or position statements from U.S. professional societies were identified that recommend cryoablation for the treatment of solid tumors other than kidney and prostate tumors.\textsuperscript{[85-93]}

Cryosurgical ablation has become a recognized standard of care in the management of tumors of the kidney and prostate. Therefore, this technique may be considered medically necessary in the treatment of these tumors.

There is not enough research to show that cryosurgical ablation for the treatment of solid organ, pulmonary, bone, and breast tumors other than tumors of the kidney or prostate improves health outcomes. In addition, there are no clinical practice guidelines that recommend the use of cryosurgical ablation of those tumors. Therefore, cryosurgical ablation as a treatment for solid organ, pulmonary, bone, and breast tumors other than those of the kidney or prostate is considered investigational.

REFERENCES

9. Kornprat, P, Jarnagin, WR, DeMatteo, RP, Fong, Y, Blumgart, LH, D'Angelica, M. Role of intraoperative thermoablation combined with resection in the treatment of hepatic...


94. BlueCross BlueShield Association Medical Policy Reference Manual "Cryosurgical Ablation of Miscellaneous Solid Tumors Other Than Liver, Prostate, or Dermatologic Tumors." 7.01.92
95. BlueCross BlueShield Association Medical Policy Reference Manual "Cryosurgical Ablation of Primary or Metastatic Liver Tumors." Policy No. 7.01.75
96. BlueCross BlueShield Association Medical Policy Reference Manual "Whole Gland Cryoablation of Prostate Cancer." Policy No. 7.01.79

<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>19105</td>
<td>Ablation, cryosurgical, of fibroadenoma, including ultrasound guidance, each fibroadenoma</td>
</tr>
<tr>
<td></td>
<td>20983</td>
<td>Ablation therapy for reduction or eradication of 1 or more bone tumors (eg, metastasis) including adjacent soft tissue when involved by tumor extension, percutaneous, including imaging guidance when performed; cryoablation</td>
</tr>
<tr>
<td></td>
<td>31641</td>
<td>Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with destruction of tumor or relief of stenosis by any method other than excision (eg, laser therapy, cryotherapy)</td>
</tr>
<tr>
<td></td>
<td>50250</td>
<td>Ablation, open, 1 or more renal mass lesion(s), cryosurgical, including intraoperative ultrasound guidance and monitoring, if performed</td>
</tr>
<tr>
<td></td>
<td>50542</td>
<td>Laparoscopy, surgical; ablation of renal mass lesion(s), including intraoperative ultrasound guidance and monitoring, when performed</td>
</tr>
<tr>
<td></td>
<td>50593</td>
<td>Ablation, renal tumor(s), unilateral, percutaneous, cryotherapy</td>
</tr>
<tr>
<td></td>
<td>55873</td>
<td>Cryosurgical ablation of the prostate (includes ultrasonic guidance and monitoring)</td>
</tr>
<tr>
<td></td>
<td>0340T</td>
<td>Ablation, pulmonary tumor(s), including pleura or chest wall when involved by tumor extension, percutaneous, cryoablation, unilateral, includes imaging guidance</td>
</tr>
</tbody>
</table>

**HCPCS**  None

*Date of Origin: March 2004*
**Deep Brain Stimulation**

**Effective:** October 1, 2017

**Next Review:** March 2018  
**Last Review:** September 2017

**IMPORTANT REMINDER**

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

**DESCRIPTION**

Deep brain stimulation (DBS) involves the stereotactic placement of an electrode into the brain [i.e., hypothalamus, thalamus, globus pallidus or subthalamic nucleus (STN)].

**MEDICAL POLICY CRITERIA**

**Notes:**

- The use of spinal cord stimulation as a treatment of chronic pain is addressed in a separate policy (see Cross References section below).
- This policy only applies to initial placement. This policy does not apply to revision(s) and replacement(s) after implantation.

I. When a multidisciplinary evaluation has confirmed both the medical intractability of the patient's symptoms and the potential value of deep brain stimulation (DBS), unilateral or bilateral DBS may be considered **medically necessary** when **both** of the following criteria (A and B) are met:

   A. One of the following is met:

      1. The request is for stimulation of the thalamus in patients with disabling, medically unresponsive tremor due to essential tremor or Parkinson's
disease. Disabling, medically unresponsive tremor defined as tremor causing significant limitation in daily activities AND inadequate symptom control despite optimal medical management for at least 3 months before implant.

2. The request is for stimulation of the subthalamic nucleus or globus pallidus in patients with previously levodopa-responsive Parkinson’s disease and symptoms such as rigidity, bradykinesia, dystonia or levodopa-induced dyskinesias.

3. The request is for stimulation of the subthalamic nucleus or globus pallidus in patients 7 years of age or above with disabling, medically unresponsive primary dystonias including generalized and/or segmental dystonia, hemidystonia and cervical dystonia (torticollis). Disabling, medically unresponsive dystonia defined as dystonia causing significant limitation in daily activities AND inadequate symptom control despite optimal medical management for at least 3 months before implant.

B. The patient does not have any of the following contraindications:

1. Patients who are not good surgical risks because of comorbid medical problems or because of the presence of a cardiac pacemaker; and

2. Patients who have medical conditions that require repeated MRI; and

3. Patients who have dementia that may interfere with the ability to cooperate.

II. Deep brain stimulation is considered *investigational* for all other conditions, including, but not limited to the following:

A. Tardive dyskinesia and tardive dystonia

B. Cerebral Palsy

C. Traumatic brain injury (TBI)

D. Chronic pain (e.g., nociceptive pain; neuropathic pain)

E. Epilepsy/intractable seizures

F. Morbid obesity

G. Multiple sclerosis

H. Cognitive decline/dementia due to Parkinson’s Disease

I. Other movement disorders

J. Post-traumatic tremor

K. Huntington’s disease

L. Cluster headaches

M. Facial pain

N. Neuropsychiatric applications, including but not limited to the following:

1. Tourette syndrome

2. Depression
3. Bipolar Disorder
4. Obsessive-compulsive disorder
5. Schizophrenia
6. Anxiety
7. Anorexia nervosa
8. Treatment of addiction including alcohol addiction

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

CROSS REFERENCES
1. Spinal Cord and Dorsal Root Ganglion Stimulation, Surgery, Policy No. 45
2. Dopamine Transporter Single-Photon Emission Computed Tomography, Radiology, Policy No. 57

BACKGROUND

The electrode is initially attached to a temporary transcutaneous cable for short-term stimulation to validate treatment effectiveness. Several days later the patient returns to surgery for permanent subcutaneous implantation of the cable and a radiofrequency-coupled or battery-powered programmable stimulator. The electrode is typically implanted unilaterally on the side corresponding to the more severe symptoms. However, the use of bilateral stimulation using two electrode arrays is also used in patients with bilateral, severe symptoms.

After implantation, noninvasive programming of the neurostimulator can be adjusted to the patient's symptoms. This feature may be important for patients with Parkinson's disease, whose disease may progress over time, requiring different neurostimulation parameters. Setting the optimal neurostimulation parameters may involve the balance between optimal symptom control and appearance of side effects of neurostimulation, such as dysarthria, disequilibrium or involuntary movements.

DBS has been investigated for a variety of indications as discussed below:

- Alternative to permanent neuroablative procedures, such as thalamotomy and pallidotomy

The technique has been most thoroughly investigated as an alternative to thalamotomy for unilateral control of essential tremor, and tremor associated with Parkinson's disease (PD). More recently, there has been research interest in the use of deep brain stimulation of the globus pallidus or STN as a treatment of other Parkinsonian symptoms such as rigidity, bradykinesia or akinesia. Another common morbidity associated with PD is the occurrence of motor fluctuations, referred to as "on and off" phenomena, related to the maximum effectiveness of drugs (i.e., the "on" state) and the nadir response during drug troughs (i.e., the "off" state). In addition, levodopa, the most commonly used antiparkinson drug, may be associated with disabling drug-induced dyskinesias. Therefore, the optimal pharmacologic treatment of Parkinson's disease may involve a balance between optimal effects on Parkinson's symptoms vs. the appearance of drug induced dyskinesias. The effect of DBS on both Parkinson's symptoms and drug-induced dyskinesias has also been studied.
• Treatment of primary and secondary dystonia

Dystonia is defined as a neurological movement disorder characterized by involuntary muscle contractions, which force certain parts of the body into abnormal, contorted, and painful movements or postures. In primary dystonia, dystonia is the only symptom and is unassociated with other pathology. Secondary dystonia is a dystonia brought on by an inciting event, such as a stroke, trauma, or drugs. Tardive dystonia is a form of drug-induced secondary dystonia. Dystonia can be classified according to age of onset, bodily distribution of symptoms, and cause. Age of onset can occur during childhood or during adulthood. Dystonia can affect certain portions of the body (focal dystonia and multifocal dystonia) or the entire body (generalized dystonia). Torticollis is an example of a focal dystonia. Treatment options for dystonia include oral or injectable medications (i.e., botulinum toxin) and destructive surgical or neurosurgical interventions (i.e., thalamotomies or pallidotomies) when conservative therapies fail.

• Cluster headaches

Cluster headaches occur as episodic attacks of severe pain lasting from 30 minutes to several hours. The pain is usually unilateral and localized to the eye, temple, forehead, and side of the face. Autonomic symptoms that occur with cluster headaches include ipsilateral facial sweating, flushing, tearing, and rhinorrhea. Cluster headaches occur primarily in men and have been classified as vascular headaches that have been associated with high blood pressure, smoking, and alcohol use. However, the exact pathogenesis of cluster headaches is uncertain. PET scanning and MRI have shown the hypothalamic region may be important in the pathogenesis of cluster headaches. Alterations in hormonal-serotonergic function may also play a role. Treatment of cluster headaches includes pharmacologic interventions for acute episodes and prophylaxis, sphenopalatine ganglion (SPG) blockade and surgical procedures such as percutaneous SPG radiofrequency rhizotomy and gamma knife radiosurgery of the trigeminal nerve.

• Other Neurologic/Psychiatric Conditions

The role of DBS in treatment of other treatment-resistant neurologic and psychiatric disorders, particularly Tourette syndrome, epilepsy, obsessive-compulsive disorder (OCD), major depressive disorders, bipolar disorder, anorexia, and alcohol addiction, is also being investigated. Ablative procedures are irreversible and, though they have been refined, remain controversial treatments for intractable illness. Interest has shifted to neuromodulation through DBS of nodes or targets within neural circuits involved in these disorders. Currently, a variety of target areas are being studied.

REGULATORY STATUS

The U.S. Food and Drug Administration (FDA) has approved the Activa® Tremor Control System (Medtronic Corp.) for deep brain stimulation. The Activa® Tremor Control System and the Activa® Dystonia Therapy System consist of the following components:

1. The implantable pulse generator
2. The deep brain stimulator lead
3. An extension that connects the lead to the power source
4. A console programmer
5. A software cartridge to set electrical parameters for simulation
6. A patient control magnet, which allows the patient to turn the pulse generator on and off or change between high and low settings

In February 2009, the FDA approved deep brain stimulation with the Reclaim device (Medtronic, Inc.) via the Humanitarian Device Exemption (HDE) process for the treatment of severe obsessive-compulsive disorder (OCD).

In June 2015, the FDA approved deep brain stimulation with the Brio Neurostimulation System, (St. Jude Medical) under the Premarket Approval Application (PMA) process (#P140009) for the following conditions:[1]

- Bilateral stimulation of the subthalamic nucleus (STN) as an adjunctive therapy to reduce some of the symptoms of advanced levodopa-responsive Parkinson’s disease that are not adequately controlled by medications.

- Unilateral or bilateral stimulation of the ventral intermediate nucleus (VIM) of the thalamus for the suppression of disabling upper extremity tremor in adult essential tremor patients whose tremor is not adequately controlled by medications and where the tremor constitutes a significant functional disability.

In September 2016, the FDA approved the St. Jude Medical Infinity™ Deep Brain Stimulation (DBS) system under the PMA process (#P140009/S001) for the same indications above.

EVIDENCE SUMMARY

The principal outcome for deep brain stimulation (DBS) for any indication is symptom reduction and improved function. Assessment of the safety and efficacy of DBS requires well-designed and well-executed randomized controlled trials (RCTs) comparing DBS with sham or on-versus off- phases to determine the following:

- whether the benefits of DBS outweigh any risks
- whether DBS offers advantages over conventional treatments.

The evidence base is sufficient that deep brain stimulation (DBS) improves the net health outcomes of selected patients with symptoms related to Parkinson's disease, essential tremor, or primary dystonias. DBS has become a standard of care for these patients and may be considered medically necessary when criteria are met. Therefore, the evidence for DBS for these indications will not be reviewed in this policy. Below is a brief synopsis of the evidence for Parkinson's disease, essential tremor, or primary dystonias.

SYMPTOMS ASSOCIATED WITH PARKINSON’S DISEASE

Systematic Reviews and Technology Assessments

The policy for PD and tremor was initially based on two BlueCross BlueShield Association Technology Evaluation Center (TEC) Assessments; a 1997 TEC Assessment focused on unilateral deep brain stimulation of the thalamus as a treatment for tremor[2] and a 2001 TEC Assessment focused on the use of deep brain stimulation of the globus pallidus and subthalamic nucleus for a broader range of Parkinson symptoms.[3]
A number of large systematic reviews have been published on the use of DBS for PD and tremor\cite{4-13} confirming the efficacy of DBS in the control of motor signs and improvement of patients' functionality and quality of life.

**Randomized Controlled Trials**

There have been additional published RCTs of deep brain stimulation for PD, which continue to report overall positive results \cite{14-22}. Some of these trials suggest that subthalamic stimulation was superior to medical therapy in patients with Parkinson's disease and early motor complications, while others did not find significant differences in overall health outcomes for patients. Surgery related adverse effects addressed in these RCTs indicate that the most common adverse effect is infection.

**PRIMARY DYSTONIA**

DBS for the treatment of primary dystonia received FDA approval through the Humanitarian Device Exemption (HDE) process.\cite{23} The HDE approval process is available for those conditions that affect less than 4,000 Americans per year. According to this approval process, the manufacturer is not required to provide definitive evidence of efficacy, but only probable benefit. As noted in the FDA’s analysis of risk and probable benefit, the only other treatment options for chronic refractory primary dystonias are neurodestructive procedures. DBS provides a reversible alternative. The FDA summary of Safety and Probable Benefit states, “Although there are a number of serious adverse events experienced by patients treated with deep brain stimulation, in the absence of therapy, chronic intractable dystonia can be very disabling and in some cases, progress to a life-threatening stage or constitute a major fixed handicap. When the age of onset of dystonia occurs prior to the individual reaching their full adult size, the disease not only can affect normal psychological development but also cause irreparable damage to the skeletal system. As the body of the individual is contorted by the disease, the skeleton may be placed under constant severe stresses that may cause permanent disfigurement. Risks associated with DBS for dystonia appear to be similar to the risk associated with the performance of stereotactic surgery and the implantation of DBS systems for currently approved indications Parkinson’s Disease and Essential Tremor), except when used in either child or adolescent patient groups.”

The FDA HDE approval was based on the results of DBS in 201 patients represented in 34 manuscripts. There were three studies that reported at least ten cases. Clinical improvement ranged from 50 to 88%. A total of twenty-one pediatric patients were studied; 81% were older than seven years. Among these patients there was approximately a 60% improvement in clinical scores.

Since the FDA approval, there have been additional published randomized controlled trials of deep brain stimulation for dystonia, which continue to report positive results.\cite{24-26} These trials included one with a long-term follow-up of five years. Two of the trials reported on the serious adverse effects of DBS, the majority of which were related to the implantation procedure. Dysarthria, involuntary movements and depression were common non-serious adverse events reported.

In 2017, Moro et al published a systematic review of literature published through November 2015 on primary dystonia (also known as isolated dystonia).\cite{27} Reviewers included studies with at least 10 cases. Fifty-eight articles corresponding to 54 unique studies were identified; most involved bilateral DBS of the GPi. There were only 2 controlled studies, 1 RCT (described
below) and 1 study that included a double-blind evaluation with and without stimulation. Twenty-four studies reported data using the Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS) and were included in a meta-analysis. These studies enrolled a total of 523 patients (mean per study, 22 patients) and had a mean follow-up of 32.3 months (range, 6-72 months). In a pooled analysis of BFMDRS motor scores (scale range, 0-120) from 24 studies, the mean increase in scores at 6 months compared with baseline was 23.8 points (95% CI, 18.5 to 29.1 points). The mean increase in the motor score at last follow-up compared with baseline was 26.6 points (95% CI, 22.4 to 30.9 points). The mean percentage improvement was 59% at 6 months and 65% at last follow-up. Fourteen studies reported BFMDRS disability scores (scale range, 0-30). Compared with baseline, the mean absolute change in the score was 4.8 points (95% CI, 3.1 to 6.6 points) at 6 months and 6.4 points (95% CI, 5.0 to 7.8 points) at last follow-up. The mean percentage improvement was 44% at 6 months and 59% at last follow-up.

The remaining literature review below will focus on the use of DBS for the investigational indications in this policy.

TARDIVE DYSKINESIA AND TARDIVE DYSTONIA

Systematic Review

Tardive dyskinesia and dystonia (TDD) are severe side effects of dopamine-blocking agents, particularly antipsychotics. Little is known about the possible psychiatric complications of DBS in psychiatric patients. The mean improvement of TDD of the combined patients 3 to 76 months after implantation was 77.5% (95% CI, 71.4%-83.3%; P < .000) on the Burke-Fahn-Marsden Dystonia Rating Scale.[28] The data suggest DBS could be effective and relatively safe for patients with treatment-resistant TDD; however, these results should be interpreted with caution, as most of the data are from case reports and small trials.

Mentzel et al. performed a systematic review to assess the effects and side-effects of deep brain stimulation (DBS) in patients that have developed a severe debilitating treatment-resistant form of TDD.[29] This review included 19 case-reports and small-scale trials without randomization or blinding (N= 52 patients). Using the Burke Fahn Marsden Dystonia Rating Scale (BFMDRS), the Abnormal Involuntary Movement Scale (AIMS) and the Extrapyramidal Symptoms Rating Scale (ESRS), the investigators assessed the average improvement in the patients' condition, reporting that improvement as a result of DBS was statistically significant (p < 0.00001) on all scales. However, limited conclusions can be drawn from this review on the efficacy and safety of DBS in this population, since there were no randomized controlled trials identified.

Randomized Controlled Trials

Stimulation of the globus pallidus has been examined as a treatment of tardive dyskinesia in a phase II double-blinded (presence and absence of stimulation) multicenter study.[30] The trial was stopped early due to successful treatment (greater than 40% improvement) in the first 10 patients.

No comparative trials were found for DBS for tardive dystonia, though one small (n=9) case series reported improvement in motor and disability scores.[31]
Koy and others recently reported data on the therapeutic outcomes of DBS in cerebral palsy.[32] Twenty articles comprising 68 patients with cerebral palsy undergoing deep brain stimulation assessed by the Burke-Fahn-Marsden Dystonia Rating Scale were identified. Most articles were case reports reflecting great variability in the score and duration of follow-up. The mean Burke-Fahn-Marsden Dystonia Rating Scale movement score was 64.94 ± 25.40 preoperatively and dropped to 50.5 ± 26.77 postoperatively, with a mean improvement of 23.6% (P < .001) at a median follow-up of 12 months. The mean Burke-Fahn-Marsden Dystonia Rating Scale disability score was 18.54 ± 6.15 preoperatively and 16.83 ± 6.42 postoperatively, with a mean improvement of 9.2% (P < .001). There was a significant negative correlation between severity of dystonia and clinical outcome (P < .05). Authors suggest DBS can be an effective treatment option for dyskinetic cerebral palsy. In view of the heterogeneous data, a prospective study with a large cohort of patients in a standardized setting with a multidisciplinary approach would be helpful in further evaluating the role of deep brain stimulation in cerebral palsy.[33]

**EPILEPSY/INTRACTABLE SEIZURES**

DBS has been investigated for the treatment of intractable seizures in patients who are not surgical candidates. To date studies show promise but these early reports of therapeutic success are not confirmed by controlled clinical trials. Questions regarding the best structures to stimulate, the most effective stimuli, and the contrasting effects of high-frequency and low-frequency stimulation remain unanswered.

**Systematic Review**

In a 2014 Cochrane review, the safety, efficacy and tolerability of DBS and cortical stimulation were assessed in patients with refractory epilepsy.[34] The review included RCTs comparing DBS to sham stimulation, resective surgery or further treatment with antiepileptic drugs. Of the 10 RCTs identified for inclusion, three trials were specific to DBS (1 anterior thalamic DBS trial, n=109 treatment periods; 2 centromedian thalamic DBS trials, n=20, 40 treatment periods). The primary outcome measures included the proportion of patients who were disease free and a 50% or greater reduction in seizure frequency after 1-3 months. The evidence was rated as moderate quality and no statistical or clinically significant differences were reported based upon the primary outcome measures. Authors concluded that there is insufficient evidence upon which to draw conclusions regarding the efficacy and safety of hippocampal DBS or centromedian DBS as a treatment for epilepsy.

**Randomized Controlled Trials**

One multicenter, RCT of bilateral stimulation of the anterior nuclei of the thalamus for epilepsy (SANTE) was found in the published literature.[35] Fisher et al randomized patients who had failed at least 3 antiepileptic drugs to one of two groups, stimulation on or stimulation off. This was a 3-month double blind phase. After this phase, all patients received unblinded stimulation. During the first and second months of the blinded phase, the difference in seizure reduction between stimulation on and stimulation off was not significantly different (-42.1% vs. -28.7%, respectively). In the last month of the blinded phase, the stimulated group had a greater reduction in seizures compared with the control group (-40.4% vs. -14.5%, respectively p=0.0017). During the blinded phase, the stimulation group experienced significantly fewer seizure-related injuries than patients in the control group (7.4% vs. 25.5%, respectively p=0.01). Cognition and mood showed no group differences, but participants in the stimulated group were more likely to report depression (8 vs. 1, respectively) or memory problems (7 vs.
1, respectively) as adverse events. Depression symptoms resolved in 4 of the 8 stimulated patients over an average of 76 days (range 14-145). There was a progressive reduction in seizure frequency over long-term follow-up. On intention-to-treat analysis, the median change in seizure frequency was -44% at 13 months and -57% at 25 months. By 2 years, 54% of patients had a seizure reduction of at least 50%, and 14 patients (13%) were seizure-free for at least 6 months. The most common device-related adverse events were paresthesias in 18.2% of participants, implant site pain in 10.9%, and implant site infection in 9.1%. Eighteen participants (16.4%) withdrew from the study after the implantation because of adverse events. There were 5 deaths, none of which were considered to be device-related. Although some patients appeared to have benefited from treatment during the extended follow-up phase, the difference between groups in the blinded portion of the study, while significant, was modest.

Thalamic stimulation for epilepsy is approved in several countries, but not presently in the U.S. Additional studies are needed to establish its role in treating patients with epilepsy and intractable seizures.

Nonrandomized Studies

Long-term outcomes of the SANTE trial, described above, were reported by Salanova et al. in 2015.[36] The uncontrolled open-label portion of the trial began after 3 months and, beginning at 13 months, stimulation parameters could be adjusted at the clinician’s discretion. Of the 110 implanted patients, 105 (95%) completed the 13-month follow-up, 98 (89%) completed the 3-year follow-up, and 83 (75%) completed 5 years. Among patients with at least 70 days of diary entries, the median change in seizure frequency from baseline was 41% at 1 year and 69% at 5 years (p<0.001 for both). During the study, 39 (35%) of 110 patients had a device-related serious adverse event, Most of which occurred in the first several months after implantation. The most frequently reported serious adverse events were implant site infection (10% of patients) and lead(s) not within target (8.2% of patients). Seven deaths occurred during the study and none were considered to be device-related. Depression was reported in 41 (37%) patients over the study; in 3 cases, this was considered device-related. Memory impairment (nonserious) was reported in 30 (27%) patients during the study, half of which had a history of the condition. Although some patients appear to have benefited from treatment during the extended follow-up phase, the difference between groups in the blinded portion of the study, while significant, was overall modest.

TRAUMATIC BRAIN INJURY

Central thalamic deep brain stimulation (CT-DBS) has been investigated as a therapeutic option to improve behavioral functioning in patients with severe traumatic brain injury (TBI)[33]; however, there are no RCTs for this indication.

NEUROPSYCHIATRIC APPLICATIONS

In addition to the areas of research discussed above, DBS is being investigated for the treatment of Tourette syndrome, depression, addiction, alcohol addiction, anorexia, and obsessive compulsive disorder.[37] Evidence remains insufficient to evaluate the efficacy of DBS for these disorders.[38]

Tourette Syndrome

Systematic Reviews
Baldermann et al. conducted a systematic review that included 57 studies on DBS for Tourette syndrome, four of which were randomized crossover studies. The studies included a total of 156 cases.\textsuperscript{[39]} Twenty-four studies included a single patient each and four had sample sizes of 10 or more (maximum, 18). Half of the patients (n=78) were stimulated in the thalamus and the next most common areas of stimulation were the global pallidus internus anteromedial part (n=44) and postventrolateral part (n=20). Two of the RCTs used thalamic stimulation, one used bilateral globus pallidus stimulation, and one used both. The primary outcome was the Yale Global Tic Severity Scale (YGTSS). In a pooled analysis of within subject pre-post data, there was a median improvement of 53\% in the YGTSS, a decline from a median score of 83 to 35 at last follow-up. Moreover, 81\% of patients showed at least a 25\% reduction in the YGTSS and 54\% and more than a 50\% improvement. In addition, data were pooled from the 4 crossover RCTs; there were a total of 27 patients receiving DBS and 27 receiving a control intervention. Targets included the thalamus and the globus pallidus. In the pooled analysis, there was a statistically significant between-group difference, favoring DBS (SMD=0.96; 95\% CI, 0.36 to 1.56). The authors noted that the effect size of 0.96 is considered to be a large effect.

A 2012 systematic review by Pansaon et al. identified 25 published studies, representing data from 69 patients that reported on the efficacy of DBS in the treatment of Tourette syndrome.\textsuperscript{[40]} However, only 3 studies with methodological quality ratings of fair to poor met the inclusion criteria for evidence-based analysis. The authors recommend that DBS continues to be considered an experimental treatment for severe, medically refractory tics.

**Randomized Controlled Trials**

Kefalopoulou et al. reported on double-blind crossover trial that included 15 patients with severe medically refractory Tourette syndrome.\textsuperscript{[41]} They received surgery for bilateral globus pallidus internus DBS and were randomized to the off-position first or the on-position first for 3 months followed by the opposite position for the next 3 months. Fifteen patients underwent surgery 14 were randomized and 13 completed assessments after both on- and off-phases. For the 13 study completers, the mean YGTSS scores were 80.7 (SD=12.0) in the off-stimulation phase and 68.3 (SD=18.6) in the on-stimulation phase. Mean difference in YGTSS scores was 12.4 (95\% CI, 0.1 to 24.7) which was statistically significant (p=0.048) after Bonferroni correction. There was no between-group difference in YGTSS scores in patients who were randomized to the on-phase first or second. Three serious adverse events were reported, 2 related to surgery and 1 related to stimulation. The authors noted that the most effective target for DBS in Tourette syndrome patients needs additional study.

Piedad et al. analyzed patient and target selection for DBS of Tourette syndrome. The majority of clinical trials for DBS in Tourette syndrome have targeted the medial thalamus at the crosspoint of the centromedian nucleus, substantia periventricularis, and nucleus ventro-oralis internus.\textsuperscript{[42]} Other targets that have been investigated include the subthalamic nucleus, caudate nucleus, globus pallidus internus, and the anterior limb of the internal capsule and nucleus accumbens. The review found no clear consensus in the literature for the best target or for which patients should be treated. Additional study is needed to clarify these issues.

In 2011, Ackermans et al. reported preliminary results of a double-blind crossover trial of thalamic stimulation in 6 patients with refractory Tourette syndrome.\textsuperscript{[43]} Tic severity during 3 months of stimulation was significantly lower than during the 3 months with the stimulator turned off, with a 37\% improvement on the Yale Global Tic Severity Scale (mean 25.6 vs. 15.5). These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
41.1) and a decrease in tic severity of 49% at 1 year after surgery compared to preoperative assessments (mean 21.5 vs. 42.2 – both respectively). Secondary outcomes (change in associated behavioral disorder and mood) were not altered by the stimulation. Serious adverse events included one small hemorrhage ventral to the tip of the electrode, one infection of the pulse generator, subjective gaze disturbances, and reduction of energy levels in all patients. The interim analysis led to the termination of the trial. The authors commented that further RCTs on other targets are urgently needed since the search for the optimal one is still ongoing.

**Depression**

**Systematic Reviews**

In a recent systematic review, the literature was identified and reviewed for research findings related to treatment-resistant BD. Therapeutic trials for treatment-resistant bipolar mania are uncommon, and provide few promising leads other than the use of clozapine. Far more pressing challenges are the depressive-dysthymic-dysphoric-mixed phases of BD and long-term prophylaxis. Therapeutic trials for treatment-resistant bipolar depression have assessed various pharmacotherapies, behavioral therapies, and more invasive therapies including electroconvulsive therapy (ECT), transcranial magnetic stimulation, and deep brain stimulation—all of which are promising but limited in effectiveness. Most studies identified in the review were small, involved supplementation of typically complex ongoing treatments, varied in controls, randomization, and blinding, usually involved brief follow-up, and lacked replication. Clearer criteria for defining and predicting treatment resistance in BD are needed, as well as improved trial design with better controls, assessment of specific clinical subgroups, and longer follow-up. Due to significant limitations within literature the effectiveness of DBS for bipolar treatment is not known at this time.

**Randomized Controlled Trials**

In 2016, a crossover RCT evaluating active and sham phases of DBS stimulation in patients with treatment-resistant depression was published by Bergfeld et al. Twenty-five patients were enrolled. Prior to the randomized phase, all patients received 52 weeks of open-label DBS treatment with optimization of the settings. Optimization ended when patients achieved a stable response of at least 4 weeks or after the 52-week period ended. At the end of the open-label phase, 10 (40%) patients were classified as responders (≥50% decrease in the Hamilton Depression Rating Scale [HAM-D] score) and 15 (60%) patients were classified as nonresponders. After the 52 weeks of open-label treatment, patients underwent 6 weeks of double-blind active and sham stimulation. Sixteen (64%) of 25 enrolled patients participated in the randomized phase (9 responders, 7 nonresponders). Nine patients were prematurely crossed over to the other intervention. Among all 16 randomized patients, HAM-D scores were significantly higher at the end of the active stimulation phase (mean HAM-D score, 16.5) than the sham stimulation phase (mean HAM-D score, 23.1; p<0.001). Mean HAM-D scores were similar after active and sham phases in initial nonresponders (19.0 vs 23.0, respectively). Among initial responders, mean HAM-D score was 9.4 after active stimulation and 23 after sham stimulation. Trial limitations include a small number of patients in the randomized phase and potential bias from having an initial year of open-label treatment; patients who had already responded to DBS over a year of treatment were those who were likely to respond to active than sham stimulation in the double-blind randomized phase;
findings may not be generalizable to treatment-resistant depressed patients who are DBS-naive.

Dougherty et al. published an industry-sponsored, double-blind RCT evaluating DBS of the ventral capsule/ventral striatum in patients with chronic treatment resistant depression, including 30 patients with a major depressive episode lasting at least 2 years and inadequate response to at least 4 trials of antidepressant therapy. Participants were randomized to 16 weeks of active (n=16) versus sham (n=14) DBS, followed by an open-label continuation phase. One patient, who was assigned to active treatment, dropped out of the study during the blinded treatment phase. The primary outcome was clinical response at 16 weeks, defined as 50% or greater improvement from baseline on the Montgomery-Asberg Depression Rating Scale (MADRS). A response was identified in 3 (20%) of 15 patients in the active treatment group and 2 (14%) of 14 patients in the sham control group. The between-group difference in response was not statistically significant (p=0.53). During the blinded treatment phase, psychiatric adverse events occurring more frequently in the active treatment group included worsening depression, insomnia, irritability, suicide ideation, hypomania, and mania. Psychiatric adverse events occurring more frequently in the sham control group were early morning awakening and purging. Findings of this study do not support the conclusion that DBS is effective for treating treatment-resistant depression.

## Obsessive-compulsive Disorder

### Systematic Reviews

Kisely et al. conducted a systematic review and meta-analyses pooling study findings evaluating DBS for OCD, including only double-blind RCTs of active versus sham DBS. Five trials (total N=50 patients) met eligibility criteria and data on 44 patients were available for meta-analysis. Three were parallel group RCTs with or without a crossover phase and 2 were only crossover trials. The site of stimulation was the anterior limb of the internal capsule (3 studies), the nucleus accumbens (1 study) and the subthalamic nucleus (1 study). Duration of treatment ranged from 2 to 12 weeks. All studies reported scores on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS). This is a 10-item scale in which higher scores reflect more intense symptoms, and a score of 24 or more (of a possible 40) is considered severe illness. Most studies designate a therapeutic response as a Y-BOCS reduction of 35% or more from the pretreatment baseline, with a reduction of 25-35% or more considered a partial response. Only one of the five studies reported proportion of responders Y-BOCS as an outcome measure and that study did not find a statistically significant difference between active and sham stimulation groups. All studies reported the outcome measure, mean reduction in Y-BOCS. When data from the 5 studies were pooled, there was a statistically significantly greater reduction in the mean Y-BOCS in the active versus sham group (mean difference, -8.49; 95% CI, 12.18 to -4.80). The outcome measure, however, does not allow conclusions on whether the difference between groups is clinically meaningful. Trial authors reported 16 serious adverse events including one cerebral hemorrhage and two infections requiring electrode removal. Additionally, nonserious transient adverse events were reported including 13 reports of hypomania, five of increase in depressive or anxious symptoms and 6 of headaches.

A 2015 systematic review and meta-analysis by Alonso et al included studies of any type (including case reports) evaluating DBS for OCD and reporting changes on the Y-BOCS. The authors identified 31 studies (total N=116 patients). They did not report study type (ie,
controlled vs uncontrolled); however, the meta-analysis was only of patients who received active treatment. Twenty-four (77%) studies included 10 or fewer patients. Most studies (24, including 83 patients) involved DBS of striatal areas including the anterior limb of the interior capsule, the ventral capsule and ventral striatum, the nucleus accumbens or the ventral caudate nucleus. Of the remaining studies, five (27 patients) addressed subthalamic nucleus stimulation and two (6 patients) addressed stimulation of the inferior thalamic peduncle. Data were available from 14 studies (105 patients) on percentage of responders (ie, >35% reduction in posttreatment Y-BOCS scores). Twelve studies provided patient-level data. A pooled analysis yielded a global percentage of responders of 60% (95% CI, 49% to 69%). The most frequent adverse events reported were worsening anxiety (25 patients), disinhibition (23 patients), throbbing or flushing (12 patients) and feeling the extension leads (10 patients). The study reported benefits and risks of DBS stimulation but conclusions cannot be drawn about stimulation to any particular region or about the safety or efficacy of DBS for OCD compared with sham stimulation or an alternative therapy.

In 2014, the American Society for Stereotactic and Functional Neurosurgery and the Congress of Neurological Surgeons conducted a systematic review which served as the basis of their evidence-based guideline regarding DBS as a treatment of OCD. The group made the following conclusions:

1. There is Level I evidence, based on a single Level I study, for the use of bilateral subthalamic nucleus DBS for the treatment of medically refractory OCD.
2. There is Level II evidence, based on a single Level II study, for the use of bilateral nucleus accumbens DBS for the treatment of medically refractory OCD.
3. There is insufficient evidence to make a recommendation for the use of unilateral DBS for the treatment of medically refractory OCD.

However, the Level I and II evidence used to support the groups conclusions were based upon studies with small sample sizes (n=18, 16) which limit the ability to rule out the possibility of chance as an explanation of findings.

In 2011, de Koning et al. published a systematic review of clinical trials for DBS for treatment resistant obsessive-compulsive disorder (OCD). Nine case studies and 7 controlled studies with a blinded on-off phase were included. Inclusion criteria were use of the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) as an outcome measure, and “some estimate of efficacy” included in the study report. The authors concluded that DBS may be a beneficial and safe therapy for refractory OCD, but further research is needed to establish appropriate patient selection criteria, determine the more effective target location, and optimize postoperative patient management. Of note, the systematic review discussed the reported outcomes of the selected studies, but failed to critically appraise their quality.

Of the studies included in the systematic review:

- Nine case studies consisted of observational case reports of 1-2 patients, or small (<10 patients) non-comparative case series. Conclusions cannot be reached from these studies as randomized trials with an appropriate comparison group are needed to control for any placebo effect and for potential patient selection and treatment bias. In addition, the lack of blinding of patients and investigators fails to control for the placebo effect and potentially leads to additional bias.
- All seven RCTs included in the systematic review were double-blind crossover studies in which both the patient and the investigators were blinded to whether the
DBS was turned on or off. However, these RCTs are considered unreliable for the following reasons:

- Small study populations (n= 4 to 16) limit the ability to rule out the role of chance as an explanation of findings
- Heterogeneity of study participants (e.g., comorbidities) and procedures (e.g., five different brain target areas) limits meaningful comparison of outcomes
- Inability to isolate the contribution of DBS from the impact of other treatments (e.g., medications) during the study period
- Short-term follow-up does not permit conclusions related to the durability of any initial beneficial effects

Anorexia Nervosa

Anorexia nervosa is an eating disorder characterized by a chronic course that is refractory to treatment in many patients and has one of the highest mortality rates of any psychiatric disorder. In a recent systematic review by McClelland et al., 2 case series and 2 case reports that applied DBS to anorexic patients were identified and reviewed with mixed results. There are no RCTs investigating DBS for this indication.

Alcohol Addiction

Alcohol dependency can be considered as a chronic mental disorder characterized by frequent relapses even when treated with appropriate medical or psychotherapeutic interventions.

A 2012 systematic review by Herremans and Baeken investigated several neuromodulation techniques including deep brain stimulation in the treatment of alcohol addiction. Previous studies investigating these neuromodulation techniques in alcohol addiction remain to date rather limited. Overall, the clinical effects on alcohol addiction were modest. Neuromodulation techniques have only recently been subject to investigation in alcohol addiction and methodological differences between the few studies restrict clear conclusions. Nevertheless, the scarce results encourage further investigation in alcohol addiction.

OTHER APPLICATIONS

There is interest in applications of DBS beyond that for essential tremors, primary dystonia and Parkinson’s disease. Clinical trials are being pursued; however, at this time, FDA approval is limited to the above indications and severe obsessive-compulsive disorder. The following discussion focuses on randomized controlled trials (RCTs) for the investigational indications noted in Policy Criteria II.A-O above.

Chronic Pain, Pain Syndromes, and Cluster Headaches

DBS for the treatment of chronic pain was investigated and largely abandoned in the 1980’s due to poor results in two trials. With improved technology and surgical techniques there has been a resurgence of interest in DBS for intractable pain. DBS of the posterior hypothalamus for the treatment of chronic cluster headaches has also been investigated as functional studies have suggested cluster headaches have a central hypothalamic pathogenesis. However, due to the lack of RCTs, conclusions cannot be reached on the effectiveness of DBS as a treatment of any type of pain, including but not limited to cluster headaches, chronic spinal pain, failed back surgery syndrome, phantom limb pain, facial deafferentation pain, and central or peripheral neuropathic pain.

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
Morbid Obesity

The study of DBS of the hypothalamus and nucleus accumbens for cluster headache and obsessive-compulsive disorder (OCD) has prompted interest in DBS for obesity and addiction, which are thought to be associated with those brain regions. However, patients with unilateral subthalamic nucleus or globus pallidus internus DBS for PD were found to have gained a mean 4.86 pounds following initiation of DBS.[60] There are currently no studies of DBS in any brain region for the treatment of obesity.

Multiple Sclerosis

No randomized controlled trials were found for DBS in the treatment of multiple sclerosis (MS) tremors. Three small nonrandomized comparative trials were found, one[61] comparing stimulation off versus on (n=9), and two[19,62] comparing thalamic stimulation versus thalamotomy (n=12 total MS patients). The small study populations do not permit conclusions on efficacy of DBS for MS tremors.

PRACTICE GUIDELINE SUMMARY

AMERICAN ACADEMY OF NEUROLOGY

In the 2013 American Academy of Neurology (AAN) guidelines on the treatment for tardive syndromes (TDS), indicated there is insufficient evidence to support or refute DBS for TDS.[63] This recommendation is based on Level U evidence (evidence is insufficient to support or refute the use of any other treatment over another). The 2011 AAN guideline regarding essential tremor was reaffirmed in 2014 indicating that, “no high quality, long-term studies exist regarding the efficacy and safety of (DBS) for ET.”[64]

AMERICAN PSYCHIATRIC ASSOCIATION

In a 2007 the American Psychiatric Association (APA) published an evidence-based guideline, which was reaffirmed in 2012, on the treatment of patients with obsessive-compulsive disorder. The APA gave their lowest level recommendation for DBS, among a list of other therapies with limited published evidence, for OCD that remains refractory “after first- and second-line treatment and well-supported augmentation strategies have been exhausted.”[65] In the 2010 APA guideline for the treatment of major depression, DBS is listed as a search term in the literature review; however, no recommendations for DBS are mentioned.[66]

VETERANS HEALTH ADMINISTRATION, DEPARTMENT OF DEFENSE (VA/DOD)

A 2010 evidence-based update of the VA/DoD practice guideline for the management of post-traumatic stress stated that the evidence is insufficient to recommend the use of biomedical somatic therapies including deep brain stimulation for first-line treatment of post-traumatic stress disorder.[67]

SUMMARY

There is enough research to show that deep brain stimulation (DBS) improves health outcomes in select patients with symptoms related to Parkinson’s disease, essential tremor, or primary dystonias. DBS has become a standard of care for these patients and therefore
may be considered medically necessary when policy criteria are met.

There is not enough research to determine the safety and effectiveness of deep brain stimulation (DBS) for other conditions. Current practice guidelines do not recommend the use of deep brain stimulation for the treatment of various neurologic and psychiatric disorders. Therefore, DBS is considered investigational for all other indications when policy criteria are not met.

**REFERENCES**


44. Poon, SH, Sim, K, Sum, MY, Kuswanto, CN, Baldessarini, RJ. Evidence-based options for treatment-resistant adult bipolar disorder patients. Bipolar disorders. 2012 Sep;14(6):573-84. PMID: 22938165

October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.


### CODES

<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>61850</td>
<td>Twist or burr hole(s) for implantation of neurostimulator electrode(s), cortical</td>
</tr>
<tr>
<td></td>
<td>61860</td>
<td>Craniectomy or craniotomy for implantation of neurostimulator electrodes, cerebral, cortical</td>
</tr>
<tr>
<td></td>
<td>61863</td>
<td>Twist drill, burr hole, craniotomy, or craniectomy for stereotactic implantation of neurostimulator array in subcortical site (e.g., thalamus, globus pallidus, subthalamic nucleus, periventricular, periaqueductal gray), without use of intraoperative microelectrode recording; first array</td>
</tr>
<tr>
<td></td>
<td>61864</td>
<td>Twist drill, burr hole, craniotomy, or craniectomy for stereotactic implantation of neurostimulator array in subcortical site (e.g., thalamus, globus pallidus, subthalamic nucleus, periventricular, periaqueductal gray), without use of</td>
</tr>
</tbody>
</table>

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>intraoperative microelectrode recording; each additional array (List separately in addition to primary procedure).</td>
<td></td>
</tr>
<tr>
<td></td>
<td>61867</td>
<td>Twist drill, burr hole, craniotomy, or craniectomy for stereotactic implantation of neurostimulator array in subcortical site (e.g., thalamus, globus pallidus, subthalamic nucleus, periventricular, periaqueductal gray), with use of intraoperative microelectrode recording; first array</td>
</tr>
<tr>
<td></td>
<td>61868</td>
<td>Twist drill, burr hole, craniotomy, or craniectomy for stereotactic implantation of neurostimulator array in subcortical site (e.g., thalamus, globus pallidus, subthalamic nucleus, periventricular, periaqueductal gray), with use of intraoperative microelectrode recording; each additional array (List separately in addition to primary procedure)</td>
</tr>
<tr>
<td></td>
<td>61885</td>
<td>Insertion or replacement of cranial neurostimulator pulse generator or receiver, direct or inductive coupling; with connection to a single electrode array</td>
</tr>
<tr>
<td></td>
<td>61886</td>
<td>;with connection to two or more electrode arrays</td>
</tr>
<tr>
<td></td>
<td>61888</td>
<td>Revision or removal of cranial neurostimulator pulse generator or receiver</td>
</tr>
<tr>
<td></td>
<td>95970</td>
<td>Electronic analysis of implanted neurostimulator pulse generator system (e.g., rate, pulse amplitude, pulse duration, configuration of wave form, battery status, electrode selectability, output modulation, cycling, impedance and patient compliance measurements); simple or complex brain, spinal cord, or peripheral (i.e., cranial nerve, peripheral nerve, sacral nerve, neuromuscular) neurostimulator pulse generator/transmitter, without reprogramming</td>
</tr>
<tr>
<td></td>
<td>95978</td>
<td>Electronic analysis of implanted neurostimulator pulse generator system (e.g., rate, pulse amplitude and duration, battery status, electrode selectability and polarity, impedance and patient compliance measurements), complex deep brain neurostimulator pulse generator/transmitter, with initial or subsequent programming, first hour</td>
</tr>
<tr>
<td></td>
<td>95979</td>
<td>;complex deep brain neurostimulator pulse generator/transmitter, with initial or subsequent programming, each additional 30 minutes after first hour</td>
</tr>
<tr>
<td></td>
<td>HCPCS</td>
<td>C1820 Generator, neurostimulator (implantable), with rechargeable battery and charging system</td>
</tr>
<tr>
<td></td>
<td>L8679</td>
<td>Implantable neurostimulator, pulse generator, any type</td>
</tr>
<tr>
<td></td>
<td>L8680</td>
<td>Implantable neurostimulator electrode, each</td>
</tr>
<tr>
<td></td>
<td>L8681</td>
<td>Patient programmer (external) for use with implantable programmable neurostimulator pulse generator, replacement only</td>
</tr>
<tr>
<td></td>
<td>L8682</td>
<td>Implantable neurostimulator radiofrequency receiver</td>
</tr>
<tr>
<td></td>
<td>L8683</td>
<td>Radiofrequency transmitter (external) for use with implantable neurostimulator radiofrequency receiver</td>
</tr>
<tr>
<td></td>
<td>L8685</td>
<td>Implantable neurostimulator pulse generator, single array, rechargeable, includes extension</td>
</tr>
<tr>
<td></td>
<td>L8686</td>
<td>Implantable neurostimulator pulse generator, single array, nonrechargeable, includes extension</td>
</tr>
<tr>
<td></td>
<td>L8687</td>
<td>Implantable neurostimulator pulse generator, dual array, rechargeable, includes extension</td>
</tr>
<tr>
<td></td>
<td>L8688</td>
<td>Implantable neurostimulator pulse generator, dual array, nonrechargeable, includes extension</td>
</tr>
</tbody>
</table>

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage.
Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>L8689</td>
<td></td>
<td>External recharging system for battery (internal) for use with implantable neurostimulator</td>
</tr>
</tbody>
</table>

*Date of Origin: April 1998*
**Medical Policy Manual**

Surgery, Policy No. 01

---

**Endometrial Ablation**

**Effective:** June 1, 2017

**Next Review:** February 2018  
**Last Review:** February 2017

---

**IMPORTANT REMINDER**

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

**PLEASE NOTE:** Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

---

**DESCRIPTION**

Endometrial ablation involves ablation or destruction of the endometrium using a variety of techniques to treat menorrhagia in women who fail standard therapy.

---

**MEDICAL POLICY CRITERIA**

1. Endometrial ablation, with or without hysteroscopic guidance, may be considered medically necessary when the clinical records document all of the following criteria (I.A-D) are met:
   
   A. There is a diagnosis of abnormally heavy uterine bleeding in a patient who is not post-menopausal.
   
   B. Hysteroscopy, sonohysterography, or pelvic ultrasound has been performed and report is provided.
   
   C. Hormonal therapy, which may include oral contraceptives or progestins cannot be used because of one or more of the following (I.C.1-5) (Note: definition for progestin includes oral progestins, progestin-releasing intrauterine devices [IUDs], or DepoProvera):
1. There is a documented contraindication to hormonal therapy including both of the following:
   a. Greater than or equal to 3 per the CDC Medical Eligibility Criteria for Contraceptive Use (see Policy Guidelines Appendix I), and
   b. Contraindication to non-contraceptive progestins.
2. Documented specific details of intolerance as one or more of the following:
   a. Intolerance develops during treatment, or
   b. Intolerance to prior hormonal therapy, or
   c. Intolerance to continuation of hormonal therapy.
3. A trial of at least 3 months of non-contraindicated hormonal therapy did not adequately treat the patient’s condition.
4. A trial of hormonal therapy is not appropriate for the severity of the patient’s condition (e.g., severe and persistent bleeding).
5. Uterine intracavitary abnormality (i.e., endometrial polyps, submucosal fibroids) is found on hysteroscopy, sonohysterography, or pelvic ultrasound and endometrial ablation is to be performed concomitantly with surgical treatment of the uterine intracavitary abnormality.

D Endometrial sampling or dilation and curettage (D&C) has been performed or is planned according to any of the following (I.D.1-3)

1. Endometrial sampling or D&C has been performed. The histopathology report is provided showing absence of endometrial hyperplasia or uterine cancer; or
2. Endometrial sampling or D&C was performed. The histopathology report is provided, but inadequate tissue was obtained for diagnosis; or
3. Cervical stenosis precludes endometrial sampling, and D&C is planned concomitantly with ablation procedure.

II Repeat endometrial ablation may be considered medically necessary when all of the following (II.A-C) criteria are met:

A The clinical records document abnormally heavy uterine bleeding in a patient who is not post-menopausal; and

B The initial endometrial ablation procedure was performed at least six months prior; and

C Endometrial sampling or D&C has been performed or is planned according to any of the following (II.C.1-3):

1. Endometrial sampling or D&C has been performed to evaluate the current abnormal bleeding episode within the past year. The histopathology report is provided showing absence of endometrial hyperplasia or uterine cancer; or
2. Endometrial sampling or D&C was performed. The histopathology report is provided, but inadequate tissue was obtained for diagnosis; or
3. Cervical stenosis precludes endometrial sampling, and D&C is planned concomitantly with ablation procedure.

III Endometrial ablation using any technique is considered not medically necessary for all other indications not meeting the criteria in I.A-D, or II.A-C.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

POLICY GUIDELINES

It is critical that the list of information below is submitted for review to determine if the policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome.

- Endometrial histopathological report
- Hysteroscopy, sonohysterography, or pelvic ultrasound report
- Clinical notes which specify hormonal therapy if applicable

CROSS REFERENCES

1. Transgender Services, Medicine, Policy No. 153
2. Cosmetic and Reconstructive Surgery, Surgery, Policy No. 12
3. Reconstructive Breast Surgery/Mastopexy, and Management of Breast Implants, Surgery, Policy No. 40
4. Autologous Fat Grafting to the Breast and Adipose-derived Stem Cells, Surgery, Policy No. 182

BACKGROUND

Ablation or destruction of the endometrium is used to treat abnormal uterine bleeding in premenopausal women who fail standard medical therapy. Standard medical management typically includes a trial of nonhormonal therapy with adequate doses of nonsteroidal anti-inflammatory medication and oral tranexamic acid. If this fails, management with hormonal treatment to thin the endometrium may be tried. Ablation is considered a less invasive alternative to hysterectomy; however, as with hysterectomy, the procedure is not recommended for women who wish to preserve their fertility.

Techniques for endometrial ablation are generally divided into two categories:

HYSTEROSCOPIC TECHNIQUES

Hysteroscopic techniques require skilled surgeons and, due to the requirement for cervical dilation, use of general or regional anesthesia. In addition, the need for the instillation of hypotonic distension media creates a risk of pulmonary edema and hyponatremia such that very accurate monitoring of fluids is required.
The initial hysteroscopic technique involved photovaporization of the endometrium using an Nd-YAG laser. This was followed by electrosurgical ablation using an electrical rollerball or electrical wire loop. The latter technique is also known as transcervical resection of the endometrium, or TCRE. Hydrothermal ablation is another technique involving hysteroscopy.

NON-HYSTEROSCOPIC TECHNIQUES

Non-hysteroscopic techniques can be performed without general anesthesia and do not involve use of a fluid distention medium. Techniques include thermal fluid-filled balloon, cryosurgical endometrial ablation, instillation of heated saline, and radio frequency (RF) ablation.

REGULATORY STATUS

The U.S. Food and Drug Administration (FDA) indicated that endometrial devices are for use in premenopausal women with menorrhagia due to benign causes for whom childbearing is complete. FDA-approved devices for endometrial ablation include, but may not be limited to, laser therapy, electrical wire loop, rollerball using electric current, and thermal ablation using a liquid-filled balloon, microwave, electrode array, or a cryosurgical device. Examples of devices for endometrial ablation are:

- The Genesys HTA™ system (Boston Scientific), This system involves the instillation and circulation of heated saline into the uterus using hysteroscopic guidance and includes features such as a smaller console and simplified set-up requirements, was approved by the FDA in May 2010.
- The Microwave Endometrial Ablation (MEA) system (Microsulis Medical): This delivers fixed-frequency microwave energy and may be performed in a physician’s office but does require use of the hysteroscope.
- The ThermaChoice® device (J&J Ethicon Gynecare): This device ablates endometrial tissue by thermal energy heating of sterile injectable fluid within a silicone balloon. Endometrial ablation will only work when there is direct contact between the endometrial wall and the fluid-filled balloon. Therefore, patients with uteri of abnormal shape, resulting from tumors such as myomas or polyps, or large size, due to fibroids, are generally not considered candidates for this procedure.
- The NovaSure™ impedance-controlled endometrial ablation system (Cytyc Corp): The system delivers RF energy to the endometrial surface. The device consists of an electrode array on a stretchable porous fabric that conforms to the endometrial surface.
- Her Option™ Uterine Cryoablation Therapy™ system (American Medical Systems): The system consists of, in part, a cryoprobe that is inserted through the cervix into the endometrial cavity. When cooled, an ice ball forms around the probe, which permanently destroys the endometrial tissue. Cryoablation is typically monitored by abdominal ultrasound.

EVIDENCE SUMMARY

SYSTEMATIC REVIEWS

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
Several published systematic reviews have evaluated the accumulated evidence for endometrial ablation. These reviews address both first-generation techniques (laser ablation, electrical wire loop, rollerball, or vaporizing electrode procedure) and second-generation techniques (newer techniques that generally do not require hysteroscopy such as balloon ablation, microwave ablation, and electrode ablation).

A 1991 BlueCross BlueShield Technology Assessment Center (TEC) Assessment concluded that endometrial ablation using either an Nd-YAG laser or a resecting loop was an effective treatment of menorrhagia unresponsive to hormone treatment or dilation and curettage.[1]

In 2013, an updated Cochrane systematic review and meta-analysis compared the efficacy and safety of different endometrial ablation techniques.[2,3] The review included RCTs that compared 2 ablation techniques and assessed amenorrhea and patient satisfaction. A total of 25 studies with 4,040 premenopausal women were eligible for the review. Five of the trials compared two “first generation” ablation methods (laser ablation, electrical wire loop, rollerball, or vaporizing electrode procedure) and five trials compared “second generation” techniques to one another. Fourteen trials compared first- to second-generation procedures. Sixteen trials had adequate randomization methods but, in most trials, blinding was not performed or was not reported. There were only 1 or 2 studies on any given comparison of techniques; the exception was balloon ablation versus rollerball for which there were 3 studies.

The investigators also conducted a meta-analysis that combined studies comparing first- and second-generation techniques. A pooled analysis of 12 studies (total n=2,085) did not find a significant difference in the rate of amenorrhea at 1 year (OR: 0.94; 95% CI: 0.74–1.20). Eleven studies (total n=1,690) reported satisfaction rates at 1 year, and there was not a significant difference between first- and second-generation techniques (OR: 1.00; 95% CI, 0.97–1.02). Pooled analysis of adverse effects did not find any significant differences in the rate of perforation (8 studies), endometritis (5 studies), or hemorrhage (5 studies) using first- versus second-generation ablation techniques. Rates of fluid overload (4 studies) and cervical lacerations (8 studies) and hematometra (5 studies) were significantly higher with first-generation techniques than with second-generation techniques.

The authors of the Cochrane review concluded that, overall, the existing evidence suggests that success rates and complications profiles of second-generation techniques compare favorably with the first generation hysteroscopic techniques.

In 2011, the Health Technology Assessment (HTA) program in the U.K. conducted a meta-analysis of individual patient data from RCTs evaluating second-line treatments for menorrhagia.[4] They identified data on 2,448 women from 14 trials comparing first- and second-generation endometrial ablation devices and data on 1,127 women from 7 trials comparing first-generation devices to hysterectomy. A limitation of the review is that individual patient data were not available for approximately 35% of women randomized in the trials. The most frequently measured outcome in the studies was patient satisfaction/dissatisfaction and this was used as the primary outcome of the meta-analysis. After 12 months of follow-up, 7.3% (57/454) of women treated with first-generation endometrial ablation devices and 5.3% (23/432) of women who had a hysterectomy were dissatisfied with their treatment outcome.
This difference was statistically significant, favoring hysterectomy (OR: 2.46, 95% CI: 1.54 to 3.93, p=0.0002). Rates of dissatisfaction were similar among women treated with first-generation endometrial ablation devices (123/1,006 [12.2%]) and second-generation devices (110/1,034 [10.6%], p=0.20). The authors noted that rates of dissatisfaction were low for all treatments.

The HTA also conducted meta-analyses on several clinical outcomes. For example, when first- and second-generation endometrial ablation devices were compared, there was not a significant difference between groups in the rate of amenorrhea after 12 months. When findings from 13 studies were pooled, rates of amenorrhea were 326/899 (36%) with first-generation devices and 464/1,261 (37%) with second-generation devices (OR: 1.12; 95% CI: 0.93 to 1.35). There were insufficient data to conduct meta-analyses of longer-term amenorrhea rates. Similarly, the rates of menorrhagia after 12 months did not differ between groups. In a pooled analysis of 12 studies, rates were 111/899 (12.3%) with first-generation devices and 151/1,281 (11.8%) after second-generation devices (pooled OR: 0.97, 95% CI: 0.74 to 1.28). In addition, a pooled analysis of 6 studies did not find a significant difference in repeat endometrial ablations over 12 months after initial treatment with first-generation devices (4/589, 0.7%) or second-generation devices (4/880, 0.5%) (OR: 0.71, 95% CI: 0.17 to 2.94). The proportion of women requiring hysterectomy within 12 months after endometrial ablation did not differ significantly when first-generation devices (39/933 [4.2%]) or second-generation devices (35/1,343 [2.6%]) were used (OR: 0.77; 95% CI: 0.47 to 1.24 [11 studies]).

In addition to the meta-analyses of data from published studies, the HTA included an analysis of individual patient data from national databases in Scotland to evaluate long-term outcomes after hysterectomy or endometrial ablation. The investigators identified a total of 37,120 women who underwent hysterectomy and 11,299 women who underwent endometrial ablation for dysfunctional uterine bleeding between 1989 and 2006. Women who received endometrial ablation were significantly older (mean of 42.5 years) compared to those receiving hysterectomy (mean of 41.0 years). The type of endometrial ablation device could not be determined. The median duration of follow-up was 6.2 years in the endometrial ablation group and 11.6 years in the hysterectomy group. During follow-up, 962 (8.5%) women who received endometrial ablation had additional gynecologic surgery compared to 1,446 (3.9%) women who had hysterectomy; this difference was statistically significant (adjusted hazard ratio [HR]: 3.56, 95% CI: 3.26-3.89). The most common types of additional surgery after endometrial ablation were intrauterine procedures (n=577, 5.1%) and repeat endometrial ablation (n=278, 2.5%). However, women who had initial endometrial ablation procedures were significantly less likely than those with initial hysterectomies to have surgery for pelvic floor repair (0.9% vs. 2.2%, respectively, adjusted HR: 0.50 to 0.77). Women were also less likely to have tension-free vaginal tape surgery for stress urinary incontinence after endometrial ablation than after hysterectomy (0.5% vs. 1.1%, respectively, adjusted HR: 0.55, 95% CI: 0.41 to 0.74).

In 2012, Daniels and colleagues compared first- and second-generation methods using 14 trials previously addressed in the HTA assessment.[5] A pooled analysis of these studies yielded conclusions that were similar to the HTA group, in that no significant difference in amenorrhea rates was observed with the 2 types of techniques (OR: 0.72, 95% CI: 0.52-1.101). In addition, 3 studies compared the second-generation techniques, thermal balloon...
ablation and bipolar radiofrequency (RF) (total n=264). A pooled analysis showed a higher rate of amenorrhea with bipolar RF (OR: 4.56; 95% CI: 2.24-9.26).

In 2013, Kroft and Liu also reported no difference in amenorrhea rates when comparing first- and second-generation methods as a treatment for menorrhagia in premenopausal women (11 randomized controlled trials were included in the review). However, authors did note a decrease in complication rates (7 studies with 1272 patients, rate ratio 0.52, 95% CI 0.35 to 0.76; P < 0.001), operating time (16.6 minutes 3 studies with 486 patients, 95% CI 12.1 to 21.2 minutes; P < 0.001) and improved compatibility with anaesthesia (3 studies with 558 patients, rate ratio 1.87, 95% CI 1.04 to 3.37; P = 0.04) in second-generation devices compared to first-generation methods. In addition, authors reported higher rates of amenorrhea in patients treated with Novasure compared to other second-generation devices (4 studies with 407 patients, rate ratio 2.60, 95% CI 1.63 to 4.14; P < 0.001).

Several medium and large nonrandomized studies have reported time to surgical reoperation rates, including repeat endometrial ablation, in women who fail initial procedure. The majority of surgical reoperations occurred at least one year after the initial procedure.

**Section Summary**

Evidence from these large systematic reviews do not demonstrate that one ablation technique is superior to another. Overall, these studies continue to report similar amenorrhea rates in first-generation and second-generation techniques.

**SAFETY**

In 2012, Brown and Blank published an analysis of adverse events associated with endometrial ablation procedures that were reported in the U.S. Food and Drug Administration (FDA’s) Manufacturer and User Facility Device Experience (MAUDE) database. There were a total of 829 reported adverse events between 2005 and 2011. Nearly two-thirds of the adverse events (540 of 829, 65%) were genital tract or skin burns and 529 of these events (98%) were associated with hydrothermal endometrial ablation. The next 2 most frequent types of adverse events were thermal bowel injury (93 of 820, 11%) and transmural uterine thermal activity (89 of 820, 11%). Of the 182 thermal injuries, 140 (77%) were associated with radiofrequency endometrial ablation. In addition, 47 instances of sepsis or bacteremia were reported, and 43 of these cases (91%) were associated with radiofrequency endometrial ablation. There were 4 reported deaths, 2 associated with radiofrequency ablation and 1 each associated with thermal balloon ablation and cryoablation. Sixty-six of the 829 events (8%) occurred when endometrial ablation was performed outside of the labeled instructions for use of the procedure. The authors did not report the total number of endometrial ablations performed during this time period, therefore the proportion of procedures with adverse events cannot be determined from these data.

A 2014 study by Dood and colleagues examined whether women who undergo endometrial ablation are at increased risk of endometrial cancer compared with those with abnormal uterine bleeding that is managed with medication. The data were collected from a population-based cohort in the U.S. and included a total of 234,721 women with abnormal
bleeding, 4776 of whom underwent endometrial ablation. During a median follow-up period of 4.1 years, 3 women with a history of endometrial ablation and 601 women who were treated medically developed endometrial cancer. There was not a statistically significant difference in endometrial cancer rates between groups (age-adjusted HR=0.61, 95% CI, 0.20 to 1.89, p=0.17). Moreover, the median time to endometrial cancer diagnosis, 237 days after ablation and 299 days with medical management, did not differ significantly between groups.

Section Summary

Adverse events have been associated with endometrial ablation procedures. Certain types of adverse events are more likely to occur with specific approaches to endometrial ablation. Due to lack of information about the total number of procedures and the number of each type of endometrial ablation procedure performed, conclusions cannot be drawn from these data about the relative safety of different types of endometrial ablation procedures.

PRACTICE GUIDELINE SUMMARY

PRACTICE COMMITTEE OF THE AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE

In 2008, the American Society for Reproductive Medicine (ASRM) reviewed their 2006 Practice Committee report and reissued their statement on indications and options for endometrial ablation.[12] Conclusions were:

- “Endometrial ablation is an effective therapeutic option for the management of menorrhagia.
- Hysteroscopic and nonhysteroscopic techniques for endometrial ablation offer similar rates of symptom relief and patient satisfaction.
- Later definitive surgery may be required in 6% to 20% of women after endometrial ablation.
- Women who undergo hysterectomy after a failed endometrial ablation report significantly more satisfaction after 2 years of follow-up.
- Endometrial ablation generally is more effective when the endometrium is relatively thin.
- Ideally, hysteroscopic methods for endometrial ablation should be performed using a fluid monitoring system to reduce the risks and complications relating to fluid overload and electrolyte imbalance.
- Nonhysteroscopic methods for endometrial ablation require less skill and operating time.”

A 2011 patient fact sheet from the ASRM states that women who meet the following criteria should not have endometrial ablation:

“Women who are pregnant, who would like to have children in the future, or have gone through menopause should not have this procedure.”[13]

AMERICAN CONGRESS OF OBSTETRICIANS AND GYNECOLOGISTS

The American Congress of Obstetricians and Gynecologists (ACOG) published a guideline on
Recommendations they assessed as being based on good and consistent evidence included the following:

“For women with normal endometrial cavities, resectoscopic endometrial ablation and nonresectoscopic endometrial ablation systems appear to be equivalent with respect to successful reduction in menstrual flow and patient satisfaction at 1 year following index surgery.”

“Resectoscopic endometrial ablation is associated with a high degree of patient satisfaction but not as high as hysterectomy.”

In addition, the ACOG practice bulletin regarding endometrial ablation included the following statement regarding preoperative evaluation:

“The structure and histology of the endometrial cavity should be thoroughly evaluated, both to assess for malignancy or endometrial hyperplasia and to ensure that the length and configuration is suitable for endometrial ablation. These parameters will vary depending on the technique or system used. Endometrial sampling, typically with an outpatient technique, can be used to evaluate all women for hyperplasia or malignancy, and results should be reviewed before ablation is scheduled. Women with endometrial hyperplasia or uterine cancer should not undergo endometrial ablation.”

In 2013, ACOG published guidelines (reaffirmed in 2015) regarding the management of acute abnormal uterine bleeding (AUB) in nonpregnant reproductive-aged women. Recommendations regarding laboratory testing and imaging of these patients are as follows:

“Endometrial tissue sampling should be performed in patients with AUB who are older than 45 years as a first-line test. Endometrial sampling also should be performed in patients younger than 45 years with a history of unopposed estrogen exposure (such as seen in patients with obesity or polycystic ovary syndrome), failed medical management, and persistent AUB.”

Recommendations regarding surgical management of women who do not respond to medical management of symptoms are as follows:

“Surgical options include dilation and curettage (D&C), endometrial ablation, uterine artery embolization, and hysterectomy.”

“Endometrial ablation, although readily available in most centers, should be considered only if other treatments have been ineffective or are contraindicated, and it should be performed only when a woman does not have plans for future childbearing and when the possibility of endometrial or uterine cancer has been reliably ruled out as the cause of the acute AUB.”

The 2013, ACOG practice bulletin regarding the management of abnormal uterine bleeding associated with ovulatory dysfunction (AUB-O) was reaffirmed in 2015. The following
recommendation is made primarily based upon consensus and expert opinion:

“Endometrial ablation is not recommended as a first-line therapy for AUB-O. Physicians must provide thorough informed consent and adequate counseling to women with AUB-O who desire endometrial ablation.”

SOCIETY FOR GYNECOLOGIC SURGEONS

In 2012, the Society for Gynecologic Surgeons (SGS) published a clinical practice guideline on treatment of abnormal uterine bleeding.[17] The guideline recommends that, in women with bleeding caused mainly by ovulatory disorders or endometrial hemostatic disorders, any of the following treatments may be chosen depending on patient values and preferences: hysterectomy, endometrial ablation, systemic medical therapies or levonorgestrel-releasing intrauterine systems. In choosing between endometrial ablation and hysterectomy, if the patient’s preference is for amenorrhea, less pain or avoiding additional therapy, hysterectomy is suggested. If the patient’s preference is for lower operative and postoperative procedural risk, and a shorter hospital stay, endometrial ablation is recommended.

SUMMARY

There is enough research to show that endometrial ablation improves net health outcomes in women who have failed prior treatment for abnormal uterine bleeding and are otherwise considering hysterectomy. Clinical guidelines recommend endometrial ablation for clinical scenarios that generally align with the policy criteria. Therefore endometrial ablation may be considered medically necessary when criteria are met. Endometrial ablation for indications or using techniques other than those specified in policy criteria are considered not medically necessary.

REFERENCES


## CODES

<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>58353</td>
<td>Endometrial ablation, without hysteroscopic guidance</td>
</tr>
<tr>
<td></td>
<td>58356</td>
<td>Endometrial cryoablation with ultrasonic guidance, including endometrial curettage, when performed</td>
</tr>
<tr>
<td></td>
<td>58563</td>
<td>Hysteroscopy, surgical, with endometrial ablation (e.g., endometrial resection, electrosurgical ablation, thermoablation)</td>
</tr>
</tbody>
</table>

**HCPCS** None

## APPENDIX I

**CDC Summary Chart of U.S. Medical Eligibility Criteria for Contraceptive Use**


*Full chart will be appended to the policy as a PDF when the word doc is converted for web push*

**Date of Origin:** September 2011
Medical Policy Manual

**Topic:** Endovascular Angioplasty and/or Stenting for Intracranial Arterial Disease (Atherosclerotic and Aneurysms)

**Date of Origin:** July 2005

**Section:** Surgery

**Last Reviewed Date:** June 2016

**Policy No:** 141

**Effective Date:** July 1, 2016

**IMPORTANT REMINDER**

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

**DESCRIPTION[1]**

It is estimated that intracranial atherosclerosis causes about 8% of all ischemic strokes. Intracranial stenosis may contribute to stroke in two ways: either due to embolism or low flow ischemia in the absence of collateral circulation. Recurrent annual stroke rates are estimated at 4%-12% per year with atherosclerosis of the intracranial anterior circulation, and 2.5%-15% per year with lesions of the posterior (vertebrobasilar) circulation. Medical treatment typically includes either anticoagulant therapy (i.e., warfarin) or antiplatelet therapy (e.g., aspirin). The WASID trial (Warfarin-Aspirin Symptomatic Intracranial Disease) was a randomized trial that compared the incidence of stroke brain hemorrhage or death among patients randomized to receive either aspirin or warfarin. The report indicated that with a mean 1.8 years of follow-up, warfarin provided no benefit over aspirin and was associated with a significantly higher rate of complications. In addition, if symptoms are attributed to low flow ischemia, agents to increase mean arterial blood pressure and avoidance of orthostatic hypotension may be recommended. However, medical therapy has been considered less than optimal. For example, in patients with persistent symptoms despite antithrombotic therapy, the subsequent rate of stroke or death has been extremely high, estimated in one study at 45%, with recurrent events occurring within a month of the initial recurrence. Surgical approaches have met with limited success. The widely quoted Extracranial-Intracranial (EC/IC) Bypass study randomized 1,377 patients with symptomatic atherosclerosis of the internal carotid or middle cerebral arteries to medical care or EC/IC bypass.
outcomes in the two groups were similar, suggesting that the EC/IC bypass is ineffective in preventing cerebral ischemia. Due to inaccessibility, surgical options for the posterior circulation are even more limited.

Percutaneous transluminal angioplasty (PTA) has been approached cautiously for use in the intracranial circulation due to technical difficulties in catheter and stent design and due to the risk of embolism, which may result in devastating complications if it occurs in the posterior fossa or brain stem. However, improvement in catheter trackability, allowing catheterization of tortuous veins, and the increased use of stents has created ongoing interest in exploring PTA as a minimally invasive treatment of this difficult-to-treat population. Most of the published studies of intracranial PTA have focused on the vertebrobasilar circulation. Intracranial vessels on which angioplasty has been performed include:

- Anterior cerebral artery
- Basilar artery
- Carotid siphon
- Internal carotid
- Middle cerebral artery
- Ophthalmic artery
- Posterior cerebral artery
- Vertebral artery (distal)

Intracranial stents are also being used in the treatment of cerebral aneurysms. Stent-assisted coil embolization began as an approach to treat fusiform or wide-neck aneurysms in which other surgical or endovascular treatment strategies may not be feasible. As experience grew, stenting was also used in smaller berry aneurysms as an approach to decrease the rate of retreatment needed in patients who receive coiling.

**Regulatory Status**

Currently, approval of intracranial stents by the U.S. Food and Drug Administration (FDA) has been through the humanitarian device exemption (HDE) process. This form of FDA approval is available for devices used in the treatment or diagnosis of conditions that affect fewer than 4,000 individuals in the United States per year; the FDA only requires data showing “probable safety and effectiveness.” An approved HDE authorizes marketing of the humanitarian use device (HUD). However, an HUD may only be used after an internal review board (IRB) approval has been obtained for the use of the device for the FDA approved indication. The labeling for an HUD must state that the device is a humanitarian use device and that, although the device is authorized by Federal Law, the effectiveness of the device for the specific indication has not been demonstrated.

**Stents for Intracranial Atherosclerosis**

There are currently two devices that have received FDA approval for humanitarian use in the treatment of intracranial atherosclerosis. Their labeled indications are as follows:

- **NEUROLINK® System** (Guidant) is "indicated for the treatment of patients with recurrent intracranial stroke attributable to atherosclerotic disease refractory to medical therapy in intracranial vessels ranging from 2.5 to 4.5 mm in diameter with greater than or equal to 50% stenosis and that are accessible to the stent system."[2]
Wingspan™ Stent System with Gateway™ PTA Balloon Catheter (Boston Scientific) is “indicated for improving cerebral artery lumen diameter in patients with intracranial atherosclerotic disease, refractory to medical therapy, in intracranial vessels with greater than or equal to 50% stenosis that are accessible to the system.”[3] The Wingspan Stent System consists of a highly flexible, microcatheter delivered self-expanding nitinol stent, which may be suitable for lesions in the distal internal carotid and middle cerebral arteries. These arteries are difficult to access with a balloon-mounted stent, such as the NEUROLINK system.[4]

Stents for Intracranial Aneurysm

Endovascular Stents for Use with Coils

The following devices have received FDA approval for humanitarian use with embolic coils in the treatment of unruptured wide-neck intracranial aneurysms:

- The Neuroform™ Microdelivery Stent System (Boston Scientific) (H020002)
- The Enterprise™ Vascular Reconstruction Device and Delivery System (Cordis Neurovascular, Inc./DePuy Companies) (H060001)
- The LVIS® or LVIS® Jr. Low-Profile Visualized Intraluminal Support Device (MicroVention®, Inc.) (H130005)

The Solitaire AB retrievable stent (Covidien) has not received FDA approval for use in the United States outside the clinical trial setting.

Flow-Diverting Stents

- In 2011, the Pipeline® Embolization Device (Covidien eV3 Neurovascular), which falls into a new device category called “intracranial aneurysm flow diverters,” or flow-diverting stent, received FDA premarket approval for endovascular treatment of large or giant wide-necked intracranial aneurysms in the internal carotid artery from the petrous to the superior hypophyseal segments in adult patients aged 22 years or older. The Pipeline device is a braided, wire mesh device that is placed within the parent artery of an aneurysm to redirect blood flow away from the aneurysm with the goal of preventing aneurysm rupture and possibly decreasing aneurysm size.
- The SILK Reconstruction device (Balt Extrusion) and the Surpass Flow Diverting Stent (Stryker) have not received FDA approval for use in the United States.

MEDICAL POLICY CRITERIA

Note: This policy does not address percutaneous angioplasty and stenting of extracranial carotid arteries or venous vessels, or the use of mechanical embolectomy or thrombectomy devices which are addressed in separate medical policies (see Cross References below).

I. Intracranial stent placement may be considered medically necessary as part of the endovascular treatment of intracranial aneurysms when all of the following criteria are met:

   A. Surgical treatment is not appropriate
B. Standard endovascular techniques do not allow for complete isolation of the aneurysm, e.g., wide-neck aneurysm (4 mm or more) or sack-to-neck ratio less than 2:1

C. Use of FDA-approved flow-diverting stents may be indicated for treatment of intracranial aneurysms when all of the following criteria are met:

1. The aneurysm is in the internal carotid artery from the petrous to the superior hypophyseal segments

2. The aneurysm is large or giant (10 mm or more) and wide-necked (4 mm or more)

II. All other intracranial endovascular angioplasty and/or stenting is considered investigational including but not limited to the following:

A. Intracranial stent placement in the treatment of intracranial aneurysms except as noted above

B. Intracranial percutaneous transluminal angioplasty with or without stenting in the treatment of atherosclerotic cerebrovascular disease

C. Intracranial angioplasty with or without stenting for acute ischemic stroke

**SCIENTIFIC EVIDENCE**

Evaluating the safety and effectiveness of intracranial endovascular angioplasty with or without stenting requires evidence from well-designed, well-conducted randomized controlled trials (RCTs) that compare the health outcomes following endovascular procedures with those following treatment with standard medical or surgical treatment. Nonrandomized comparative studies and uncontrolled studies can provide useful information on health outcomes such as adverse events (AEs), but are prone to biases such as noncomparability of treatment groups, nonspecific effects such as the placebo effect, and the variable natural history of the condition.

**Intracranial Atherosclerotic Disease**

Data Included in U.S. Food and Drug Administration (FDA) Submissions

- **NEUROLINK® System**[2]

The clinical study investigating the NEUROLINK device is known as the SSYLVIA study (Stenting of Symptomatic Atherosclerosis Lesions in the Vertebral or Intracranial Arteries), a prospective, nonrandomized, multicenter, international study of 61 patients. Patients were eligible for participation in the study if they were symptomatic (previous stroke or TIA) attributed to an angiographically demonstrated, discrete stenosis ≥50%, in an extracranial or intracranial artery. The primary endpoint was a composite of stroke and death clinical outcomes at 30 days; 4 patients experienced strokes (6.6%) and there were no deaths. Mean follow-up was 216 days and lower bound for ipsilateral stroke at 12 months was estimated to be 11.5%. The FDA summary notes that in the WASID study of aspirin and warfarin therapy, the rate of fatal or nonfatal stroke was 14.6%
and total stroke or death was 22.5% with a follow-up of 15-19 months, suggesting a potentially superior outcome with the NEUROLINK device. However, the short length of follow-up in the NEUROLINK study prevents meaningful comparisons. The FDA Summary of Safety and Probable Benefit concludes, “Therefore, it is reasonable to conclude that the probable benefit to health from using the NEUROLINK System for intracranial stenting for recurrent stroke attributable to intracranial atherosclerosis refractory to medical therapy outweighs the risk of illness or injury, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment, when used as indicated in accordance with the directions of use.”

- **Wingspan Stent System**[^3]

The Wingspan was studied in a prospective, multicenter, single arm trial of 45 patients enrolled at 12 international centers. Patients were considered eligible if they presented with evidence of recurrent stroke, refractory to medical therapy and thought to be secondary to intracranial stenosis of 50% or greater. The primary safety endpoint was similar to the SSYLVIA study, i.e., a composite of stroke and death clinical outcomes at 30 days, which occurred in 4.5% of patients (2/45), 1 with death following a hemorrhagic stroke and 1 stroke.

The FDA summary provided a comparison of various outcomes of the NEUROLINK and Wingspan device studies as follows:

<table>
<thead>
<tr>
<th>Clinical study</th>
<th>Follow-up</th>
<th>All Stroke</th>
<th>Death</th>
<th>Stroke + Death</th>
<th>Ipsilateral Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSYLVIA (n=61)</td>
<td>Mean: 216 days (n=48 at 6 mos)</td>
<td>13.1%</td>
<td>6.6%</td>
<td>13.1%</td>
<td>11.5%</td>
</tr>
<tr>
<td>Wingspan (n=45)</td>
<td>Mean: 174 days (n=42 at 6 mos)</td>
<td>9.5%</td>
<td>2.4%</td>
<td>9.5%</td>
<td>7.1%</td>
</tr>
</tbody>
</table>

The FDA offered the following conclusions concerning the Wingspan device and appeared to base its approval, in part, on the favorable comparison to the NEUROLINK device:

“The Wingspan clinical study treated 45 patients with symptomatic atherosclerotic lesions in intracranial arteries who were refractory to medical therapy. The lesions were predilated and stented. Clinical follow-up (42 patients) and angiographic follow up (40 patients) were performed at 6 months. The type and frequency of observed adverse events including stroke are consistent with or lower than similar neurovascular procedures. Therefore, it is reasonable to conclude that the probable benefit to health from using the Wingspan Stent System with Gateway PTA Balloon Catheter for treating intracranial stenosis outweighs the risk of illness or injury when used in accordance with the Instructions for Use and when taking into account the probable risks and benefits of currently available alternative forms of treatment.”

**Elective Treatment of Symptomatic Intracranial Stenosis**

The following literature review focused on systematic reviews, RCTs, and nonrandomized comparative studies of stent-assisted angioplasty for stroke prevention in patients with intracranial artery stenosis. This review did not include treatments for acute stroke.

**Systematic Reviews**
In 2014, Abuzinadah conducted a systematic review and meta-analysis of studies reporting the rates of stroke recurrence or death (the primary outcome) in symptomatic intracranial vertebrobasilar stenosis with medical or endovascular treatment.\[5\] The authors identified 23 studies involving 592 medical treatment patients and 480 endovascular treatment patients. In pooled analysis, the stroke or death rate was 14.8 per 100 person-years (95% CI, 9.5 to 20.1) in the medical therapy group and 8.9 per 100 person-years (95% CI, 6.9 to 11.0) in the endovascular group (incidence rate ratio [IRR], 1.3; 95% CI, 1.0 to 1.7). The stroke recurrence rate was 9.6 per 100 person-years (95% CI, 5.1 to 14.1) in the medical group and 7.2 per 100 person-years (95% CI, 5.5 to 9) in the endovascular group (IRR=1.1; 95% CI, 0.8 to 1.5). However, the wide confidence interval in some outcomes increases the uncertainty of the accuracy of the reported effects and generally indicates that more data are needed.

In 2012 Zhou et al. conducted a systematic review of “double-blind” RCTs of angioplasty with stenting for symptomatic intracranial atherosclerosis defined as more than 50% stenosis on angiogram.\[6\] A comprehensive literature search was described which included English language databases, Chinese academic journals, and the reference lists of selected articles. Participants with acute ischemic events were excluded. The primary outcome of interest was the occurrence of post-procedure stroke. No studies were found that met inclusion criteria. However, the SAMMPRIS trial\[7\] was reviewed. This RCT, which was terminated early due to the risk of stroke or periprocedural death in the stent group, is summarized below. The authors concluded that more RCT evidence is needed before widespread application of stent-assisted intracranial angioplasty can be recommended.

In 2009 Groschel et al. conducted a systematic review on outcomes after stenting for intracranial atherosclerosis.\[8\] The authors identified 31 studies including 1,177 procedures, which had mainly been performed in patients with a symptomatic (98%) intracranial high-grade stenosis (mean: 78.7%) with high technical success rates (median: 96%; interquartile range: 90% to 100%). The periprocedural minor or major stroke and death rates ranged from 0% to 50%, with a median of 7.7%. Periprocedural complications were significantly higher in the posterior versus the anterior circulation (12.1% vs. 6.6%, p<0.01), but did not differ between patients treated with a balloon-mounted (n=906) versus those who had been treated with a self-expandable stent (n=271; 9.5% vs. 7.7%, p=0.47). Restenosis greater than 50% occurred more frequently after the use of a self-expandable stent (16/92; 17.4%, mean follow-up time: 5.4 months) than a balloon-mounted stent (61/443; 13.8%, mean follow-up time: 8.7 months; p<0.001). The authors concluded that although intracranial stenting appears to be feasible, adverse events vary widely and thus given a high rate of restenoses and no clear impact of new stent devices on outcome, the widespread application of intracranial stenting outside the setting of randomized trials and in inexperienced centers currently does not seem to be justified.

**Randomized Clinical Trials (RCTs)**

VAST is the largest RCT published to date on stenting versus medical therapy in patients with symptomatic vertebral artery disease.\[9\] This multicenter phase 2 study included 115 patients who had a transient ischemic attack or minor stroke attributed to vertebral artery stenosis. Randomization to stenting or medical therapy was stratified by center and by the level of stenosis; 83.5% of patients had extracranial lesions and the rest had intracranial lesions. The median interval between symptoms and randomization was 25 days, with a median interval between randomization and stenting of 7 days. The particular stent used was by surgeon preference. All patients received best medical therapy and were followed yearly by telephone. The primary outcome was the composite of vascular death, stroke, or myocardial infarction within 30 days. Secondary outcomes were stroke in the territory of the symptomatic artery, the composite outcome measure during follow-up, and the degree of restenosis. The
median follow-up was 3.0 years (range, 1.3 to 4.1)

Endovascular therapy plus best medical therapy was not superior to best medical therapy alone in this trial. The primary outcome occurred in 3 of 57 (5%, 95% confidence interval [CI] 0-11) patients in the stenting group and 1 of 58 (2%, 95% CI 0-5) patients in the medical treatment group. Of these four patients, all had a vertebrobasilar stroke and 2 of the 4 occurred in the group of 9 patients with intracranial stenosis who received endovascular therapy. One of the strokes in the stenting group was fatal. During follow-up, the composite outcome occurred in 11 (19%) patients in the stenting group compared to 10 (17%) patients in the medical therapy group. The periprocedural risk of a major vascular event in the stenting group was 5%. The authors questioned the need and feasibility of a phase 3 trial, given the low risk of recurrent stroke with best medical therapy. However, recruitment of 540 patients for the phase 3 VIST be completed as of March 2016. Enrollment was originally planned for 1302 patients. In VIST, patients with symptomatic extracranial or intracranial vertebral artery stenosis and vertebrobasilar transient ischemic attacks or stroke in the previous three months will be randomly assigned to vertebral artery stenting or best medical therapy alone.

In 2015, Zaidat et al. published results of the VISSIT trial, an RCT comparing a balloon-expandable stent plus medical management to medical management alone among patients with symptomatic intracranial stenosis of 70% or greater.[10] Eligible patients had stenosis of 70% to 99% of the internal carotid, middle cerebral, intracranial vertebral, or basilar arteries with a transient ischemic attack (TIA) or stroke attributable to the territory of the target lesion within the prior 30 days. Enrollment was planned for up to 250 participants. However, an early unplanned analysis was conducted by the trial sponsor after the results of the SAMMPRIS trial were published (see below). A total of 112 patients were enrolled from 2009 to 2012 and randomized to balloon-expandable stent (Vitesse stent) plus medical management (stent group; n=59) or medical management alone (medical group; n=53). Medical management included clopidogrel (75 mg daily) for the first 3 months postenrollment and aspirin (81-325 mg/d) for the duration of the study, along with management of hypercholesterolemia and/or hypertension, if necessary. The study used a primary composite end point that included any stroke in the same territory as the presenting event within 1 year of randomization and “hard TIA” in the same territory as the presenting event from 2 days to 1 year after randomization. Among 29 patients who met one of the primary end points within 1 year of randomization, 8 (15.1%) patients were in the medical group and 21 (36.2%) were in the stent group (risk difference, 21.1%; 95% CI, 5.4% to 36.8%; p=0.02). The rates of stroke within 30 days of randomization or TIA were 9.4% in the medical group and 24.1% in the stent group (risk difference, 14.7%; 95% CI, 1.2% to 28.2%; p=0.05). The 30-day all-cause mortality rate was 5.2% and 0% in the stent and the medical groups, respectively (risk difference, 5.2%; 95% CI, -0.5% to 10.9%; p=0.25). The authors concluded that results did not support the use of a balloon-expandable stent for patients with symptomatic intracranial stenosis.

The Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS) randomized 16 patients with symptomatic vertebral artery stenoses in a 1:1 ratio to receive best medical treatment plus endovascular therapy (balloon angioplasty or stenting) or best medical treatment alone.[11] Endovascular intervention was technically successful in all 8 patients, but 2 patients experienced transient ischemic attack at the time of endovascular treatment. During a mean follow-up period of 4.7 years, no patient in either treatment group experienced a vertebrobasilar territory stroke, but 3 patients in each treatment arm died of myocardial infarction or carotid territory stroke, and 1 patient in the endovascular arm had a nonfatal carotid territory stroke. The investigators concluded that patients with vertebral artery stenosis were more likely to have carotid territory stroke and myocardial infarction during follow up than have recurrent vertebrobasilar stroke. While they noted that the trial failed to show a benefit of endovascular treatment of vertebral artery stenosis, the small number of patients enrolled severely limits conclusions.
In 2015, Lutsep et al. published a subgroup analysis of the SAMMPRIS trial results to evaluate whether outcomes differed for patients whose qualifying events occurred on or off antithrombotic therapy.\[12\] Similar to the overall trial results, outcomes were worse in the stent group than in the best medical management group: of the 284 patients on antithrombotic therapy at the time of the qualifying event, 140 patients were randomized to medical management and 144 to stenting; in Kaplan-Meier analysis, 2-year rates of the primary end point were 15.6% in the medical management group and 21.6% in the stent group (p=0.043). In other subgroup analyses of the SAMMPRIS trial results, 2-year event rates were higher in the stent group for most variables evaluated.\[13\] The interaction between treatment and the subgroup variables was not significant for any variable.

In 2013, the SAMMPRIS investigators published results from long-term subject follow up.\[14\] Primary end points included stroke or death within 30 days of enrollment, ischemic stroke in the territory of the qualifying artery beyond 30 days after enrollment, or stroke or death within 30 days after a revascularization procedure of the qualifying lesion. During a median follow up of 32.4 months, 34 of 227 (15%) of patients in the best medical management group and 52 of 224 (23%) of patients in the stenting group had a primary end point event, with a significantly higher cumulative probability of a primary end point in the stenting group than in the best medical management group (p=0.025). Compared with the best medical management group, subjects in the stenting group had higher rates of any stroke (59/224 [26%] vs 42/227 [19%], p=0.047) and major hemorrhage (29/224 [13%] vs 10/227 [4%], p<0.001). The authors concluded that the benefits of aggressive medical management over percutaneous angioplasty and stenting among patients with intracranial stenosis persist over long-term follow up.

The Stenting versus Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) trial was an RCT comparing aggressive medical management alone to aggressive medical management plus stenting in patients with symptomatic cerebrovascular disease and an intracranial stenosis of between 70-99%.\[7\] This trial used the Wingspan stent system implanted by experienced neurointerventionists who had been credentialed to participate in the trial. The authors had planned for an enrollment of approximately 750 patients based on power calculations. However, the trial was stopped early for futility after 451 patients had been randomized. The trial was terminated due to an excess of the primary outcome, stroke or death, at 30 days in the stenting group. In the stenting group, the rate of stroke or death at 30 days was 14.7% (95% confidence interval [CI] 10.7-20.1) compared to a rate of 5.8% (95% CI 3.4-9.7, p=0.002) in the medical management group.

At the time of termination, the mean follow-up was 11.9 months. Kaplan-Meier estimates of the primary outcome of stroke or death at one year was 20.5% (95% CI 15.2-26.0) in the stenting group compared to 12.2% (95% CI 8.4-17.6, p=0.009) in the medical management group. These results represented an excess rate of early adverse events with stenting over what was expected together with a decreased rate of stroke and death in the medical management group compared to expected values.

Nonrandomized Trials

A number of nonrandomized studies have compared outcomes of endovascular procedures with medical therapy.\[15-18\] These studies have either been retrospective, or based on registry data, and provided relatively weak evidence on the efficacy of endovascular procedures compared with medical therapy for intracranial atherosclerosis.

Numerous single arm non-comparative case series have also been published.\[19-25\] These studies provide
some information on the success rates and the adverse events that occur with this procedure, but the lack of a control group does not provide evidence on the comparative efficacy of endovascular approaches versus medical therapy.

Conclusion

The strongest evidence on the efficacy of endovascular treatment for symptomatic intracranial stenosis is from the SAMMPRIS RCT. This trial was stopped early due to harms, as the rate of stroke or death at 30 days following treatment was higher in the patients who received percutaneous angioplasty with stenting compared to the medical management arm. Follow up of the SAMMPRIS subjects demonstrated no long-term benefit from endovascular therapy. This supports the conclusion that outcomes of endovascular treatment are worse than medical therapy in patients with symptomatic intracranial stenosis.

Stent-Assisted Treatment of Intracranial Aneurysm

Systematic Reviews

In 2015, Ryu et al. conducted a systematic review of studies reporting complications after stent-assisted coiling of ruptured intracranial aneurysms, with a focus on complications related to antiplatelet therapy. The review included 33 studies, 3 of which were prospective and the remaining 30 retrospective (total N=1090 patients). In pooled analysis, thromboembolic complications occurred in 108 patients (event rate, 11.2%; 95% CI, 9.2% to 13.6%). Intraprocedural hemorrhage occurred in 46 (event rate, 5.4%; 95% CI, 4.1% to 7.1%).

In 2014, Hong et al. reported the results of a systematic review and meta-analysis of studies that compared stent-assisted coiling (N=753) with coiling alone (N=1,813) for the treatment of intracranial aneurysms. The authors included ten retrospective cohort studies, ranging in size from 9 to 1109 patients (N=2,566). In pooled analysis, compared to coiling alone, stent-assisted coiling was associated with higher rates of progressive thrombosis (37.5% vs 19.4%; OR 2.75; 95% CI 1.95 to 3.86; P<0.00001) and lower rates of recurrence (16.2% vs 34.4%; OR 0.35; 95% CI 0.25 to 0.49; P<0.00001). Mortality was 9.1% for stent-assisted coiling, compared with 2.6% for coiling alone; this difference was not statistically significant (OR 2.31; 95% CI 0.68 to 7.82; P=0.18). Similarly, permanent complication rates and thromboembolic complication rates were not significantly different between the two groups. The authors recommended cautious interpretation of their study, noting methodological limitations of their analysis and of the included studies. These limitations included the pooling of data from observational studies with variable baseline characteristics among the included studies such as the location of the aneurysms treated, ruptured and non-ruptured aneurysms, and different interventions.

A 2012 systematic review by Shapiro et al. identified 39 articles reporting on 1517 patients, most of which were single-arm, retrospective series. The majority of patients treated had unruptured aneurysms, but 22% of patients had ruptured aneurysms. The authors noted a large amount of heterogeneity in reporting outcome data, particularly for adverse events. The periprocedural mortality rate was 2.1%, and the overall complication rate was 19%. Immediately following treatment, approximately 45% of patients had occlusion of the aneurysm. At an average of 13 months posttreatment, the stroke rate in the stented area was 3.2%.

A systematic review that was restricted to ruptured aneurysms was published by Bodily et al. in 2011. This review included 17 articles that described treatment in 212 patients. Technical success was high at
93%, and 2% of patients required open surgery due to stent failure or intraoperative aneurysm rupture. A total of 63% (130/207) of aneurysms were successfully occluded. The overall mortality rate was 19%, and 14% of patients had poor clinical outcomes. There was a relatively high rate of adverse events reported, with 8% of patients having an acute intracranial bleed related to the procedure, and 6% (16/288) having a clinically significant thromboembolic event.

**Randomized Controlled Trials (RCTs)**

No RCTs were identified for stent-assisted intracranial aneurysm repair.

**Nonrandomized Comparative Studies**

**Stent-assisted Aneurysm Repair vs. Standard Surgical Treatment**

No trials were found in the published literature that compared stent-assisted treatment of intracranial aneurysms with standard neurosurgical treatment (i.e., surgical clipping or endovascular coils). This contrasts with therapy of ruptured aneurysms in which a randomized trial compared treatment with coiling versus surgical clipping.

**Coiling with vs. without Stenting**

The largest clinical case series describing use of stents in treating intracranial aneurysms was a retrospective cohort study reported by Piotin and colleagues. This study was included in the Hong et al. systematic review summarized above. The authors reported on a series of 1,137 patients (1,325 aneurysms) treated between 2002 and 2009. In this series, coiling was performed without stent-assist in 1,109 aneurysms (83.5%), and with stent assistance in 216 aneurysms (16.5%) (15 balloon-expandable and 201 self-expandable stents). Stents were delivered after coiling in 55% (119/216) and before coiling in 45% (97/216) of the cases. Permanent neurological procedure-related complications occurred in 7.4% (16 of 216) of the procedures with stents versus 3.8% (42 of 1,109) in the procedures without stents (logistic regression p=0.644; odds ratio: 1.289; 95% CI: 0.439–3.779). Procedure-induced mortality occurred in 4.6% (10 of 216) of the procedures with stents versus 1.2% (13 of 1,109) in the procedures without stents (logistic regression p=0.006; odds ratio: 0.116; 95% CI: 0.025–0.531). Thus far, the authors have followed 53% (114 of 216) of aneurysms treated with stents and 70% (774 of 1,109) of aneurysms treated without stents, with angiographic recurrence in 14.9% (17 of 114) versus 33.5% (259 of 774), respectively (p<0.0001; odds ratio: 0.3485; 95% CI: 0.2038–0.5960). Based on this series, the authors concluded that use of stents was associated with a significant decrease of angiographic recurrences but with more lethal complications compared with coiling without stents.

Hetts et al. compared outcomes for patients treated with stent-assisted coiling (n=137) with those treated with coiling alone (n=224) for patients with unruptured intracranial aneurysms enrolled in the prospective, nonrandomized, multicenter Matrix and Platinum Science (MAPS) Trial, which was designed to compare bare-metal aneurysm coils and polymer-coated aneurysm coils. Patients treated with stent-assisted coiling more often had wide-neck aneurysms (62% vs 33%; p<0.000) and had aneurysms with lower dome-to-neck ratio (1.3 vs 1.8; p<0.000). Periprocedural serious AEs occurred in 6.6% of those treated with stent-assisted-coiling, compared with 4.5% of those treated with coiling alone (p=0.039). At 1 year, ischemic strokes were significantly more common in patients who received a stent-assisted coil than in patients who received a coil alone (8.8% vs 2.2%; p=0.005). However, in multivariable analysis, stent use did not independently predict ischemic stroke at 2 years (adjusted OR=1.1; p=0.94). This study has a number of methodological limitations that hinder conclusions such as
post hoc data analysis of a prospective trial that was conducted to compare different coils. Thus, the use of stents was at the discretion of the operating physician. Some centers used no stents, and a higher rate of stent use was found in North America. They also noted that some aneurysm morphologies (e.g., wide neck) were not conducive to treatment with coils alone and required stent-assist. In addition, use of postprocedure antiplatelet medication was not uniform, a limitation which the authors considered significant since the delayed stroke rate for stent-assisting coiling could be associated with antiplatelet management. Other limitations included poor image quality of angiograms and the inability to directly visualize stent struts on digital subtraction angiography.

Liu et al. compared the aneurysms recurrence rates for patients with posterior communicating artery aneurysms treated with stent-assisted coiling with those treated with coiling alone in a retrospective comparative study. They conducted a total of 291 coiling procedures, including 56 aneurysms treated with a self-expandable stent. Complete aneurysm occlusion on initial angiography occurred in 41.1% of stent-assisted coiling patients compared with 35.3% of nonstented patients (statistical comparison not reported). At last follow-up (mean, 14.3 months for stent-assisted coiling and 13.2 months for nonstent patients), aneurysms recurred in 10.6% of stent-assisted coiling patients compared with 28.1% of nonstent patients (p=0.014). Procedural complications occurred in 10.7% of stent-assisted coiling patients compared with 11.5% of nonstent patients (stated to be nonsignificantly different).

A nonrandomized comparative study reported on 126 aneurysms that were treated with stent-assisted coiling compared with 86 patients treated with coil alone. At 2-year follow-up, the authors reported rates of occlusion and recurrence. Progressive occlusion was noted in 42.5% of the stent group (17/40) compared with 39.5% of the nonstented group (34/86), a difference that was not statistically significant. The rates of aneurysm recurrence were also not statistically different between groups. Recurrence occurred in 17.5% of patients in the stent group versus 21.0% in the nonstent group.

**Coiling with Stenting vs. Coiling with Balloon**

Consoli et al. compared stent-assisted coiling with balloon-assisted coiling in patients with unruptured wide-necked intracranial aneurysms treated at a single center. The study included 268 patients (286 aneurysms), 117 (122 aneurysms) of whom were treated with stent-assisted coiling and 151 (164 aneurysms) of whom were treated with balloon-assisted coiling. At discharge, 97.9% and 97.3% of those in the balloon-assisted and stent-assisted groups, respectively, had mRS scores of 0 or 1 (statistical comparison not reported). After 6 months, 97.9% and 98% of those in the balloon-assisted and stent-assisted groups, respectively, had mRS score of 0 or 1, while mortality rates were 2.6% and 1.7% in the balloon-assisted and stent-assisted groups, respectively (statistical comparisons not reported). At 6 months, aneurysm recurrence rates were 11.1% and 5.8% in the balloon-assisted and stent-assisted groups, respectively. In multivariable analysis, the use of stent-assisted coiling was significantly associated with complete occlusion at the end of the procedure (regression coefficient not reported; p=0.024) and complete occlusion after 6 months (regression coefficient not reported; p=0.05).

**Comparisons between Stents**

Nonrandomized studies, summarized in a 2015 systematic review by King et al., have compared devices used for stent-assisted coiling of intracranial aneurysms. King et al. reviewed published studies reporting on stent-assisted coiling with the Neuroform and Enterprise systems to assess outcomes between the devices. The analysis included 47 studies with a total of 4039 patients (4238 aneurysms; 2111 treated with Neuroform and 2127 with Enterprise). Most (81%) studies were retrospective. Compared with those treated with the Enterprise system, patients treated with the Neuroform system...
were more likely to have deployment failure (2.3% vs 0.2%, p<0.001) and have a higher mortality rate (2.8% vs 1.8%, p=0.04), less likely to have 100% aneurysm occlusion at last follow-up (61.1% vs 74.7%, p<0.001), and more likely to have recanalization (13.9% vs 10.6%, p=0.02).

In 2013, Kadkhodayan et al. reported results from a nonrandomized comparison of the Neuroform and Enterprise systems in the treatment of intracranial aneurysms not amenable to surgical clipping based on evaluation of prospectively collected registry data.[36] Patients who received the Neuroform device (n=160) were enrolled starting in February 2003, and patients who received the Enterprise device (n=98) were enrolled starting in March 2007. Indications for the devices differed slightly based on FDA HDE criteria: both have an indication for wide-necked aneurysms (neck ≥4 mm or a dome-to-neck ratio <2 mm) not amenable to surgical clipping. For the Enterprise, stents were used for sacular or fusiform aneurysms arising from a parent vessel with a diameter of ≥2.5 mm and ≤4 mm; for the Neuroform, stents were used for sacular aneurysms arising from a parent vessel with a diameter of ≥2 mm and ≤4.5 mm. The authors reported that Enterprise deployment success was high (108 of 115 attempts, 93.9%) compared with Neuroform (173 of 214 attempts, 80.8%, p=0.001). Rates of stent movement, misplacement, and symptomatic hemorrhage were similar for the 2 stent types, but symptomatic thromboembolic events were more frequent with the Enterprise stent (8.7% vs 1.4%, p=0.002).

Nonrandomized Single-arm Studies

Since the publication of the Shapiro and Bodily systematic reviews, a number of noncomparative studies evaluating the use of stent-assisted endovascular treatments in intracranial aneurysms have been published.[37-47] In general, these series demonstrate high rates of technical success of stent deployment with high rates of aneurysm occlusion; however, variable complication rates, particularly related to thromboembolic events were observed. Long-term follow up, particularly beyond 1 year, was limited. Interpretation of these studies is limited by significant methodologic limitations, including but not limited to the lack of a control group for comparison, short-term outcomes, and potential selection bias.

Flow-diverting Stents for Intracranial Aneurysm

Systematic Reviews and Meta-analyses

Zhou et al reported results of a systematic review of studies comparing flow-diverting devices with endovascular coiling for intracranial aneurysms, which included nine retrospective comparative studies (total N=863 subjects).[48] This review included studies of patients with ruptured or unruptured aneurysms. Across the nine studies, 305 patients were treated with flow-diverting devices, 558 with coil embolization therapy, and 324 with stent-assisted coiling alone. In pooled analysis, the use of flow-diverting devices was associated with a significantly higher complete occlusion rate compared with coil embolization therapy (OR=3.13; 95% CI, 2.11 to 4.65; I²=18%) or with stent-assisted coiling (OR=2.08; 95% CI, 1.34 to 3.24; I²=0%). Rates of overall morbidity did not differ significantly between patients treated with flow-diverting devices and coil embolization therapy, or between flow-diverting devices and stent-assisted coiling.

The largest meta-analysis by Brinjikji et al., published in 2013, included 1451 patients with 1654 aneurysms reported in a total of 29 studies published through 2012.[49] The authors evaluated aneurysmal occlusion rates at 6 months, and procedure-related morbidity, mortality, and complications across studies. They found a high rate of complete aneurysmal occlusion (76% [95% CI, 70% to 81%], but also a high rate of procedure-related morbidity and mortality (5% [95% CI, 4% to 7%] and 4% [95% CI, 3% to 6%], respectively). This systematic review included the study upon which the FDA approval
Also in 2013, Arrese et al. reported results of a meta-analysis that used somewhat more restrictive inclusion criteria that included 897 patients with 1018 aneurysms reported in a total of 15 studies. All but two of the studies were included in the Brinjikji meta-analysis. The authors determined rates of complete or nearly complete occlusion of the treated aneurysm with a patent parent artery and early procedure-related mortality and neurologic morbidity. Similar to the Brinjikji meta-analysis, this study found a high overall rate of complete aneurysmal occlusion (76.2% [95% CI, 72.1 to 80.2]), but also a high rate of procedure-related morbidity and mortality (2.8% [95% CI, 1.7%–3.8%] and 7.3% [95% CI, 5.7% to 9%], respectively). The authors assessed for publication bias using funnel plots and the Egger’s test to assess whether the study estimate size is related to the size of the study, and found p<0.001 for the Egger’s test for both early and late morbidity and aneurysmal occlusion, suggestive of publication bias.

Randomized Controlled Trials (RCTs)

No RCTs were found in which flow-diverting stents were used for the treatment of intracranial aneurysms.

Nonrandomized Comparative Studies

Since the publication of the systematic reviews summarized above, several additional studies have been published.

Guedon et al reported on late ischemic complications after flow-diverting stent placement. Among 86 patients treated at a single institution, mean angiographic follow up was available to 15.7 months (SD=11.8 months; range, 8-21 months) and mean clinical follow-up was available to 16.9 months (SD=12.9 months; range 10-22 months). Five (5.8%) patients developed ischemic complications. The longest follow-up reported is from a series of 98 patients with 119 aneurysms treated with the Pipeline Embolization Device and followed for at least two years. Of the 119 aneurysms, all had clinical follow-up and 88.8% had imaging follow-up for two or more years postprocedure. Aneurysm occlusion rates were 81.6%, 84.1%, and 93.2% at 6-month, 1-year, and 2-year follow-ups, respectively. Three (2.8%) cases of in-stent stenosis occurred. From 0 to 6 months, rates of TIA, minor stroke, and major stroke were 4.2%, 3.4%, and 0.8%, respectively.

Kallmes et al, who conducted a retrospective analysis of patients treated with the Pipeline device at 17 centers worldwide. The authors identified 793 patients with 906 aneurysms who were enrolled in the International Retrospective Study of Pipeline Embolization Device (IntrePED) registry. Of the total number of aneurysms, 311 were in the anterior ICA circulation and at least 10 mm, 349 of which were in the anterior circulation and less than 10 mm, 59 of which were in the posterior circulation, 179 of which were in a non-ICA anterior circulation location and less than 10 mm, and 10 of which had no aneurysm size specified. Overall neurologic morbidity and mortality was 8.4%, highest in the posterior circulation group (16.4%) and lowest in the less than 10-mm ICA group (4.8%; p=0.01). The overall spontaneous rupture rate was 0.6%, and the intracranial hemorrhage rate was 2.4%. Ischemic stroke rates were 4.7%, again highest in the posterior circulation group (7.3%) and lowest in the less than 10-mm ICA group (2.7%; p=0.16). In a subsequent study using data from the same registry, Brinjikji et al reported on risk factors for hemorrhagic complications after Pipeline device placement. Twenty patients had an intraparenchymal hemorrhage, most often (75%) within 30 days of treatment. The only procedure- or device-related variable associated with intraparenchymal hemorrhage was receiving 3 or 4 coils.
more Pipeline devices (OR=4.10; 95% CI, 1.34 to 12.58; p=0.04). Additional analyses from this registry have evaluated the effect of age on outcomes after Pipeline placement and differences in complication rates between aneurysms treated with the Pipeline with or without coil embolization.

In 2014, van Rooij et al reported outcomes for 550 consecutive patients treated with endovascular methods for intracranial aneurysms at a single European center from 2009 to 2013. Endovascular treatments consisted of selective coiling in 445 (80.8%), stent-assisted coiling in 68 (12.4%), balloon-assisted coiling in 13 (2.4%), parent vessel occlusion in 12 (2.2%), and flow-diverter treatment in 12 (2.2%). Among the 11 patients treated with flow diverters, two patients had ruptured dissecting aneurysms, two deaths occurred, one patient had permanent morbidity, and two aneurysms were not occluded at 30 months follow-up. Direct comparisons with outcomes from alternative treatments were not reported. However, based on these poor outcomes and the high complication rates reported in other studies, the authors recommended against the use of flow-diverter devices in aneurysms that are amenable to other techniques.

A comparative study based on registry data of health outcomes following insertion of the Pipeline device versus endovascular coiling. They identified a total of 229 patients enrolled during their data collection period from 2004-2013, 54 treated with the Pipeline device and 175 with coiling. Patients treated with the Pipeline device were significantly older and had significantly larger aneurysms that were more likely to be fusiform. Because of this, the authors excluded patients with fusiform or anterior communicating artery aneurysms and conducted their analysis in 160 patients (40 Pipeline and 120 coil patients) who were matched in a 1:3 ratio on the basis of patient age and aneurysm size. Aneurysm neck size, overall size, and anterior versus posterior circulation location were similar between the groups. Of the patients treated with the Pipeline device, 4 patients (10%) also required adjunctive coil placement. Of the patients treated with endovascular coiling, 67 (56%) were treated with coiling, while 52 (43%) were treated with stent-assisted coiling and 1 (1%) with balloon-assisted coiling. Primary outcomes included obliteration of the aneurysm on follow-up imaging and clinical outcomes, measured by Modified Rankin Scale score of 0-2 (vs 3-6).

At the time of latest follow up, a higher proportion of aneurysms treated with the Pipeline device compared with those treated with coiling achieved complete obliteration (30/35 [86%] vs 37/90 [41%], p<0.001). However, angiographic follow-up was available for a greater proportion of patients treated with the Pipeline (35 /40 [87.5%]) than those treated with coiling (90/120 [75%]), and the median angiographic follow-up time differed significantly between the groups (7 months in the Pipeline group and 12 months in the coil group, p<0.001). In terms of clinical outcomes, similar proportions of the Pipeline and coil groups had a Modified Rankin Scale score 0 to 2 (35/38 [92%] in the Pipeline group vs 97/103 [94%], p=0.8). Similar to the angiographic follow up results, the median clinical follow-up time differed significantly between the groups. Treatment type was not significantly associated with rates of procedure-related complications. While this study directly compares patients treated with the Pipeline endovascular device and those treated with coiling, it is limited by its nonrandomized, retrospective design. In particular, patients treated with coiling were treated in an earlier period (2004-2011) than those treated with the Pipeline device (2011-2012); this may have systematically biased the study in favor of the Pipeline device because aspects of neurointerventional care other than the device used may have differed over time.

The remaining studies were single-arm studies showing feasibility and short-term outcomes up to one year. Interpretation of these studies is limited by significant methodologic limitations, including but not limited to the lack of a control group for comparison, short-term outcomes, and small sample size.
**Acute Stroke**

There are currently no randomized controlled trials for intracranial angioplasty with or without stenting for acute ischemic stroke. A number of case series have been published including the Stent-Assisted Recanalization for Acute Ischemic Stroke (SARIS) trial.\[70\] This study was a prospective series of 20 patients with acute ischemic stroke who presented within 8 hours of symptom onset, with a NIH stroke score of at least 8, and for whom thrombolysis was either contraindicated or ineffective. All patients were treated with the Wingspan intracranial self-expanding stent, aspirin, and clopidogrel. At six months follow-up, mortality was 35% (7/20), NIH stroke score was 3 or less in 60% of patients (12/20), and 55% (11/20) had an NIH stroke score of 2 or less. A total of 11/13 (85%) patients who were alive at six months had a follow-up angiogram and all showed patency of the stent graft with TIMI level 3 flow or greater.

**Clinical Practice Guidelines and Position Statements**

**Intracranial Atherosclerosis**

*The Society for NeuroInterventional Surgery (SNIS)*

In 2012, the SNIS published consensus-based recommendations in a clinical standards statement on endovascular angioplasty and/or stenting of intracranial atherosclerosis.\[71\] The only randomized controlled trial found was the SAMMPRIS trial, described above. This trial was ranked as AHA evidence level B, defined as limited evidence from a single randomized trial or other nonrandomized studies. The remaining included studies were nonrandomized studies that were uncontrolled or did not have objective outcome measures; these were classified as AHA evidence level C, defined as based on expert opinion, case studies, or standard of care. The following recommendations were made:

- Medical therapy was recommended over angioplasty and stent therapy (Class IIa recommendation: Weight of evidence/opinion is in favor of usefulness/efficacy).
- For symptomatic 70-99% intracranial stenosis refractory to aggressive maximal medical therapy, angioplasty or stenting may be considered (Class IIb recommendation: Usefulness/efficacy less well-established by evidence/opinion).
- There is insufficient evidence to recommend between angioplasty and balloon mounted drug eluting or self-expanding stent systems (Class III recommendation: Intervention is not useful/effective and may be harmful).

*The American Society of interventional and Therapeutic Neuroradiology (ASITN), the Society of interventional Radiology (SIR), and the American Society of Neuroradiology (ASNR)*

In 2005 the ASITN, SIR, and ASNR jointly published a position paper on intracranial endovascular procedures.\[72\] This position statement reviewed a number of case series and also the SSYLVIA and Wingspan studies. It was republished in 2009 without an updated evidence review.\[73\] The following statement was offered, although the underlying rationale and process for development for the position statement was not provided:

“The ASITN, SIR, and ASNR concur that sufficient evidence now exists to recommend that intracranial angioplasty with or without stenting should be offered to symptomatic patients with intracranial stenoses who have failed medical therapy. Endovascular interventions are intensive services provided to patients who are at very high risk for stroke and typically have multiple comorbidities. Similar to revascularization for extracranial carotid artery stenosis, patient benefit
from revascularization for symptomatic intracranial arterial stenosis is critically dependent on a low periprocedural stroke and death rate and should thus be performed by experienced neurointerventionists. We recommend reimbursement by third party insurers so that these patients may have access to such interventions. Continued attempts to improve the benefits of endovascular therapy are warranted.”

*The American Heart Association (AHA)*

In April 2009, the AHA, along with several other organizations, published a statement on indications for intracranial endovascular neuro-interventional procedures.[74] The statement recommended that angioplasty and/or stenting be considered for patient with symptomatic severe intracranial stenoses (>70% luminal narrowing) that has been unresponsive to optimal medical therapy (Class IIb, Level of Evidence C, defined above).

**Intracranial Aneurysm**

No clinical practice guidelines or position statements from U.S. professional societies were found that provided recommendations for stenting in the treatment of intracranial aneurysms. The 2009 AHA statement mentioned that stent deployment is being investigated to assist in coil embolization of certain aneurysms, but did not include stenting in their recommendations.

**Acute Stroke**

*The American Heart Association (AHA) and the Society for NeuroInterventional Surgery (SNIS)*

In separate position statements, the AHA[74] and the SNIS[75] recommended that the usefulness of endovascular devices other than mechanical thrombectomy devices “is not yet established, but may be beneficial and may be considered” (Class IIb, Level of Evidence C, defined above).

**Summary**

Use of endovascular stents in the treatment of intracranial aneurysms is generally reserved for cases in which successful occlusion of the aneurysm cannot be obtained with standard surgical or endovascular techniques, e.g., wide-neck aneurysms. Despite the lack of evidence from well-designed randomized controlled trials, stent-assisted coil embolization is becoming more widely used for certain intracranial aneurysms. Thus, use of stents may be considered medically necessary as part of the endovascular treatment of intracranial aneurysms in selected cases that meet the medical policy criteria.

For elective treatment of symptomatic intracranial artery stenosis, the current evidence is insufficient to determine the effectiveness and rate of adverse events of endovascular angioplasty with or without stenting compared with best medical therapy. The evidence suggests that the adverse event rate with endovascular angioplasty is relatively high and may outweigh the benefit in preventing recurrent ischemic events. In addition, there are no clinical practice guidelines from U.S. professional societies that recommend angioplasty with or without stenting for treatment of intracranial artery stenosis. Therefore, endovascular angioplasty with or without stenting is considered investigational for the elective treatment of symptomatic intracranial stenosis.

In individuals who have extracranial vertebral artery stenosis who receive percutaneous transluminal angioplasty with or without stent implantation, the evidence includes two RCTs that found no advantage...
of endovascular intervention compared to best medical therapy alone. Evidence from non-comparative studies indicates that vertebral artery stenting can be performed with high rates of technical success with low periprocedural morbidity and mortality, and that vessel patency can be achieved in a high percentage of cases. However, long-term follow-up demonstrates high rates of in-stent stenosis. Therefore, percutaneous transluminal angioplasty with or without stenting is considered investigational for the treatment of atherosclerotic cerebrovascular disease.

For elective treatment of acute ischemic stroke, the current evidence is insufficient to determine the effectiveness and rate of adverse events of endovascular angioplasty with or without stenting compared with best medical therapy. The evidence for small case series suggests that the adverse event rate with endovascular angioplasty is relatively high and may outweigh the benefit in preventing recurrent ischemic events. However, there have been no randomized controlled trials to confirm the net benefit on health outcomes. In addition, there are no clinical practice guidelines from U.S. professional societies that recommend angioplasty with or without stenting for treatment of acute ischemic stroke. Therefore, endovascular angioplasty with or without stenting is considered investigational for the elective treatment of acute ischemic stroke.

REFERENCES

1. BlueCross BlueShield Association Medical Policy Reference Manual "Endovascular Procedures (Angioplasty and/or Stenting) for Intracranial Arterial Disease (Atherosclerosis and Aneurysms)." Policy No. 2.01.54
2. FDA Website with link to H010004b. [cited 05/19/2016]; Available from: http://www.accessdata.fda.gov/cdrh_docs/pdf/H010004b.pdf
3. FDA Website with link to H050001. [cited 05/18/2016]; Available from: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cftopic/pma/pma.cfm?num=H050001
11. Coward, LJ, McCabe, DJ, Ederle, J, Featherstone, RL, Clifton, A, Brown, MM. Long-term outcome after angioplasty and stenting for symptomatic vertebral artery stenosis compared with


60. Lin, LM, Colby, GP, Kim, JE, Huang, J, Tamargo, RJ, Coon, AL. Immediate and follow-up results for 44 consecutive cases of small (<10 mm) internal carotid artery aneurysms treated with the pipeline embolization device. *Surg Neurol Int*. 2013;4:114. PMID: 24083050


**CROSS REFERENCES**

- **Extracranial Carotid Angioplasty/Stenting**, Surgery, Policy No. 93
- **Percutaneous Angioplasty and Stenting of Veins**, Surgery, Policy No. 109
- **Mechanical Embolectomy for Treatment of Acute Stroke**, Surgery, Policy No. 158

<table>
<thead>
<tr>
<th>CODES</th>
<th>NUMBER</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>61630</td>
<td>Balloon angioplasty, intracranial (e.g., atherosclerotic stenosis), percutaneous</td>
</tr>
<tr>
<td></td>
<td>61635</td>
<td>Transcatheter placement of intravascular stent(s), intracranial (e.g., atherosclerotic stenosis), including balloon angioplasty, if performed</td>
</tr>
<tr>
<td>HCPCS</td>
<td>None</td>
<td></td>
</tr>
</tbody>
</table>

*These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.*
Extracorporeal Membrane Oxygenation (ECMO) for the Treatment of Cardiac and Respiratory Failure in Adults

Effective: October 1, 2017

Next Review: September 2018
Last Review: September 2017

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Extracorporeal Membrane Oxygenation (ECMO) is a complex treatment which utilizes a modified cardiopulmonary bypass circuit for temporary life support as a treatment for reversible cardiac and/or respiratory failure.

MEDICAL POLICY CRITERIA

Note: This policy does not address the use of ECMO in children or neonates, which may be considered medically necessary. In addition, this policy does not address the use of short-term extracorporeal support, including ECMO, such as during surgical procedures. The Policy Guidelines section below includes information regarding weaning and/or discontinuation of ECMO.

I. Extracorporeal Membrane Oxygenation (ECMO) in adults (18 years or older) may be considered medically necessary as a treatment of respiratory or cardiac failure that is potentially reversible when both of the following criteria I.A. and I.B. are met:

   A. At least one of the following criteria is met:

      1. Hypoxic respiratory failure despite maximal lung-protective ventilation (see Policy Guidelines) as demonstrated by any one or more of the following:
a. Murray Lung Injury Score three or higher (see Policy Guidelines for Murray Lung Injury Score); or

b. PaO2/FiO2 of less than 100 mm Hg on fraction of inspired oxygen (FiO2) greater than 90%; or

c. Inability to maintain airway plateau pressure (Pplat) less than 30 cm H2O despite a tidal volume of four to six mL/kg ideal body weight (IBW); or

d. Oxygenation Index greater than 30: Oxygenation Index equals FiO2 times 100 times MAP divided by PaO2 mm Hg. [FiO2 times 100 equals FiO2 as percentage; MAP equals mean airway pressure in cm H2O; PaO2 equals partial pressure oxygen in arterial blood].

2. Respiratory failure despite maximal lung-protective ventilation (see Policy Guidelines) as demonstrated by any one of the following:
   a. Significant hypercapnea despite high Pplat (greater than 30 cm H2O); or
   b. A pH of less than 7.20 due to significant uncompensated hypercapnia

3. Severe air leak syndromes including, but not limited to:
   a. Significant tracheal airway injuries; or
   b. An air-leak or broncho-pleural fistula that prevents adequate ventilation with lung-protective ventilation (see Policy Guidelines) strategies.

4. Refractory cardiogenic shock as demonstrated by one of the following:
   a. Inadequate tissue perfusion manifested as hypotension and low cardiac output despite adequate intravascular volume; or
   b. Shock which persists despite volume administration, inotropes and vasoconstrictors, and intra-aortic balloon counterpulsation.

5. Hypothermia with a core temperature of less than 28 degrees centigrade.

6. As a bridge to heart, lung or heart-lung transplantation.

B. None of the following contraindications are present:

1. Ventilation with high ventilator pressure (Pplat greater than 30 cm H2O) sustained throughout a seven day period and/or high FiO2 (greater than 80%) sustained throughout a seven day period; or

2. Signs of intracranial bleeding, or other major central nervous system injury without the potential to recover meaningful function; or

3. Presence of an irreversible, terminal illness; or

4. Cardiac decompensation and not meeting medical necessity criteria for heart transplant or ventricular assist device; or

5. Chronic organ failure without the potential to recover meaningful function; or

6. Prolonged CPR without adequate tissue perfusion; or

7. Patient choice to decline extraordinary life support interventions. (see Policy Guidelines)
II. The continued use of Extracorporeal Membrane Oxygenation (ECMO) in adult patients meeting criteria I., is considered **not medically necessary** if any one or more of the following conditions are present for five or more days:

A. Neurologic devastation determined by at least two physicians agreeing after evaluation, (including neurologic examination, head CT, and EEG), that the patient has sustained irreversible cessation of all functioning of the brain, including the brain stem and an outcome better than “persistent vegetative state” at six months is unlikely. At least one of these physicians should be a neurologist, neurosurgeon, and/or neuro-intensivist.

B. End stage fibrotic lung disease confirmed by lung biopsy. The presence of end stage fibrotic lung disease is suggested by PA systolic pressures sustained at greater than 75% of systemic pressures.

C. Hypotension and/or hypoxemia recalcitrant to all maneuvers which causes inadequate aerobic metabolism demonstrated by evidence of profound tissue ischemia [creatine phosphokinase (CPK), lactate, lactate to pyruvate (L/P) ratio, near-infrared spectroscopy (NIRS)].

D. End-stage cardiac or lung failure without alternative long-term plan (i.e., ineligible for assist device and/or transplant).

III. The use of Extracorporeal Membrane Oxygenation (ECMO) in adult patients is considered **investigational** in all other situations, including but not limited to when the above criteria I. is not met.

**NOTE:** A summary of the supporting rationale for the policy criteria is at the end of the policy.

**POLICY GUIDELINES**

**RESPIRATORY FAILURE REVERSIBILITY**

The reversibility of the underlying respiratory failure is best determined by the treating physicians, ideally physicians with expertise in pulmonary medicine and/or critical care. Some of the underlying causes of respiratory failure which are commonly considered reversible are as follows:

- Acute respiratory distress syndrome (ARDS)
- Acute pulmonary edema
- Acute chest trauma
- Infectious and noninfectious pneumonia
- Pulmonary hemorrhage
- Pulmonary embolism
- Asthma exacerbation
- Aspiration pneumonitis.

**MAXIMAL LUNG-PROTECTIVE VENTILATION**

The Society of Critical Care Medicine (SCCM) has made the following recommendations regarding lung-protective ARDS ventilation management:[1]
• Low tidal volume ventilation (4-6 mL/kg of ideal body weight)
• Plateau pressure (pPlat) < 30 cm H2O

In addition, the SCCM recommends optimal recruitment pressures.

Additional lung protective options include prone positioning[2] and neuromuscular blockade[3].

MURRAY LUNG INJURY SCORE

The Murray Lung Injury Score is a system for classifying the severity of respiratory failure. It was developed for use in ARDS, but has been applied to other indications.[4] This score includes four subscales, each of which is scored from 0 to 4. The final score is obtained by dividing the collective score by the number of subscales used. A score of 0 indicates no lung injury; a score of 1-2.5 indicates mild or moderate lung injury; and a score of 2.5 indicates severe lung injury, e.g. ARDS. Table 1 shows the components of the Murray scoring system.

Table 1: Murray Lung Injury Score

<table>
<thead>
<tr>
<th>Subscale</th>
<th>Criteria</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest x-ray score</td>
<td>No alveolar consolidation</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Alveolar consolidation confined to 1 quadrant</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Alveolar consolidation confined to 2 quadrants</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Alveolar consolidation confined to 3 quadrants</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Alveolar consolidation in all 4 quadrants</td>
<td>4</td>
</tr>
<tr>
<td>Hypoxemia score</td>
<td>PaO2/FiO2 &gt;300</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>PaO2/FiO2 225-299</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>PaO2/FiO2 175-224</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>PaO2/FiO2 100-174</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>PaO2/FiO2 ≤ 100</td>
<td>4</td>
</tr>
<tr>
<td>PEEP score (when ventilated)</td>
<td>PEEP ≤ 5 cm H2O</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>PEEP 6-8 cm H2O</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>PEEP 9-11 cm H2O</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>PEEP 12-14 cm H2O</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>PEEP ≥ 15 cm H2O</td>
<td>4</td>
</tr>
<tr>
<td>Respiratory system compliance</td>
<td>Compliance &gt;80 mL/cm H2O</td>
<td>0</td>
</tr>
<tr>
<td>score (when available)</td>
<td>Compliance 60-79 mL/cm H2O</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Compliance 40-59 mL/cm H2O</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Compliance 20-39 mL/cm H2O</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Compliance ≤ 19 mL/cm H2O</td>
<td>4</td>
</tr>
</tbody>
</table>

CPAP – continuous positive airway pressure; FiO2 – fraction of inspired oxygen; PaO2 – partial pressure of oxygen in arterial blood; PEEP – peak end expiratory pressure.

In addition to the Murray Lung Injury Score, the Berlin Definition is gaining acceptance for classifying acute respiratory distress syndrome (ARDS).[5]

WEANING AND DISCONTINUATION OF ECMO

The Extracorporeal Life Support Organization (ELSO) has published guidelines regarding the weaning and discontinuation of ECMO.[6] The general ECMO guidelines indicate: "(e)xtracorporeal support is decreased as native organ function improves. When ECC [extracorporeal circulation] support is less than 30% of total, native heart or lung function may be adequate to allow coming off ECLS, and a trial off is indicated. Note: As long as ECC support is more than 30 to 50%, there is no indication to trial off, except in special..."
circumstances such as uncontrolled bleeding. ECLS should be discontinued promptly if there is no hope for healthy survival (severe brain damage, no or heart or lung recovery, and no hope of organ replacement by VAD or transplant). The definition of irreversible heart or lung damage depends on the patient and the resources of the institution. In each case a reasonable deadline for organ recovery or replacement should be set early in the course.”

In addition, ELSO has published specific weaning guidelines for cardiac failure:

**Cardiac Failure**

ELSO suggests the general guidelines summarized above should be used for weaning in cases of cardiac failure.[7] In addition, ELSO guidelines for Adult Cardiac Failure list the following for bridge to recovery, including for postcardiotomy, acute MI, and myocarditis:

1. Expect early signs of recovery within one week of support.
2. With evidence of improved aortic pulsatility and contraction on echocardiography, optimize inotropes and reduce flow to 50%, then 25% of adequate cardiac output.
3. Use echo to visualize ventricular function and major valvular pathology.
4. Clamp circuit and allow recirculation for trial period of 30 minutes to four hours.
5. Flush cannulae with heparinized saline continuously or flash from the circuit every 10 minutes to avoid cannula thrombosis.
6. If hemodynamics and oxygen delivery are adequate on less than maximum inotropic infusions, consider decannulation.

**Respiratory Failure**

Methods of weaning and discontinuing ECMO treatment may vary based upon a variety of factors, including but not limited to, individual patient clinical considerations and the current established practice of specialty ECMO centers. Weaning guidelines for respiratory failure used regionally include the following:[8]

1. **Indications of recovery:**
   a. Absence of signs of active inflammation and/or shock
   b. Reduced pressor requirements
   c. Improvements in laboratory findings, including white blood counts (WBCs), C-reactive protein (CRP), lactate, and base deficit
   d. Evidence of improving respiratory status on chest X-ray (CXR) arterial blood gases (ABGs) and ventilation parameters (compliance, etc.). A specific measure is the Cilley test: daily "step up" ABGs measuring responses to transient FiO2 of 100% on vent.
   e. Evolution of negative fluid balance
   f. Decreasing sweep requirements

2. **"Recruitment" measures may be considered:**
   a. If effusions are present, consider draining effusions to improve functional residual capacity (FRC)
   b. Central venous pressure (CVP) < 9 and total body water (TBW) euvoolemia with diuresis or continuous renal replacement therapy (CRRT)
   c. Regional atelectasis may be addressed with positional therapy
   d. Possible lightened sedation to encourage spontaneous breathing and coughing
   e. Bronchoscopy for pulmonary toilet
f. Ventilator settings to encourage recruitment, assuring mean arterial pressure (MAP) < 24

3. Consider a trial off ECMO when indications of recovery are present.

PATIENT CHOICE TODECLINE EXTRAORDINARY LIFE SUPPORT INTERVENTIONS

Choices to decline extraordinary life support interventions may include, but is not limited to, the presence of an advanced directive, healthcare directive, Physician Orders for Life Sustaining Treatment (POLST), or Physician Orders for Scope of Treatment (POST) to indicate the patient or the patient’s health care representative or agent has selected any of the following upon which life-sustaining support would be withheld or withdrawn:

- A Do Not Resuscitate (DNR, DNAR, No Code) order; or
- Allow Natural Death; or
- No CPR or advanced cardiac life support interventions; or
- An equivalent choice.

CROSS REFERENCES

1. Ventricular Assist Devices and Total Artificial Hearts, Surgery, Policy No. 52

BACKGROUND

Extracorporeal Membrane Oxygenation (ECMO), also referred to as extracorporeal life support (ECLS), or extracorporeal lung assist (ELA), has been proposed as an alternative treatment for cardiac and respiratory failure in adult patients and is described by the Extracorporeal Life Support Organization (ELSO) as, “the use of a modified cardiopulmonary bypass circuit for temporary life support for patients with potentially reversible cardiac and/or respiratory failure. ECMO provides a mechanism for gas exchange as well as cardiac support thereby allowing for recovery from existing lung and/or cardiac disease.”[9] ECMO is used for prolonged time periods (days to weeks) and involves removing a portion of the patient’s blood, pumping it through a membrane oxygenator, removing carbon dioxide, rewarming the blood, and returning it to the patient. ECMO is a complex treatment requiring a specialized staff and specific equipment. The ELSO specialty group maintains a registry of detailed data from a voluntary international consortium of health care centers which utilize ECMO.[9]

Historically, ECMO has been used in neonatal and pediatric populations to treat respiratory failure related to a variety of respiratory diseases. The treatment may be used in newborn infants with neonatal respiratory distress due to congenital diaphragmatic hernia, meconium aspiration, hyaline membrane disease, pulmonary hypertension and pulmonary hypoplasia, and pneumonia with sepsis. ECMO is associated with a 55% survival rate in this subgroup and has become an accepted treatment for respiratory failure in pediatric and neonatal patients, despite the lack the randomized trials.[10-12]

With improvements in ECMO circuit technology and methods of supportive care, ECMO has been proposed as salvage therapy to prevent irreversible neurologic damage in adults with acute, reversible respiratory or cardiac failure. In critically ill adult patients, ECMO also may be considered a non-ventilatory treatment by which to avoid ventilator induced lung injury (VILI) associated with mechanical ventilation. In these situations, death would be imminent unless medical interventions can immediately reverse the underlying disease process or physiologic
functions can be supported for long enough that normal reparative processes or treatment can occur (e.g., resolution of ARDS or treatment of infection) or other life-saving intervention can be delivered (e.g., provision of a lung transplant).

**DISEASE-SPECIFIC INDICATIONS FOR ECMO**

Venoarterial (VA) and venovenous (VV) ECMO have been investigated for a wide range of adult conditions that can lead to respiratory or cardiorespiratory failure, some of which overlap clinical categories (e.g., H1N1 influenza infection leading to ARDS and cardiovascular collapse), which makes categorization difficult. ARDS has been defined by consensus in the Berlin definition, which includes criteria for the timing of symptoms, imaging findings, exclusion of other causes, and degree of oxygenation.[13] However, in general, indications for ECMO can be categorized as follows:

- **Acute respiratory failure due to potentially reversible causes.** Acute respiratory failure refers to the failure of either oxygenation, removal of carbon dioxide, or both, and may be due to a wide range of causes. In these cases, ECMO is most often used as a bridge to recovery. Specific potentially reversible or treatable indications for ECMO may include ARDS, acute pneumonias, and a variety of other pulmonary disorders.

- **Bridge to lung transplant.** Lung transplant is used for management of chronic respiratory failure, most frequently in the setting of advanced chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis, cystic fibrosis, emphysema due to alpha-1-antitrypsin deficiency, and idiopathic pulmonary arterial hypertension. In the end stages of these diseases, patients may require additional respiratory support while awaiting an appropriate donor. In addition, patients who have undergone a transplant may require retransplantation due to graft dysfunction after the primary transplant.

- **Acute-onset cardiogenic or obstructive shock** is defined as shock that is due to cardiac pump failure or vascular obstruction, refractory to inotropes and/or other mechanical circulatory support. Examples of this category include postcardiotomy syndrome (i.e., failure to wean from bypass), acute coronary syndrome, myocarditis, cardiomyopathy, massive pulmonary embolism, and prolonged arrhythmias.

- **ECMO-assisted cardiopulmonary resuscitation (E-CPR).** ECMO can be used as an adjunct to CPR in patients who do not respond to initial resuscitation measures.

**TECHNOLOGY DESCRIPTION**

The basic components of ECMO include a pump, an oxygenator, sometimes referred to as a “membrane lung,” and some form of vascular access. Based on the vascular access type, ECMO can be described as VV or VA. VA ECMO has the potential to provide cardiac and ventilatory support.

More recently, these include ventilation support devices that provide oxygenation and removal of CO₂ without the use of a pump system or interventional lung assist devices (e.g., iLA® Membrane Ventilator, Novalung GmbH). These technologies are not the focus of this evidence review, but are described briefly because there is overlap in patient populations treated with extracorporeal carbon dioxide removal (ECCO₂R) and those treated with ECMO, and some studies have reported on both technologies.

In contrast to VA and VV ECMO, which use large-bore catheters and generally high flow
through the ECMO circuits, other systems use pumpless systems to remove CO₂. These pumpless devices achieve ECCO₂R via a thin double-lumen central venous catheter and relatively low extracorporeal blood flow. They have been investigated as a means to allow low tidal volume ventilator strategies, which may have benefit in ARDS and other conditions where lung compliance is affected. Although ECMO systems can effect CO₂ removal, dedicated ECCO₂R systems are differentiated by simpler mechanics and the fact that they do not require dedicated staff.[14]

**Venovenous ECMO**

**Technique**

In venovenous extracorporeal membrane oxygenation (VV ECMO), the ECMO oxygenator is in series with the native lungs, and the ECMO circuit provides respiratory support. Venous blood is withdrawn through a large-bore intravenous line; oxygen is added and CO₂ removed, and oxygenated blood is returned to the venous circulation near the right atrium. Venous access for VV ECMO can be configured through two single lumen catheters (typically in the right internal jugular and femoral veins), or through one dual lumen catheter in the right internal jugular vein. In the femorojugular approach, a single large multiperforated drainage cannula is inserted in the femoral vein and advanced to the cavo-atrial junction, and the return cannula is inserted into the superior vena cava via the right internal jugular vein. Alternatively, in the bi-femorojugular approach, drainage cannulae are placed in both the superior vena cava and the inferior vena cava via the jugular and femoral veins, and a femoral return cannula is advanced to the right atrium. In the dual-lumen catheter approach, a single bicaval cannula is inserted via the right jugular vein and positioned to allow drainage from the inferior vena cava and superior vena cava and return via the right atrium.

**Indications**

VV ECMO provides only respiratory support, and therefore is used for conditions in which there is progressive loss in ability to provide adequate gas exchange due to abnormalities in the lung parenchyma, airways, or chest wall. Right ventricular (RV) dysfunction due to pulmonary hypertension that is secondary to parenchymal lung disease may sometimes be effectively treated by VV ECMO.

However, acute or chronic obstruction of the pulmonary vasculature (e.g., saddle pulmonary embolism) may require VA ECMO. There may be cases in which RV dysfunction due to pulmonary hypertension caused by severe parenchymal lung disease may be severe enough to require VA ECMO. In adults, VV ECMO is generally used only in situations in which all other reasonable avenues of respiratory support have been exhausted, including mechanical ventilation with lung protective strategies, pharmacologic therapy, and prone positioning.

**Venoarterial ECMO**

**Technique**

In venoarterial extracorporeal membrane oxygenation (VA ECMO), the ECMO oxygenator is in parallel with the native lungs and the ECMO circuit provides both cardiac and respiratory support. In VA ECMO, venous blood is withdrawn and oxygen is added and CO₂ removed similar to VV ECMO, but blood is returned to the arterial circulation. Cannulation for VA ECMO can done peripherally, with withdrawal of blood from a cannula in the femoral or internal jugular vein and return of blood through a cannula in the femoral or subclavian artery. Alternatively, it
can be done centrally, with withdrawal of blood directly from a cannula in the right atrium and return of blood through a cannula in the aorta. VA ECMO typically requires a high blood flow extracorporeal circuit.

**Indications**

VA ECMO provides both cardiac and respiratory support. Thus, it is used in situations of significant cardiac dysfunction that is refractory to other therapies, when significant respiratory involvement is suspected or demonstrated, such as treatment-resistant cardiogenic shock, pulmonary embolism, or primary parenchymal lung disease severe enough to compromise right heart function. Echocardiography should be used before ECMO is considered or started to identify severe left ventricular dysfunction which might necessitate the use of VA ECMO. The use of peripheral VA ECMO in the presence of adequate cardiac function may cause severe hypoxia in the upper part of the body (brain and heart) in the setting of a severe pulmonary shunt.

**MEDICAL MANAGEMENT DURING ECMO**

During ECMO, patients require supportive care and treatment for their underlying medical condition, including ventilator management, fluid management, and systemic anticoagulation to prevent circuit clotting, nutritional management, and appropriate antimicrobials. Maintenance of the ECMO circuit requires frequent (i.e., multiple times in 24 hours) monitoring by medical and nursing staff and evaluation at least once per 24 hours by a perfusion expert.

ECMO may be associated with significant complications, which can be related to the vascular access required to the need for systemic anticoagulation, including hemorrhage, limb ischemia, compartment syndrome, cannula thrombosis, and limb amputation. Patients are also at risk of progression of their underlying disease process.

**EVIDENCE SUMMARY**

The ideal study design to evaluate the specific therapeutic effects of (VA) or venovenous (VV) extracorporeal membrane oxygenation (ECMO) for adult respiratory and cardiorespiratory conditions would be multicenter randomized controlled trials (RCTs) that compare ECMO with best standard therapy, such as mechanical ventilation. RCTs are needed to adequately control for confounding factors, evaluate adverse effects, safety, effectiveness and individual patient differences (age, condition, and severity of illness) compared to standard therapy. The RCT is the most rigorous and reliable study design for demonstrating a causal relationship between the therapy under investigation and the health outcomes of interest. Specifically, questions regarding appropriate patient selection, standardization and duration of ECMO treatment and complication and survival rates, would be addressed. However, there are challenges in conducting RCTs to evaluate ECMO due to several factors, such as small patient populations and the urgent and emergent setting in which ECMO is typically utilized. Given these confounding factors, data from large randomized controlled trials are not expected in the near future.

Current guidelines for establishing causality require direct evidence which demonstrates that the effect of utilizing ECMO as a treatment of respiratory or cardiac failure in adults is greater than the combined influence of all confounding factors for the given condition. Given that RCTs are unlikely, evidence from non-randomized trials may be considered when treatment with ECMO results in an improvement of symptoms which is so sizable that the health
improvement rules out the combined effect of all other possible concurrent treatments or natural progression of the disease. Currently, there is limited evidence of this magnitude regarding patient selection, timing and therapeutic strategies in adult patients with respiratory or cardiac failure.[16,17] Therefore large studies with adequate follow-up are needed in order to validate appropriate patient selection criteria, treatment strategies and timing of ECMO use.

EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO) IN ADULTS WITH ACUTE RESPIRATORY FAILURE

The current evidence regarding ECMO in adult patients is primarily limited to nonrandomized studies with heterogenous patient populations, treated at various healthcare institutions with differing ECMO treatment protocols. In addition, ECMO technology and treatment protocols have evolved over the past several decades with the use of lung-protective ventilation systems.[16,17] Therefore, the following literature review focuses on systematic reviews and meta-analyses regarding the use of ECMO in adults in the past two decades.

Systematic Reviews and Technology Assessments

In 2015 the Washington State Health Care Authority published a health technology assessment (HTA) for ECMO in adults.[18] Evidence of clinical efficacy of ECMO compared to conventional treatment included RCTs, good-quality comparative cohort studies, and good-quality systematic reviews. The review identified two RCTs, both of good quality. Among the 41 comparative cohort studies identified, 16 were of good quality, eight of fair quality and 17 of poor quality. The bulk of the good quality evidence was for pulmonary support, including two randomized control trials[19,20] and six observational studies. Based on the evidence, which was admitted to have significant limitations for some indication, and expert consensus, the committee determined that ECMO is effective for patients with severe life-threatening respiratory or cardiac dysfunction that is not responding to conventional management but is potentially reversible; as a bridging therapy for patients in pulmonary and/or cardiac failure for transplantation.

In 2015, Tramm published a Cochrane review on the use of ECMO for critically ill adults. The reviewers included RCTs, quasi-RCTs, and cluster RCTs that evaluated VV or VA ECMO compared with conventional respiratory and cardiac support.[21] Four RCTs were identified (Peek [2009][20], Morris [1994][22], Bein [2013][19], Zapol [1979][23]), which described below. Combined, the trials included 389 subjects. Inclusion criteria (acute respiratory failure with specific criteria for arterial oxygen saturation and ventilator support) were generally similar across studies. Risk of bias was assessed as low for the trials by Peek, Bein, and Zapol, and high for the trial by Morris. The reviewers were unable to perform a meta-analysis due to clinical heterogeneity across studies. The Morris and Zapol trials were not considered to represent current standards of care. The reviewers summarized the outcomes from these studies (findings described individually above). They concluded: “We recommend combining results of ongoing RCTs with results of trials conducted after the year 2000 if no significant shifts in technology or treatment occur. Until these new results become available, data on use of ECMO in patients with acute respiratory failure remain inconclusive.”

In 2015, Schmidt conducted a systematic review of studies reporting outcomes for extracorporeal gas exchange, including both ECMO and ECCO2R, in adults with acute respiratory failure.[24] The review identified 56 studies, of which four were RCTs, seven were case-control studies, and 45 were case series. Two of the RCTs evaluated ECCO2R in ARDS patients, while the other two evaluated ECMO in ARDS. One RCT evaluating ECMO in ARDS
was from the 1970s and was noted to have significant methodologic issues. The second RCT evaluating ECMO in ARDS was the CESAR trial (described above). The reviewers have reported that retrospective cohort studies of ECMO using more updated technology reported high rates (approximately 60%-80%) of short-term survival. The RCTs reporting on ECCO2R in ARDS patients included those by Morris (1994) and Bein (2013). As noted in the Randomized Controlled Trials section below, the Morris trial was stopped early due to futility. In the second RCT of ECCO2R in ARDS (Bein), the number of ventilator-free days did not differ significantly between groups.

In 2013, Zampieri, reports results of a systematic review and meta-analysis evaluating the role of VV ECMO for severe acute respiratory failure in adults.[25] The authors searched for RCTs and observational case-control studies with severity-matched patients that evaluated the use of ECMO in severe acute respiratory failure in adults. Three studies were included in the meta-analysis that comprised a total of 353 patients of whom 179 received ECMO, one RCT (CESAR trial,[26] described below) and two case control studies[27,28] with severity-matched patients. For the primary analysis, the pooled in-hospital mortality in the ECMO-treated group was not significantly different from the control group (odds ratio [OR], 0.71; 95% CI, 0.34 to 1.47; p=0.358). Both nonrandomized studies included only patients treated for H1Noneinfluenza A infection, which may limit their generalizability to other patient populations.

Also in 2013, Zangrillo, reported the results of a systematic review and meta-analysis that evaluated the role of ECMO for respiratory failure due to H1N1 influenza A infection in adults.[29] The meta-analysis included eight studies, all observational cohort studies, that included 1357 patients with confirmed or suspected H1N1 infection requiring ICU admission, 266 (20%) of whom were treated with ECMO. The median age of those receiving ECMO was 36 years, with 43% men. In 94% of cases, VV ECMO was used, with VA ECMO used only in patients presenting with respiratory and systolic cardiac failure or unresponsive to VV ECMO. The median ECMO use time was 10 days. Reported outcomes were variable across the studies, but in a random-effects pooled model, the overall in-hospital mortality was 27.5% (95% CI, 18.4% to 36.7%), with a median ICU stay of 25 days and an overall median length of stay of 37 days.

In 2013, Hirshberg conducted a review of evidence regarding ECMO use in critically ill adults with ARDS.[30] Studies included in the review were limited to the two most recent years’ publications. A total of 12 case series and 12 review articles were considered in the assessment. Successful ECMO treatment of ARDS secondary to H1N1 was reported within the literature; however, studies were limited in the discussion of alternative modes of ventilation or other interventions. In addition, two national registry reports published conflicting conclusions regarding H1N1-related ARDS and ECMO treatment.[27,28] The authors made key observations, concluding:

- Increase in ARDS survival over time makes historical controls and comparisons to determine the efficacy of ECMO challenging and likely unreliable.
- Scientifically credible evidence to support the use of ECMO in the routine management of patients with ARDS is lacking.
- The use of ECMO as a salvage therapy in practice biases the interpretation of case series results.

Additional systematic reviews[31,32] were identified which also noted the heterogeneous nature of patients studied as well as a lack of well-designed randomized trials comparing ECMO to
other therapies.

There are some older systematic reviews on H1N1-related respiratory distress/failure published prior to 2013 that will not be described in detail here.[33-35]

**Randomized Controlled Trials (RCTs)**

In 2013, Bein reported results of the Xtravent study, which randomized patients with ARDS to a strategy of low tidal volume ventilation combined with ECCO₂R (n=40) or a conventional ventilation strategy (n=39).[19] For the study’s primary end point (28- and 60-day ventilator-free days), there was no significant difference between treatment groups. However, the interventions evaluated are better characterized as pumpless extracorporeal lung assist devices (CO₂ removal only), making them less relevant to the evaluation of ECMO.

In 2010, Peek conducted an RCT and economic evaluation of conventional ventilatory support versus extracorporeal membrane oxygenation in adults with severe respiratory failure (CESAR trial).[26] Patients were 18-65 years old with severe, but reversible, respiratory failure (defined as a Murray score ≥ 3.0), or uncompensated hypercapnia with a pH < 7.20. The primary study outcome was death or severe disability at six month follow-up. Secondary outcomes included: duration of ventilation, use of high frequency/oscillation/jet ventilation, use of nitric oxide, prone positioning, use of steroids, length of intensive care unit stay, and length of hospital stay - and (for ECMO patients only) mode (venovenous/veno-arterial), duration of ECMO, blood flow and sweep flow. Exclusion criteria were: high pressure (>30 cm H₂O for peak inspiratory pressure) or high FIO₂ (>0.8) ventilation for more than seven days; intracranial bleeding; other contraindication to limited heparinization; or any contraindication to continuation of active treatment. A total of 180 patients (90 in each arm) were randomized from 68 centers. Data from 87 patients in the conventional management (CM) group and 68 patients from the ECMO group were available at 6-month follow-up. Authors reported significantly better mortality and disability rates in the ECMO arm compared to the CM arm six months after randomization, [33/90 (36.7%) versus 46/87 (52.9%) respectively]. However, these outcomes included the 22 patients who were randomized to the ECMO treatment arm, but who never received ECMO due to death or improvement with conventional treatment. A comparison of patients actually treated with ECMO to those treated with CM did not result in a significant difference between groups [33/68 (49%) versus 46/87 (52.9%) respectively] at 6-month follow-up. The study is further limited by a lack of standardized mechanical ventilation management in the CM group.

Two early small RCTs were identified that compared some form of extracorporeal support with standard care. They are described here briefly. In 1994, Morris reported the results of an RCT comparing a ventilator strategy of low-frequency positive-pressure ventilation (LFPPV) ECCO₂R (ECCO₂R; n=21) to standard care (n=19) in adults with ARDS.[22] In this trial, there was no significant difference in 30-day survival between groups (33% for LFPPV-ECCO₂R patients vs 42% for conventional ventilation patients; p=0.8), although the trial was stopped early due to futility. The clinical practices in this trial are likely not representative of current practice. In a very early RCT, Zapol (1979)[23] compared mechanical ventilation with partial VA bypass (n=42) to conventional ventilation (n=48) in individuals with severe hypoxemic respiratory failure.

**Nonrandomized Studies**

Numerous nonrandomized comparative and non-comparative studies have been published regarding outcomes in patients treated with ECMO for cardiac or respiratory failure due to a
variety of conditions. Several key nonrandomized studies are reviewed below:

In 2009, Brogan evaluated survival data from the Extracorporeal Life Support Organization (ELSO) registry regarding the use of ECMO in adult patients with respiratory failure. A total of 1,473 patient data from 1986-2006 and 2002-2006 were analyzed with a 50% survival rate reported at discharge. The median patient age was 34 years with an average of 154 hours on ECMO. Advanced patient age, increased pre-ECMO ventilation duration, diagnosis category and complications while on ECMO were associated with mortality. Limitations of this study included the voluntary nature of reported outcomes. Authors concluded that additional studies were needed in order to evaluate the role of ECMO in patients with respiratory failure.

In 2009, Davies published an observational series to characterize patients with influenza A (H1N1)-associated ARDS treated with ECMO. A total of 61 patients with confirmed H1N1 influenza (n=53) or influenza A, not otherwise subtyped (n=8) and an additional 133 influenza patients treated with mechanical ventilation were included in the study. Compared to the 133 patients who improved with conventional care, median days of mechanical ventilation were longer in patients treated with ECMO (18 [9-27] vs. 8 [4-14] days, p = .001), median ICU days were higher (22 [13-32] vs. 12 [7-18] days; p = .001) and ICU mortality was higher (23% vs. 9%; p = 0.01). At the point of data assessment, 48 (71%) of the ECMO patients had survived to ICU discharge, 14 (21% mortality) had died, and six remained in the ICU. Of the 22 patients still remaining in the hospital, 16 had survived to ICU discharge. By comparison, the non-ECMO cohort had 13% mortality at the time of reporting, suggesting no observable benefit with ECMO treatment.

Additional nonrandomized studies regarding the use of ECMO for a variety of conditions have been published, with a majority of studies reporting an overall survival to discharge ranging from 50-68% in patients with severe respiratory failure. Overall these publications suggest some survival benefit with ECMO treatment; however, these studies should be interpreted with caution due to the following limitations:

- Results from small sample sizes (n<100), limit the ability to rule out the role of chance as an explanation of study findings.
- Results from studies with short-term follow-up (hospital discharge) are not adequate to determine the durability of the treatment effect.
- A lack of comparison group, without which it is not possible to account for the many types of bias that can affect study outcomes.

Conclusion

Although evidence to establish standardized protocols regarding patient selection and treatment strategies is lacking, there is sufficient evidence to suggest the use of ECMO in patients with severe acute respiratory or cardiac failure may provide some survival benefit when the risks associated with mechanical ventilation are very high. Questions remain about the generalizability of findings from the CESAR trial and nonrandomized study results to other patient populations, and further clinical trials in more specific patient populations are needed.

EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO) IN ADULTS AS A BRIDGE TO TRANSPLANTATION

The evidence related to the use of ECMO as a bridge to transplantation consists of two large nonrandomized comparative studies and small case series ranging from 13 to 46
Some retrospective studies have compared outcomes for patients treated with and without ECMO preoperatively. Overall, these studies report success rates of 81-87%, and one-year survival rates of 74-100%. Adverse events reported in these series include: renal failure requiring temporary dialysis, pulmonary infections, sepsis, tracheostomy required, and distal digital ischemia. Since ECMO is generally determined to be medically necessary as a bridge to transplant, the published studies are not described in detail. Of note, two large studies are described below.

In 2016, Schechter published a survival analysis comparing types of preoperative support prior to lung transplantation, using data from the United Network for Organ Sharing (UNOS).\[57\] Included in the analysis were 12,403 adult lung transplantations from 2005 through 2013: 11,607 (94.6%) did not receive invasive support prior to transplantation, 612 (4.9%) received invasive mechanical ventilation (iMV) only, 119 (1%) received iMV plus ECMO, and 65 (0.5%) received ECMO only. Table 2 shows the cumulative survival for patients at six months, one year, and three years, by support prior to transplantation. Compared to patients with no invasive support, patients receiving iMV with or without ECMO had an increased mortality risk. The mortality of patients receiving ECMO alone was not significantly different from patients receiving no support at three years. A limitation of the study is related to the use of registry data, in that complications due to the bridge strategy and certain details such as equipment and technique of ECMO, are not available. In addition, underlying demographic differences are not represented in the comparisons.

<table>
<thead>
<tr>
<th>Support</th>
<th>N</th>
<th>6 Months</th>
<th>1 Year</th>
<th>3 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>No support</td>
<td>11,607</td>
<td>89.4%</td>
<td>84.2%</td>
<td>67.0%</td>
</tr>
<tr>
<td>Invasive mechanical ventilation only</td>
<td>612</td>
<td>79.9%</td>
<td>72.0%</td>
<td>57.0%</td>
</tr>
<tr>
<td>Invasive mechanical ventilation plus ECMO</td>
<td>119</td>
<td>68.1%</td>
<td>61.0%</td>
<td>45.1%</td>
</tr>
<tr>
<td>ECMO only</td>
<td>65</td>
<td>75.2%</td>
<td>70.4%</td>
<td>64.5%</td>
</tr>
</tbody>
</table>

ECMO: extracorporeal membrane oxygenation.

In 2014, Jayarajan evaluated survival rates of ECMO and mechanical ventilation (MV) treatment as a bridge to heart-lung transplantation (HLT).\[58\] The primary study outcome was risk-adjusted all-cause mortality. Of 542 adult patients who received HLT between 1995-2011, 15 (2.8%) received ECMO and 22 (4.1%) received MV as a bridge to transplantation. At 30-day survival, the ECMO group had worse survival than the control group (patients who did not receive either ECMO or MV) (20% vs. 83.5%, respectively). Similar results were reported at 5-year survival (20% vs. 47.4%, respectively; P<0.001). Both ECMO (hazard ratio [HR]=3.820, P=0.003) and MV (HR=2.011, P=0.030) were independently associated with mortality. The authors concluded that HLT recipients receiving ECMO or MV as a bridge to transplantation had increased short and long-term mortality and that additional studies were needed in order to establish optimal treatment protocols and patient selection criteria for ECMO as a bridge to HLT.

**EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO) IN ADULTS WITH REFRACTORY CARDIOGENIC SHOCK**

Systematic Reviews
In 2015, Xie reported on a meta-analysis evaluating VA ECMO for cardiogenic shock and cardiac arrest that included observational studies and clinical trials with at least 10 adult patients. Twenty-two studies, all observational, with a total of 1199 patients (12 studies [n=659 patients] with cardiogenic shock; five studies [n=277 patients] with cardiac arrest; five studies [n=263 patients] with both patient types) met inclusion criteria. Across the 16 studies (n=841 patients) that reported survival to discharge, the weighted average survival was 40.2% (95% CI, 33.9% to 46.7%). Across the 14 studies that reported 30-day survival, the weighted average survival was 52.8% (95% CI, 43.9% to 61.6%), with similar survival rates at three, six, and 12 months across studies that reported those outcomes. Across studies that reported on cardiogenic shock only, the weighted average survival to discharge was 42.1% (95% CI, 32.2% to 52.4%; \(I^2=79\%\)). Across all studies, complications were common, most frequently acute kidney injury (pooled incidence, 47.4%; 95% CI, 30.2% to 64.9%; \(I^2=92\%\)), followed by renal dialysis (pooled incidence, 35.2%; 95% CI, 23% to 47.4%; \(I^2=95\%\)) and reoperation for bleeding (pooled incidence, 30.3%; 95% CI, 1.8% to 72.2%; \(I^2=98\%\)). However, the authors noted that it is uncertain that the complications were entirely due to ECMO, given the underlying illness in patients who receive ECMO.

Nonrandomized Studies

In 2017 Le Pennec-Prigent analyzed outcomes of 26 patients with intractable refractory arrhythmic storm and cardiogenic shock. Stable sinus rhythm was restored in all patients, 61.5% immediately and the rest after a median of three hours after ECMO implantation. No patients died from life support-related complications and thirteen patients died overall, mostly due to multiple organ failure.

Aso (2016) analyzed 5263 patients from the Japanese Diagnosis Procedure Combination database who received VA ECMO during hospitalization. Reasons for receiving VA ECMO included: cardiogenic shock (88%), pulmonary embolism (7%), hypothermia (2%), trauma (2%), and poisoning (1%). Among patients in the cardiogenic shock group, 33% died during VA ECMO, 40% died after weaning from VA ECMO, and 25% were discharged following weaning from VA ECMO. Multivariate logistic regression for in-hospital mortality showed an increased risk among patients 60 years of age and older, a BMI less than 18.5 kg, a BMI of 25 kg or more, ischemic heart disease, myocarditis, use of intra-aortic balloon pumping, use of continuous serial replacement therapy, and cardiac arrest.

Lorusso (2016) reported on a series of 57 adults with acute fulminant myocarditis treated with VA ECMO identified from institutional databases from 13 centers. Primary inclusion criteria were the presence of sudden and refractory cardiogenic shock, cardiac arrest, or severe hemodynamic instability despite aggressive inotropic drugs with or without intraaortic balloon pump (IABP), demonstration of normal coronary artery anatomy and echocardiographic signs of myocardial tissue swelling and biventricular involvement. The series excluded patients with organic valvular or coronary artery disease, chronic dilated cardiomyopathy, toxic myocarditis, mediastinal radiotherapy, or other mechanical circulatory support other than IABP. Mean VA ECMO time was 9.9 days (range, 2-24 days), and 43 patients (75.5%) had cardiac recovery. Complications were common (40 patients [70.1%]), most frequently acute kidney injury (10 patients [17.5%]) and neurologic complications (10 patients [17.5%]). Sixteen (28.1%) patients died before hospital discharge.

In the largest series identified, Diddle 2015 reported on 147 patients (150 ECMO runs), treated with ECMO for acute myocarditis, who were identified from the Extracorporeal Life Support
Organization database [61] Patients in this group were relatively young (median age, 31 years) and were most often treated with VA ECMO (91%). Of the cohort, 101 (69%) were decannulated from ECMO and 90 (61%) survived to discharge. In multivariable analysis, the occurrence of pre-ECMO cardiac arrest and the need for higher ECMO support at four hours were significantly associated with in-hospital mortality (odds ratio [OR], 2.4; 95% CI, 1.1 to 5.0; p=0.02 for pre-ECMO arrest; OR=2.8; 95% CI, 1.1 to 7.3; p=0.03 for increased ECMO support at four hours).

Chamogeorgakis (2013) conducted a retrospective chart review of patients with cardiogenic shock at a single center, comparing outcomes of 18 patients treated with a temporary miniaturized percutaneous ventricular assist device (mpVAD) with 61 patients who underwent ECMO. [62] The patient population was mostly male adults who had had myocardial infarction documented during the same hospital admission. Mean follow-up time was 14.3 months. No benefit from use of ECMO was found on in-hospital survival (ECMO 50.0% mp-VAD 49.2%), successful weaning off mechanical support (ECMO 33.3% mp-VAD 19.7%), or bridging to long-term support or transplant (ECMO 27.8% mp-VAD 31.1%).

Conclusion

The evidence on ECMO for refractory cardiogenic shock includes case series and case reports. The largest body of literature relates to the use of ECMO in the failure-to-wean from bypass population. For this indication, case series report some successful cases of weaning patients from ECMO in the setting of very high expected morbidity and mortality rates. However, without comparative studies, it is difficult to assess whether rates of weaning from bypass are better with ECMO than with standard care.

EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO) ASSISTED CARDIOPULMONARY RESUSCITATION

Systematic Review

In 2017, Debaty published a systematic review and meta-analysis on prognostic factors for patients receiving ECPR following out-of-hospital refractory cardiac arrest, to inform the decision of which patients benefit most from ECPR. [63] The search included literature through September 2016. Fifteen retrospective and prospective cohort studies were included (total N=841 patients). The overall rate of a favorable outcome following ECPR was 15%, though the range among the studies was wide (0% to 50%) due to heterogeneity of inclusion criteria, outcome definition, and compliance with protocol. Favorable outcomes occurred more frequently among patients with initial shockable cardiac rhythms, shorter low-flow duration, higher arterial pH, and lower serum lactate concentration on hospital admission. No significant differences were found when age, gender, and bystander CPR attempt were evaluated.

Nonrandomized Studies

Park (2014) developed a predictive score for survival to discharge using a series of 152 consecutive patients who received ECPR for in-hospital cardiac arrest. [64] In this series, in-hospital death occurred in 104 (68.4%) patients. Factors significantly associated with improved survival were an age of 66 years or less, the presence of an arrest rhythm of pulseless electrical activity or ventricular fibrillation or pulseless ventricular tachycardia, shorter CPR to ECMO time, higher initial mean arterial pressure, and higher Sequential Organ Failure Assessment scores. A score developed from these factors and evaluated in a test set
generated from the initial sample using a bootstrap method was associated with a sensitivity and specificity of 89.6% and 75.0%, respectively, for predicting survival to discharge. This score may help select patients for ECMO, but further validation is needed.

Maekawa (2013) reported results from a prospective observational cohort of adult patients who underwent ECPR after prolonged conventional CPR after out-of-hospital cardiac arrest. The study included 162 patients, 53 in the ECPR group and 109 in the conventional CPR group. After propensity score matching, 24 patients in each group were analyzed. The survival rate was higher in the matched ECPR group (29.2%) than in the matched conventional CPR group (8.3%; p=0.018).

In 2011, Shin compared ECPR with conventional CPR in adult patients who had undergone CPR for more than 10 minutes after witnessed in-hospital cardiac arrest. Four hundred six patients were included, 85 who underwent ECPR and 321 who underwent conventional CPR. The cause of arrest was considered cardiac in most cases (n=340 [83.7%]) and noncardiac (secondary to respiratory failure or hypovolemia) in the remainder (n=66 [16.3%]). The decision to initiate ECPR was made by the CPR team leader. Typically, the ECMO device was available in the catheterization laboratory, coronary care unit, and operating room, and an ECMO cart was transported to the CPR site within five to 10 minutes during the day and within 10 to 20 minutes at night. After propensity score matching, 120 patient pairs were included; in the matched group, ECPR was associated with significantly higher rates of survival to discharge with minimal neurologic impairment (OR for mortality or significant neurologic deficit, 0.17; 95% CI, 0.04 to 0.68; p=0.012) and survival at six months with minimal neurologic impairment (hazard ratio [HR], 0.48; 95% CI, 0.29 to 0.77; p=0.003).

In contrast, in a single institution cohort of 122 patients with in-hospital cardiac arrest of cardiac origin with prolonged (>10 minutes) conventional CPR, Lin demonstrated no survival difference between patients who had return of spontaneous breathing after ECMO and those who had return of spontaneous circulation after conventional CPR. After propensity score matching, 59 patients experienced return of spontaneous breathing after ECPR and 63 patients experienced sustained return of spontaneous circulation after conventional CPR. Acute coronary syndrome was the most common etiology of cardiac arrest, occurring in 73% of the ECPR patients and 50.9% of the conventional CPR patients. In the 27 ECPR response group, eight (29.6%) patients survived to discharge, while in the conventional CPR response group, five (18.5%) patients survived to discharge. In a multivariable model, ECPR was not associated with reduced mortality (adjusted HR=0.618; 95% CI, 0.325 to 1.176; p=0.413).

In an earlier prospective study, Chen (2008) compared ECPR with conventional CPR in adult patients who had undergone prolonged (>10 minutes) conventional CPR after in-hospital cardiac arrest of cardiac origin. One hundred seventy-two patients were included, 59 in the ECPR group and 113 in the conventional CPR group. The decision to call the extracorporeal life-support team was made by the physician in charge. The average duration from the call to team arrival was five to seven minutes during the day and 15 to 30 minutes overnight. Survival to discharge occurred in 17 (28.8%) patients in the ECPR group and in 14 (12.3%) patients in the conventional CPR group. In a multivariable logistic regression model to predict survival at discharge, use of ECPR was associated with reduced risk of death before discharge (adjusted HR=0.50; 95% CI, 0.33 to 0.74; p=0.001).
Other noncomparative case series have described the use of ECPR for refractory cardiac arrest.[69-80] Overall, these studies suggest that ECPR is feasible, particularly for in-hospital cardiac arrests, although mortality rates are high.

**Conclusion**

The most direct evidence related to the use of ECPR in cardiac arrest consists of several nonrandomized comparative studies, the largest of which consisted of 406 patients, most of which have demonstrated a survival benefit with ECPR. However, selection for ECMO in these studies was at the discretion of treating physicians, and treatment groups were not likely to be comparable. Multiple unanswered questions remain about the role of ECPR in refractory cardiac arrest, including appropriate patient populations, duration of conventional CPR, and assessment of futility.

**EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO) IN ADULTS WITH OTHER CONDITIONS**

**Systematic Reviews**

In 2013, Lazzeri evaluated the use of ECMO to improve outcomes after refractory cardiac arrest (CA).[81] Authors concluded that analyses of the available observational studies were characterized by heterogeneity and controversial results. In addition, authors noted, “the impact of ECMO implantation in CA patients can be considered a clinical challenge, since it is strictly linked to the ‘clinical selection of patients’”, as well as the technical skills and experience of the team. The study concluded that improved outcomes from the use of ECMO, in patients with refractory CA, could not be established but that, “…optimal utilization requires a dedicated local health-care organization and expertise in the field (both for the technical implementation of the device and for the intensive care management of these patients). A careful selection of patients guarantees optimal utilization of resources and a better outcome.”

In 2009, Cardarelli conducted a meta-analysis regarding the use of ECMO in adult patients in cardiac arrest or immediately after cardiopulmonary resuscitation (CPR).[35] Data was collected from observational studies published between: 1990-2007, and included 11 case series and nine case reports. A total of 135 patients were included in the analysis with a median age of 56 years (18-83). Overall survival to discharge in patients receiving ECMO was 40% (54 of 135 patients). Survival was notably improved in younger patients (17-41 years) and in patients where ECMO was used for short periods of time (0.875-2.3 days, odds ratio 0.2). Authors noted that major complications such as neurologic sequelae were not well described in the pooled studies.

**Nonrandomized Studies**

In a 2017 study of patients admitted to the ICU for pheochromocytoma crisis, Sauneuf evaluated the use of ECMO in 34 patients, 14 of whom received ECMO.[82] Ninety-day mortality was not significantly different between patients who were or were not treated with ECMO, despite the ECMO group having higher severity scores at admission.

Ramanathan (2017) analyzed data from the Extracorporeal Life Support Organization Registry database of 1,055 patients treated with ECMO for community-acquired pneumonia. Their data came from a 10-year period, over which time an increase in the number of patients treated with ECMO. Overall, 66% of the cohort survived. Duration of mechanical ventilation prior to extracorporeal membrane oxygenation, lower arterial pressure, fungal pneumonia, and
advancing age were all factors indicated as predictors of mortality via a multiple regression analysis.

Dangers (2017) reported the outcomes from 105 patients implanted with venoarterial-ECMO for acute decompensated heart failure at one ICU.[83] One-year survival was 42%. Independent predictors of one-year mortality were determined with multivariable analyses to be pre-extracorporeal membrane oxygenation Sequential Organ Failure Assessment score of more than 11, idiopathic cardiomyopathy, cardiac disease duration greater than two-years pre-ECMO, pre-ECMO blood lactate greater than 4 mmol/L.

**ADVERSE EFFECTS OF ECMO IN ADULTS**

**Systematic Reviews**

In 2013, Zangrillo conducted a systematic review and meta-analysis regarding outcomes and complications related to ECMO.[84] Studies reporting complications and mortality in 100 or more patients were included in the analysis. The primary outcome was mortality at the longest follow-up date, while secondary outcomes were fatal and non-fatal complications. A total of 12 studies were included (1763 patients) with ECMO treatment utilized for acute respiratory failure, cardiogenic shock, or both. The most common ECMO-associated complications were as follows:

- renal failure requiring continuous venovenous hemofiltration (52%)
- bacterial pneumonia (33%)
- any bleeding (33%)
- oxygenator dysfunction requiring replacement (29%)
- sepsis (26%)
- hemolysis (18%)
- liver dysfunction (16%)
- leg ischemia (10%)
- venous thrombosis (10%)
- central nervous system complications (8%)
- gastrointestinal bleeding (7%)
- aspiration pneumonia (5%)
- disseminated intravascular coagulation (5%).

The overall mortality at 30-day follow-up was 54%, with 45% of fatal events occurring during ECMO and 13% occurring after ECMO.

In 2013, Cheng conducted a systematic review and meta-analysis evaluating complications related to ECMO treatment of cardiogenic shock or cardiac arrest in adult patients.[85] Studies reporting complication rates and including at least 10 patients were included for a total of 20
studies (1,866 patients). The pooled estimated complication rates with 95% confidence were as follows:

<table>
<thead>
<tr>
<th>Complication</th>
<th>Pooled Estimated Complication Rate (%)</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute kidney injury</td>
<td>55.6</td>
<td>35.5% to 74.0%</td>
</tr>
<tr>
<td>Renal replacement therapy</td>
<td>46.0</td>
<td>36.7% to 55.5%</td>
</tr>
<tr>
<td>Rethoracotomy for bleeding or tamponade in postcardiotomy patients</td>
<td>41.9</td>
<td>24.3% to 61.8%</td>
</tr>
<tr>
<td>Major or significant bleeding</td>
<td>40.8</td>
<td>26.8% to 56.6%</td>
</tr>
<tr>
<td>Significant infection</td>
<td>30.4</td>
<td>19.5% to 44.0%</td>
</tr>
<tr>
<td>Lower extremity ischemia</td>
<td>16.9</td>
<td>12.5% to 22.6%</td>
</tr>
<tr>
<td>Neurologic complications</td>
<td>13.3</td>
<td>9.9% to 17.7%</td>
</tr>
<tr>
<td>Fasciotomy or compartment syndrome</td>
<td>10.3</td>
<td>7.3% to 14.5%</td>
</tr>
<tr>
<td>Stroke</td>
<td>5.9</td>
<td>4.2% to 8.3%</td>
</tr>
<tr>
<td>Lower extremity amputation</td>
<td>4.7</td>
<td>2.3% to 9.3%</td>
</tr>
</tbody>
</table>

In addition, 17 studies reported survival to discharge with a pooled survival rate of 534 of 1,529 patients, ranging from 20.8%-65.4%. The authors concluded that, “[a]lthough ECMO can improve survival of patients with advanced heart disease, there is significant associated morbidity with performance of this intervention.” Similar complication rates were reported in a 2014 review by Xie. [32]

Given the significant complications associated with ECMO, additional studies are needed which compare ECMO to other standard treatments, such as mechanical ventilation (MV), in order to better define appropriate patient selection criteria and treatment strategies in these high-risk patients.

Nonrandomized Studies

Numerous nonrandomized studies were identified which demonstrated that ECMO was associated with other serious complications[10], including, but not limited to: brachial plexus injury[86], thoracic complications (including bleeding and pneumothorax)[36,87,88], infection[89-92] (e.g. systemic, surgical site, respiratory tract, urinary tract), limb ischemia[93], neurological injury[94], abdominal compartment syndrome[95]. Furthermore, a recent analysis of ELSO database indicated that ECMO-related infections were higher in adults compared to children and neonates (30.6 vs. 20.8 vs. 10.1 infections per 1,000 ECMO days, respectively).[96]

**PRACTICE GUIDELINE SUMMARY**

**EXTRACORPOREAL LIFE SUPPORT ORGANIZATION (ELSO)**

In 2014, ELSO[9] published updated practice guidelines regarding the use of ECMO at specialty centers which highlighted the importance of institutional support, staff experience and implementation of specific procedures. However, these guidelines are not based on evidence or consensus, but rather intended to be used as a model for institutional requirements regarding appropriate ECMO use. ELSO authors noted, “[t]his guideline describes useful and safe practice, but these are not necessarily consensus recommendations. These guidelines are not intended as a standard of care...”
Adult Respiratory Failure

ELSO published guidelines regarding the use of ECMO for adult respiratory failure.[8] ELSO indicated ECMO could be considered in patients who met the following criteria:

1. In hypoxic respiratory failure due to any cause (primary or secondary) ECLS should be considered when the risk of mortality is 50% or greater, and is indicated when the risk of mortality is 80% or greater.
   a) 50% mortality risk is associated with a PaO2/FiO2 < 150 on FiO2 > 90% and/or Murray score 2-3.
   b) 80% mortality risk is associated with a PaO2/FiO2 < 100 on FiO2> 90% and/or Murray score 3-4 despite optimal care for six hours or more.
2. CO2 retention on mechanical ventilation despite high Pplat (>30 cm H2O)
3. Severe air leak syndromes
4. Need for intubation in a patient on lung transplant list
5. Immediate cardiac or respiratory collapse (PE, blocked airway, unresponsive to optimal care)

ELSO noted there are no absolute contraindications to ECMO; however, ELSO listed conditions associated with a poor outcome despite ECMO treatment in patients with adult respiratory failure:[8]

1. Mechanical ventilation at high settings (FiO2 > .9, P-plat > 30) for 7 days or more.
2. Major pharmacologic immunosuppression (absolute neutrophil count <400/mm3).
3. CNS hemorrhage that is recent or expanding.
4. Non recoverable comorbidity such as major CNS damage or terminal malignancy.
5. Age: …increasing risk with increasing age.

ELSO has published specific weaning guidelines for respiratory failure:[8]

Respiratory Failure Weaning

- Decrease flow in steps to 1L/min at sweep 100% OR decrease flow to 2L/min then decrease sweep FiO2 to maintain SaO2 > 95%.
- When SaO2 stable on these settings, on VV [vein to vein], trial off by clamping sweep on vent rest settings PSV [pressure support ventilation] or CPAP 20 cm H2O. If SaO2 >95 and PaCO2 <50 x 60 mins, come off.
- If PaCO2 >50 stay on at low flow, go to selective CO2 clearance mode.

Adult Cardiac Failure

ELSO published guidelines regarding the use of ECMO for adult cardiac failure due to cardiogenic shock.[7] ELSO indicated ECMO could be considered in patients who met the following criteria:

1. Inadequate tissue perfusion manifested as hypotension and low cardiac output despite adequate intravascular volume.
2. Shock persists despite volume administration, inotropes and vasoconstrictors, and intraaortic balloon counterpulsation if appropriate.
3. Septic shock is an indication in some centers.

ELSO also listed contraindications for ECMO in patients with cardiac failure:
1. Absolute: Unrecoverable heart and not a candidate for transplant or VAD, advanced age, chronic organ dysfunction (emphysema, cirrhosis, renal failure), compliance (financial, cognitive, psychiatric, or social limitations), prolonged CPR without adequate tissue perfusion.

2. Relative: Contraindication for anticoagulation, advanced age, obesity.

**AMERICAN HEART ASSOCIATION**

In 2015, the American Heart Association (AHA) issued updated guidelines on cardiopulmonary resuscitation (CPR) and emergency cardiovascular care, which included a new systematic review of the evidence for ECPR and recommendations about the use of ECPR for adults with in- or out-of-hospital cardiac arrest.\[^97^\] The systematic review identified no RCTs evaluating ECPR for cardiac arrest and variability in the inclusion and exclusion criteria of the studies was noted, which potentially affects generalizability. The guidelines make the following recommendations related to ECPR:

“There is insufficient evidence to recommend the routine use of ECPR for patients with cardiac arrest. In settings where it can be rapidly implemented, ECPR may be considered for select cardiac arrest patients for whom the suspected etiology of the cardiac arrest is potentially reversible during a limited period of mechanical cardiorespiratory support” (Class IIb, level of evidence C—limited data).”

**SUMMARY**

The research for extracorporeal membrane oxygenation (ECMO) for adult respiratory or cardiac failure has limitations. Despite these limitations, the research shows that ECMO for adult respiratory or cardiac failure improves health outcomes, including survival rates comparable to conventional therapy. Therefore, ECMO may be considered medically necessary as a treatment of respiratory or cardiac failure in adults when policy criteria are met.

Due to a lack of research and clinical practice guidelines, the use of ECMO is considered investigational when policy criteria are not met and in all other situations not specified in the policy criteria.

**REFERENCES**


<table>
<thead>
<tr>
<th>Procedure Code</th>
<th>Description</th>
<th>ICD Procedure Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>33964</td>
<td>Reposition central cannula(e) by sternotomy or thoracotomy, 6 years and older</td>
<td>Extracorporeal membrane oxygenation [ECMO]</td>
</tr>
<tr>
<td>33966</td>
<td>Removal of peripheral (arterial and/or venous) cannula(e), percutaneous, 6 years and older</td>
<td>None</td>
</tr>
<tr>
<td>33984</td>
<td>Removal of peripheral (arterial and/or venous) cannula(e), open, 6 years and older</td>
<td>39.65</td>
</tr>
<tr>
<td>33986</td>
<td>Removal of central cannula(e) by sternotomy or thoracotomy, 6 years and older</td>
<td></td>
</tr>
</tbody>
</table>
Gastric Electrical Stimulation

**Effective:** June 1, 2017

**Next Review:** April 2018
**Last Review:** April 2017

**IMPORTANT REMINDER**

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

**DESCRIPTION**

Gastric electrical stimulation (GES) is performed using an implantable device designed to treat chronic drug-refractory nausea and vomiting secondary to gastroparesis of diabetic or idiopathic etiology. Gastric electrical stimulation is also proposed as a treatment of obesity. The device may also be referred to as a gastric pacemaker or gastric pacing.

**MEDICAL POLICY CRITERIA**

**Note:** This policy only applies to the initial placement of the device. This policy does not apply to revision(s) or replacement(s) after the device has been placed.

1. Gastric electrical stimulation may be considered **medically necessary** in the treatment of chronic intractable nausea and vomiting secondary to gastroparesis of diabetic, idiopathic or post-surgical etiology when all of the following criteria are met:
   
   A. Significantly delayed gastric emptying as documented by standard scintigraphic imaging of solid food; and
   
   B. Patient is refractory or intolerant of 2 out of 3 classes of prokinetic medications and 2 out of 3 antiemetic medications. (see Appendices for classes); and
C Patient’s nutritional status is sufficiently low that weight has decreased to 90% or less of normal body weight for a patient’s height and age in comparison with pre-illness weight.

II Gastric electrical stimulation is investigational for all other indications including but not limited to the treatment of obesity.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

CROSS REFERENCES

1. Bariatric Surgery; Surgery, Policy No. 58
2. Vagus Nerve Blocking Therapy for Obesity; Surgery, Policy No. 200
3. Vagus Nerve Stimulation; Surgery, Policy No. 74

BACKGROUND

A subcutaneously implanted pulse generator delivers electrical stimulation to the stomach via intramuscular leads that are implanted on the outer surface of the greater curvature of the stomach either laparoscopically or during a laparotomy. Stimulation parameters are typically programmed at an “on time” (ON) (e.g., 0.1 second) alternating with an “off time” (OFF) (e.g., 5.0 seconds).

GASTRIC STIMULATION FOR THE TREATMENT OF INTRACTABLE NAUSEA AND VOMITING DUE TO GASTROPARESIS

Gastroparesis is a chronic disorder of gastric motility characterized by delayed emptying of a solid meal. Symptoms include bloating, distension, nausea, and vomiting. When severe and chronic, gastroparesis can be associated with dehydration, poor nutritional status, and poor glycemic control in diabetics. While most commonly associated with diabetes, gastroparesis is also found in chronic pseudo-obstruction, connective tissue disorders, Parkinson disease, and psychological pathology. Idiopathic gastroparesis refers to symptoms of gastroparesis which are not associated with an identifiable cause. Treatment of gastroparesis includes prokinetic agents such as metoclopramide, and antiemetic agents such as metoclopramide, granisetron, or ondansetron. Severe cases may require enteral or total parenteral nutrition.

GASTRIC STIMULATION FOR THE TREATMENT OF OBESITY

GES has also been investigated as a treatment of obesity as a technique to increase a feeling of satiety with subsequent reduced food intake and weight loss. The exact mechanisms resulting in changes in eating behavior are uncertain but may be related to neurohormonal modulation and/or stomach muscle stimulation.

REGULATORY STATUS

The Enterra™ Therapy System (formerly named Gastric Electrical Stimulation [GES] System; manufactured by Medtronic) is the only device approved for treatment of chronic refractory gastroparesis. It received approval for marketing from the U.S. Food and Drug Administration (FDA) in 2000 through the humanitarian device exemption (HDE) process.[1] This process requires the manufacturer to provide adequate information for the FDA to determine that the device has “probable” benefit but does not pose an unreasonable or significant risk; it does not
require data confirming the efficacy of the device. The HDE process is available for devices treating conditions that affect fewer than 4,000 Americans per year.

### EVIDENCE SUMMARY

**GASTRIC STIMULATION FOR THE TREATMENT OF INTRACTABLE NAUSEA AND VOMITING DUE TO GASTROPARESIS**

**Systematic Reviews**

Several systematic reviews of studies of gastric electrical stimulation (GES) for gastroparesis have been published, the most recent of which was conducted by Levinthal et al in 2017.[2-4]

To be included in the Levinthal review, studies had to include adults with established gastroparesis, report patient symptom scores and administer treatment for at least 1 week. Five randomized controlled trials (RCTs) and 13 non-RCTs meeting criteria were identified. Pooled analysis of data from the 5 RCTs (n=185 patients) did not find a statistically significant difference in symptom severity when the GES was turned on versus off (standardized mean difference [SMD], 0.17; 95% confidence interval [CI], -0.06 to 0.40; p=0.15). Another pooled analysis did not find a statistically significant difference in nausea severity scores when the GES was on or off (SMD = -0.143; 95% CI, -0.50 to 0.22; p=0.45). In a pooled analysis of 13 open-label single-arm studies and data from open-label extensions of 3 RCTs, mean total symptom severity score decreased 2.68 (95% CI, 2.04 to 3.32) at follow-up from a mean of 6.85 (95% CI, 6.28 to 7.42) at baseline. The rate of adverse events in the immediate postoperative period (reported in 7 studies) was 8.7% (95% CI, 4.3% to 17.1%). The in-hospital mortality rate within 30 days of surgery was 1.4% (95% CI, 0.8% to 2.5%), the rate of reoperations (up to 10 years of follow-up) was 11.1% (95% CI, 8.7% to 14.1%), and the rate of device removal was 8.4% (95% CI, 5.7% to 12.2%).

**Randomized Controlled Trials**

The data presented to the FDA documenting the “probable benefit” of the GES (Enterra™) system was based on a multicenter double-blind cross-over study referred to as the Worldwide Anti-Vomiting Electrical Stimulation Study (WAVESS).[1] The study included 33 patients with intractable idiopathic or diabetic gastroparesis. The primary endpoint of the study was a reduction in vomiting frequency, as measured by patient diaries. In the initial phase of the study, all patients underwent implantation of the stimulator and were randomly and blindly assigned to stimulation ON or stimulation OFF for the first month, with crossover to OFF and ON during the second month. The baseline vomiting frequency was 47 episodes per month, which significantly declined in both ON and OFF groups to 23 and 29 episodes, respectively. However, there were no significant differences in the number of vomiting episodes between the 2 groups, suggesting a placebo effect.

After the first 2 months of therapy, patients were asked which month of the cross-over stimulation they preferred. Twenty-one of the 33 patients selected the ON mode as their preferred month, compared to 7 who preferred the OFF mode, and 5 who had no preference. The greater preference for ON stimulation suggested some short-term effect that was not placebo.

In a continuing open phase of the trial, the patients then received the stimulation consistent with their preference. However, by 4 months all patients had the device turned ON (it was not...
clear whether this phase was by preference or design). At 6 and 12 months’ follow-up, the mean number of vomiting episodes continued to decline, although only 15 patients were followed for a period of 12 months. Data regarding quality of life were also obtained at 6 and 12 months and showed improvement. At 6 months, there was a significant improvement in 2-hour gastric retention (from 80% retention to 60% retention), but not in 4-hour gastric retention. (Fifty percent gastric retention at 2 hours was considered the upper limits of normal.)

The results of the randomized portion of the study suggest a placebo effect. Therefore, long-term results of GES must be validated in a longer-term randomized trial. It is interesting to note that GES did not return gastric emptying to normal in the majority of the patients tested. In as much as the device is intended to improve gastric emptying, as a proof of principle, it would be interesting to investigate the correlation between the degree of gastric emptying and symptom improvement.

In an update to WAVESS, Abell and colleagues reported 12-month outcomes for all of the patients.\(^5\) Statistically significant improvements were found for weekly vomiting frequency, total abdominal symptom score, and scintigraphic solid food emptying. At baseline the median vomiting frequency was 17.3 episodes per week with gastroparetic symptoms over a mean of 6.2 years. All patients had scintigraphic evidence of delayed gastric emptying at 2 and 4 hours, all patients were refractory to prokinetic and antiemetic medications, and 14 required some form of parenteral or enteral feedings. Results at the end of phase 1 (the blinded phase) showed a 50% decreased vomiting frequency for patients whose devices were ON compared to patients whose devices were OFF (p=0.05).

Symptom severity trended toward improvement in the ON versus OFF period, although these changes did not reach statistical significance in phase 1. In a second phase of the study all patients were switched to the ON position with 6- and 12- months follow-up. Vomiting at 12 months was compared to baseline; 72% for the combined group, 63% for diabetics with gastroparesis, and 83% for patients with idiopathic gastroparesis. Total symptom score improved significantly (p<0.05) at 6 and 12 months. Physical and mental quality of life scores improved significantly compared to baseline (p= less than 0.025). Baseline gastric retention was 78% at 2 hours. This decreased significantly with electrical stimulation to 65% at 6 months and 56% at 12 months for the combined group. The changes in 2-hour gastric emptying were not significant for the diabetic and idiopathic groups separately. Four-hour gastric emptying improved from 34% retention at baseline to 22% retention at 12 months. The difference was statistically significant for the combined group as well as the diabetic and idiopathic groups separately.

McCallum and colleagues performed a multicenter prospective study to evaluate Enterra™ therapy in patients with chronic intractable nausea and vomiting from diabetic gastroparesis (DGP).\(^6\) In this study, 55 patients with refractory DGP (5.9 years of DGP) were implanted with the Enterra™ system. After surgery, all patients had the stimulator turned ON for 6 weeks and then were randomly assigned to groups that had consecutive 3-month cross-over periods with the device ON or OFF. After this period, the device was turned ON in all patients and they were followed up unblinded for 4.5 months. During the initial 6-week phase with the stimulator turned ON, the median reduction in weekly vomiting frequency (WVF) compared with baseline was 57%. There was no difference in WVF between patients who had the device turned ON or OFF during the 3-month cross-over period. At 1 year, the WVF of all patients was significantly lower than baseline values (median reduction, 68%; P < 0.001). One of the patients had the
device removed due to infection; 2 patients required surgical intervention due to lead-related problems.

In a later study, McCallum and colleagues evaluated GES (Enterra™ system) in patients with chronic vomiting due to idiopathic gastroparesis in a randomized, double-blind crossover trial.[7] In this study, 32 patients with nausea and vomiting associated with idiopathic gastroparesis, which was unresponsive or intolerant to prokinetic and antiemetic drugs, received Enterra™ implants and had the device turned on for 6 weeks. Subsequently, 27 of these patients were randomized to have the device turned on or off for 2 consecutive 3 month periods. Twenty five of these subjects completed the randomized phase; of note, 2 subjects had the device turned on early, 2 subjects had randomization assignment errors, and 1 subject had missing diaries. During the initial 6-week on period, all subjects demonstrated improvements in their WVF, demonstrating a median reduction of 61.2% compared with baseline (17.3 episodes/week at baseline vs 5.5 episodes/week at 6 week postimplant, p<0.001). During the on-off crossover phase, subjects demonstrated no significant differences between the on and off phase in the study’s primary end point, median WVF (median 6.4 in the on phase vs 9.8 in the off phase; p=1.0). Among the 19 subjects who completed 12 months of follow up, there was an 87.1% reduction in median WVF compared with baseline (17.3 episodes/week at baseline vs 2 episodes/week at 12-month follow-up, p<0.001). Two subjects required surgical intervention for lead migration/dislodgement or neurostimulator migration.

Nonrandomized Studies

In 2016, Heckert and colleagues reported on GES as a treatment for refractory symptoms of gastroparesis in 138 patients (65 diabetic, 68 idiopathic, and 5 other) with delayed gastric emptying at one-year follow-up (1.4 ± 1.0 years).[8] Patients reported their response to GES using the Clinical Patient Grading Assessment Scale (CPGAS), of which, 75% of patients felt their symptoms had improved, and 25% felt their symptoms were the same or worsened (diabetics had a greater response than idiopathic patients). Symptom severity was assessed by analyzing Patient Assessment of GI Symptoms (PAGI-SYM) questionnaires, before insertion of GES and at the last follow-up visit. PAGI-SYM scores were improved for all symptoms, though the authors report nausea, early satiety and loss of appetite to have been most improved; and constipation, diarrhea, and abdominal distension to have been least improved. In this selected group of patients, the authors concluded GES to be beneficial in the majority of patients.

In 2013, Keller and colleagues reported complication rates and need for a second surgery in 233 patients who had GES implantation surgery over a ten year period at a single institution.[9] Additional surgery was required in 58% of patients. The majority of reoperations were due to the following complications: nutritional access (45 patients, requiring 77 procedures), subcutaneous pocket issues (n = 21), gastroparetic symptoms (n = 11), mechanical issues (n = 9) and infection (n = 4). The study reported that patient BMI was predictive of additional surgeries, with 4.45 overall increased risk of pocket revision surgery. Although 70% of patients reported improved symptoms of pain, bloating and nausea, GES had a significantly high reoperation rate due to complications associated with the initial procedure.

In 2007, Anand et al. reported on a study of 214 consecutive drug-refractory patients with the symptoms of gastroparesis (146 idiopathic, 45 diabetic, 23 after surgery).[10] A GES device was implanted in 156 patients. The remaining 58 patients, designated as the control group, were either on the waiting list for permanent implantation or consented to not receive a permanent
implant. At last follow-up (median 4 years), most patients who received implants (135 of 156) were alive with intact devices, significantly reduced gastrointestinal symptoms, and improved health-related quality of life, with evidence of improved gastric emptying. Also, 90% of the patients had a response in at least 1 of 3 main symptoms. Most patients that explanted, usually for pocket infections, were later successfully reimplanted.

GES placement using minimally invasive surgical approaches has also been evaluated in several publications. Laparoscopy has been reported in at least two studies as a feasible approach in placement of GES for patients with medically refractory diabetic or idiopathic gastroparesis\[^{11,12}\].

Several small case series and retrospective reviews have been reported, some with long-term outcomes up to 5 years\[^{11,13-29}\]. The data indicate that GES may be associated with improvements in gastrointestinal symptom scores, nutrition and quality-of-life for patients; these improvements were sustained over time. However, gastric emptying rates were mixed.

**Adverse Events**

Bielefeldt analyzed the number, severity and type of voluntarily reported adverse events related to Enterra™ in the Manufacturer and User Device Experience (MAUDE) databank of the FDA\[^{30}\]. Data were retrieved for 2001 through October 31, 2015, of which 1472 reports were abstracted. Thirty-six perioperative complication reports were reviewed; 6 were serious events, including three deaths (1 due to cardiac arrest, 2 due to septic complications with resulting multi organ failure), one stroke, and one myocardial infarction complicated further by a pulmonary embolism. Overall, most of the reports were regarding patient concerns, local complications, or system failure. Limitations of these findings include reporting bias (the MAUDE data are voluntarily submitted), and report misclassification bias (MAUDE data sources vary from patient reports to published articles and inconsistencies in reporting have been found). Risk-benefit could not directly be assessed given the nature of the MAUDE database, though the author cites other studies for outcomes measurement, most of which are included in the other sections of this evidence review. Overall, 35% of the reported adverse events prompted an additional surgery.

**Section Summary**

The evidence regarding the clinical utility of GES for gastroparesis due to intractable nausea and vomiting is limited to 3 small crossover RCTs. However, long-term, 12-month data suggest improvements in gastrointestinal symptom scores, nutrition, and quality-of-life scores, suggesting some benefit with GES treatment. Given the lack of alternative treatment options in this specific patient population, GES may be considered reasonable treatment of symptoms of gastroparesis.

**GASTRIC STIMULATION FOR THE TREATMENT OF OBESITY**

**Systematic Review**

In 2014, Cha and colleagues published a review of 33 studies evaluating various methods of gastric stimulation as a treatment of obesity, including implantable GES\[^{31}\]. The majority of included studies were small in nature with 24 studies evaluating 30 or fewer patients. In addition, many of the studies reported high dropout rates of more than 50% of patients at the end of the study follow-up period. A major limitation of the review was the inclusion of studies which did not include the treatment of obesity (i.e., BMI or weight loss) as a primary outcome measure. Furthermore, there were methodological difference in the patient inclusion criteria.
and most of the studies included in the review were limited by short-term follow-up of less than 1 year. The authors concluded that the level of evidence regarding GES as a treatment of obesity was low. Long-term RCTs which compare GES to other treatments of obesity and sham are needed in order to assess the safety and efficacy of GES in this population.

Randomized Controlled Trials

There is 1 published RCT on GES for the treatment of obesity. In 2009, Shikora et al. reported on a randomized controlled, double-blind study (SHAPE trial) to evaluate GES for the treatment of obesity.[32] All 190 patients participating in the study received an implantable gastric stimulator and were randomized to have the stimulator turned on or off. All patients were evaluated monthly, participated in support groups and reduced their diet by 500-kcal/day. At 12 month follow-up, there was no difference in excess weight loss between the treatment group (weight loss of 11.8% +/- 17.6%) and the control group (weight loss of 11.7% +/- 16.9%) using intention-to-treat analysis (p=0.717).

Nonrandomized Studies

Additional, small studies – including one patient population with comorbidities of gastroparesis and morbid obesity – have reported positive outcomes in weight loss and maintenance of weight loss along with minimal complications.[33-38] However, due to lack of long-term outcomes from well-designed randomized clinical trials, conclusions cannot be made concerning the safety and efficacy of chronic gastric stimulation as a treatment for morbid obesity.

PRACTICE GUIDELINE SUMMARY

AMERICAN COLLEGE OF GASTROENTEROLOGY[39]

The American College of Gastroenterology (ACG) published a clinical practice guideline on management of gastroparesis in 2013. The recommendations for this guideline were based on review of the evidence-base through 2011. The ACG concluded that GES treatment does not adequately address the clinical needs of these patients, but that, “GES may be considered for compassionate treatment in patients with refractory symptoms, particularly nausea and vomiting. Symptom severity and gastric emptying have been shown to improve in patients with diabetic gastroparesis (DG), but not in patients with idiopathic gastroparesis (IG) or postsurgical gastroparesis (PSG). (Conditional recommendation, moderate level of evidence.).”

SUMMARY

It appears that gastric electrical stimulation (GES) may improve intractable nausea and vomiting for patients with gastroparesis. Clinical guidelines based on research state GES may be considered for compassionate treatment in patients with refractory symptoms, particularly nausea and vomiting. Therefore, given the lack of treatment options in this very specific patient population, GES may be medically necessary in carefully selected patients with gastroparesis when policy criteria are met.

Due to limited evidence on the efficacy and safety GES, when policy criteria are not met, all other indications including treatment for obesity are considered investigational.

2. Levinthal, DJ, Bielefeldt, K. Systematic review and meta-analysis: Gastric electrical stimulation for gastroparesis. Autonomic neuroscience : basic & clinical. 2017 Jan;202:45-55. PMID: 27085627


15. van der Voort, IR, Becker, JC, Dietl, KH, Konturek, JW, Domschke, W, Pohle, T. Gastric electrical stimulation results in improved metabolic control in diabetic patients suffering
from gastroparesis. Exp Clin Endocrinol Diabetes. 2005 Jan;113(1):38-42. PMID: 15662594


20. McKenna, D, Beverstein, G, Reichelderfer, M, Gaumnitz, E, Gould, J. Gastric electrical stimulation is an effective and safe treatment for medically refractory gastroparesis. Surgery. 2008 Oct;144(4):566-72; discussion 72-4. PMID: 18847640


32. Shikora, SA, Bergenstal, R, Bessler, M, et al. Implantable gastric stimulation for the
2009;5:31-7. PMID: 19071066
33. Favretti, F, De Luca, M, Segato, G, et al. Treatment of morbid obesity with the
Transcend Implantable Gastric Stimulator (IGS): a prospective survey. *Obes Surg.* 2004
May;14(5):666-70. PMID: 15186636
34. Shikora, SA. Implantable gastric stimulation for the treatment of severe obesity. *Obes
35. Cigaina, V, Hirschberg, AL. Gastric pacing for morbid obesity: plasma levels of
gastrointestinal peptides and leptin. *Obes Res.* 2003 Dec;11(12):1456-62. PMID:
14694209
summary of results of the European multi-center study. *Obes Surg.* 2004 Sep;14 Suppl
1:S33-9. PMID: 15479588
37. D'Argent, J. Gastric electrical stimulation as therapy of morbid obesity: preliminary
11969104
PMID: 25595741
39. Camilleri, M, Parkman, HP, Shafi, MA, Abell, TL, Gerson, L. Clinical guideline:
management of gastroparesis. *Am J Gastroenterol.* 2013;108:18-37; quiz 8. PMID:
23147521
40. BlueCross BlueShield Association Medical Policy Reference Manual "Gastric Electrical
Stimulation." Policy No. 7.01.73

**CODES**

The CPT code book instructs that, after January 1, 2012, procedures related to gastric
stimulation electrodes for morbid obesity should be reported using code unlisted procedure
codes 43659 for laparoscopic approach and 43999 for open laparotomy approach.

<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>43647</td>
<td>Laparoscopy, surgical; implantation or replacement of gastric neurostimulator electrodes, antrum</td>
</tr>
<tr>
<td></td>
<td>43648</td>
<td>Laparoscopy, surgical; revision or removal of gastric neurostimulator electrodes, antrum</td>
</tr>
<tr>
<td></td>
<td>43659</td>
<td>Unlisted laparoscopy procedure, stomach</td>
</tr>
<tr>
<td></td>
<td>43881</td>
<td>Implantation or replacement of gastric neurostimulator electrodes, antrum, open</td>
</tr>
<tr>
<td></td>
<td>43882</td>
<td>Revision or removal of gastric neurostimulator electrodes, antrum, open</td>
</tr>
<tr>
<td></td>
<td>43999</td>
<td>Unlisted procedure, stomach</td>
</tr>
<tr>
<td></td>
<td>64590</td>
<td>Insertion or replacement of peripheral or gastric neurostimulator pulse generator or receiver, direct or inductive coupling.</td>
</tr>
<tr>
<td></td>
<td>64595</td>
<td>Revision or removal of peripheral or gastric neurostimulator pulse generator or receiver</td>
</tr>
<tr>
<td>Codes</td>
<td>Number</td>
<td>Description</td>
</tr>
<tr>
<td>--------</td>
<td>--------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td></td>
<td>95980</td>
<td>Electronic analysis of implanted neurostimulator pulse generator system (eg, rate, pulse amplitude and duration, configuration of wave form, battery status, electrode selectability, output modulation, cycling, impedance and patient measurements) gastric neurostimulator pulse generator/transmitter; intraoperative, with programming</td>
</tr>
<tr>
<td></td>
<td>95981</td>
<td>; subsequent, without programming</td>
</tr>
<tr>
<td></td>
<td>95982</td>
<td>; subsequent, with reprogramming</td>
</tr>
<tr>
<td>HCPCS</td>
<td>C1767</td>
<td>Generator, neurostimulator (implantable), nonrechargeable</td>
</tr>
<tr>
<td></td>
<td>C1778</td>
<td>Lead neurostimulator</td>
</tr>
<tr>
<td></td>
<td>C1883</td>
<td>Adaptor/Extension, pacing lead or neurostimulator lead (implantable)</td>
</tr>
<tr>
<td></td>
<td>C1897</td>
<td>Lead neurostimulator test kit (implantable)</td>
</tr>
<tr>
<td></td>
<td>E0765</td>
<td>FDA approved nerve stimulator, with replaceable batteries, for treatment of nausea and vomiting</td>
</tr>
<tr>
<td></td>
<td>L8679</td>
<td>Implantable neurostimulator, pulse generator, any type</td>
</tr>
<tr>
<td></td>
<td>L8680</td>
<td>Implantable neurostimulator electrode, each</td>
</tr>
<tr>
<td></td>
<td>L8685</td>
<td>Implantable neurostimulator pulse generator, single array, rechargeable, includes extension</td>
</tr>
<tr>
<td></td>
<td>L8686</td>
<td>; non-rechargeable, includes extension</td>
</tr>
<tr>
<td></td>
<td>L8687</td>
<td>Implantable neurostimulator pulse generator, dual array, rechargeable, includes extension</td>
</tr>
<tr>
<td></td>
<td>L8688</td>
<td>; non-rechargeable, includes extension</td>
</tr>
</tbody>
</table>

**Appendix 1: Prokinetic Medications**

<table>
<thead>
<tr>
<th>Class</th>
<th>Common Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholinergic Agonists</td>
<td>dextanthenol (Illopan®), betahanechol (Urecholine®)</td>
</tr>
<tr>
<td>Motolin receptor agonists</td>
<td>erythromycin</td>
</tr>
<tr>
<td>Dopamine receptor antagonists</td>
<td>metoclopramide (Reglan®)</td>
</tr>
</tbody>
</table>

**Appendix 2: Antiemetic Medications**

<table>
<thead>
<tr>
<th>Class</th>
<th>Common Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antihistamines</td>
<td>diphenhydramine (Benadryl®), dimenhydrinate (Dramamine®), meclizine (Antivert®), hydroxyzine (Vistaril®), trimethobenzamidet (Tigan®)</td>
</tr>
<tr>
<td>Serotonin (5HT₃) receptor antagonists</td>
<td>ondansetron (Zofran®), granisetron (Kytril®), dolasetron (Anzemet®)</td>
</tr>
<tr>
<td>Dopamine receptor antagonists</td>
<td>Metoclopramide (Reglan®), perphenazine (Trilafon®), prochlorperazine (Compazine®), promethazine (Phenergan®), thiethylperazine (Torecan®), cyclizine (Marezine®)</td>
</tr>
</tbody>
</table>

_Date of Origin: February 2001_
Regence

Medical Policy Manual

Topic: Gastroesophageal Reflux Surgery

Section: Surgery

Policy No: 186

Date of Origin: November 2012

Last Reviewed Date: February 2017

Effective Date: March 1, 2017

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Surgical fundoplication involves wrapping the fundus of the stomach around the lower esophagus in order to create a high pressure zone that reduces gastroesophageal reflux.

Background

Gastroesophageal reflux disease (GERD) is a chronic medical condition, defined as “troublesome symptoms and/or complications” caused by reflux or regurgitation of stomach acid.[1] GERD is a common disorder; the proportion of North American adults with GERD (those who report experiencing symptoms such as heartburn or acid reflux at least once a week, or those with a physician diagnosis of GERD) is estimated to be around 19.8-20%.[2] GERD has also been associated with extraesophageal symptoms or conditions, such as cough, laryngitis, asthma and pulmonary fibrosis, although a direct causal relationship with GERD has not been established.

Standard treatment of GERD may address lifestyle modifications as appropriate to individual patients such as weight loss, smoking cessation, avoidance of specific foods that may precipitate reflux or heartburn, elevating the head of the bed, and avoiding recumbent positions until 2-3 hours after a meal.[1] When these actions are not successful, treatment generally consists of a daily regimen of proton pump inhibitors (PPIs). However, some patients with chronic GERD are unable or unwilling to continue ongoing medical treatment. For these patients, surgical treatment may be considered.
Surgical fundoplication involves wrapping the fundus of the stomach around the lower esophagus in order to create a high pressure zone that reduces gastroesophageal reflux. The fundal wrap can be either total (360 degrees) or partial (<360 degrees). Fundoplication may be performed as an open procedure but is more commonly performed laparoscopically.

**Esophagogastric Fundoplication with Paraesophageal Hiatal Hernia Repair**

The hiatus is an opening in the diaphragm where the distal esophagus passes through to enter the abdomen. A hiatal hernia occurs when the stomach bulges up into the thorax (chest) through the hiatus. Hiatal hernias are classified according to their severity and location:

- **Type I** - Protrusion of the upper part of the stomach and esophagus (gastroesophageal junction) into chest is a sliding hiatal hernia and is the most common type (over 95% of hiatal hernias are of the sliding type).
- **Type II** - A paraesophageal hiatal hernia occurs when the esophagus and gastroesophageal junction to the stomach remains in their normal location but part of the stomach protrudes through the hiatus next to the esophagus.
- **Type III** – Combination of both type I and II hiatal hernias when the stomach and esophagus protrude into the chest and the fundus of the stomach lies above the gastroesophageal junction. A "giant" hiatal hernia is a subset of type III hiatal hernias and defined when greater than 50% of the stomach has protruded into the chest.
- **Type IV** – Defined as the presence of a structure other than the stomach that protrudes into the chest (e.g. colon, small bowel).

In some cases, patients may exhibit a paraesophageal hiatal hernia with symptoms of GERD, requiring hernia repair in conjunction with fundoplication. Paraesophageal hiatal hernias, also known as Type II or III hiatal hernias, occur when the stomach, and in some cases the gastroesophageal junction (GEJ), herniates through the diaphragmatic esophageal hiatus into the mediastinum. These cases are rare, representing only 5% of all hiatal hernias compared to the more common Type I or “sliding” type hiatal hernia. Diagnosis of a “true” paraesophageal hiatal hernia is confirmed through endoscopy or imaging studies. Prophylactic surgical treatment of paraesophageal hiatal hernias are common as they account for most of the complications associated with hiatal hernias, including but not limited to obstruction, perforation and strangulation.

**Esophagogastric Fundoplication in Patients with Pulmonary Fibrosis**

Idiopathic pulmonary fibrosis (IPF) is a progressive lung disease which is often associated with additional comorbidities (e.g., pulmonary hypertension and gastroesophageal reflux) and symptoms (e.g., dyspnea, exercise limitation, fatigue, anxiety, mood disturbance, sleep disorders) that negatively affect patients’ lives. GERD is highly prevalent in patients with IPF with up to 50% of patients with asymptomatic disease. Although the pathological significance of GERD in IPF remains uncertain, studies indicate that medical or surgical treatment of GERD may stabilize lung function and increase oxygenation. It is hypothesized that fundoplication surgery may offer increased benefit over medication treatment by reducing acid as well as microaspirations of the gastric contents in to the lungs.

Due to the complexities of IPF, treatment protocols are not rigid or standardized and often require a management approach which is tailored to the patients’ specific conditions and symptoms. Nissen
Fundoplication surgery is one option which may be considered for treating patients with pulmonary fibrosis with symptomatic or asymptomatic GERD.

Note: This policy does not address transesophageal endoscopic therapies for GERD, which are addressed separately in Surgery Policy No. 110 (see Cross References).

MEDICAL POLICY CRITERIA

Notes: This policy addresses adults only. For the purposes of this policy, adult is defined as age 18 years or older. This policy does not address fundoplication in children and adolescents, which may be considered medically necessary.

I. Initial esophagogastric fundoplication may be considered medically necessary for the treatment of symptomatic gastroesophageal reflux disease (e.g., heartburn, regurgitation) when all of the following criteria I.A-C are met:

A. Lifestyle Modifications Symptoms are unresponsive to one or more of the following lifestyle modifications as appropriate to the individual patient:

1. Weight loss for overweight or obese patients
2. Avoidance of late meals, specific foods that cause heartburn (coffee, alcohol, chocolate, fatty foods, citrus, carbonated drinks, spicy foods)
3. Avoidance of specific activities that may cause heartburn, such as recumbency within 2-3 hours after a meal
4. Elevation of the head of the bed for patients who develop heartburn or regurgitation when recumbent

B. Medication therapy that meets at least one of the following:

1. A 6-month total trial of proton pump inhibitors (PPIs), including at least two different PPIs, is ineffective, contraindicated, or not tolerated. A minimum 2 month trial is required for each PPI trial; or
2. PPIs adequately control symptoms but are continuously required for 12 or more months and surgery is considered an alternative to long term medication use.

C. There is objective diagnostic confirmation of reflux and/or esophagitis via endoscopy. If endoscopy is normal, objective evidence of reflux should include at least one of the following: 24-hour ambulatory esophageal pH monitoring or barium swallow.

II. Repeat esophagogastric fundoplication for a failed previous antireflux procedure may be considered medically necessary when either of the following criteria (II.A or II.B) are met:

A. Criteria I. A-C for esophagogastric fundoplication above are met; or
B. Repeat surgery is for a documented mechanical failure of previous antireflux procedure (e.g., obstruction).

III. Initial or repeat esophagogastric fundoplication may be considered medically necessary for any of the following:
   A. In patients with pulmonary fibrosis with symptomatic or asymptomatic gastroesophageal reflux disease; or
   
   B. When the procedure is performed with a paraesophageal hiatal hernia, and documentation of a paraesophageal type of hiatal hernia (type II, III, or IV) is confirmed by imaging. (Types are listed in policy Description section.) A paraesophageal hernia must be documented for coverage of paraesophageal hernia repair; or
   
   C. When the procedure is performed with esophageal myotomy in patients with achalasia.

IV. Esophagogastric fundoplication is considered not medically necessary for the treatment of symptomatic gastroesophageal reflux disease (e.g., heartburn, regurgitation) when the criteria above are not met.

V. The following surgical procedures are considered investigational for the treatment of gastroesophageal reflux:
   
   A. Distal or partial gastrectomy performed with or without any of the following:
      1. Gastroduodenostomy
      2. Gastrojejunostomy
      3. Roux-en-Y reconstruction

   B. Hiatal hernia repair without fundoplication, including repair of sliding or paraesophageal hernia.

SCIENTIFIC EVIDENCE

In order to determine whether the benefits of surgical fundoplication in patients with chronic GERD outweigh the risks, well-designed randomized controlled trials (RCTs) are necessary, comparing medical therapy (proton pump inhibitors) with surgical fundoplication and reporting on relevant clinical outcomes.

The focus of the following literature review is on systematic reviews, randomized trials published after the systematic reviews, and clinical practice guidelines.

Fundoplication

Systematic Reviews

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
In 2010, The Cochrane Collaboration published a systematic review on medical versus surgical management for GERD in adults.[9] Included in the review were all randomized or quasi-randomized controlled trials comparing laparoscopic fundoplication with medical management; nonrandomized studies were excluded. Four trials with a total of 1232 patients were included.[10-13] All reported outcomes at one year, with only one reporting outcomes up to three years. There were no studies that followed patients longer than three years. Overall, the authors concluded that in the short- to medium-term there is evidence that laparoscopic fundoplication is more effective than medical management.

A 2015 update concluded that there is considerable uncertainty in the balance of benefits versus harms of laparoscopic fundoplication compared to long-term medical treatment with proton pump inhibitors.[14] Four randomized controlled trials were included for meta-analysis, consisting of three studies previously reported in the 2010 review, and longer term follow-up for the Anvari study.[15] The available evidence was rated low or very low, and further high-quality studies are needed.

Randomized Controlled Trials

Included in the publication of the 2015 Cochrane review, Anvari and colleagues reported 3-year outcomes from a prospective RCT (one-year results were included in the 2010 Cochrane review).[15] Of note, a priori, a sample size of 216 was calculated for this study at a statistical significance level of \( \alpha = 0.05 \); however only 104 participants were ultimately randomized which may have impacted the ability of the study to detect significant changes.

Of the original 104 subjects, 93 were available for the 3-year follow-up assessment. The authors reported the following outcomes:

- Improvement from baseline in GERD symptoms was significant in both the medical treatment and surgical groups. Differences between the two groups were not significant. (Primary outcome)
- Surgical patients experienced a mean of 1.35 more heartburn-free days per week compared with the medical group, a significant difference. (Primary outcome)
- Both groups demonstrated improvements in acid reflux and did not differ significantly in change from baseline. (Secondary outcome)
- The surgical group had significantly better lower esophageal sphincter pressure than the medical group. (Secondary outcome)
- With respect to global symptom control compared with baseline measurements, medically treated patients maintained their control, but the surgical patients demonstrated a statistically significant improvement from baseline. (Secondary outcome)
- Significant improvements in quality of life scores were also seen in the surgical group compared with the medical group. (Secondary outcome)
- 6 (11.8%) patients in the surgical group and 8 (16%) patients in the medical group failed their primary treatment.
- No adverse events were reported in the medical treatment group. In the surgical group:
  - There were no intraoperative complications, major morbidities, or mortality
  - 7 patients experienced minor postoperative complications
  - 4 patients reported dysphagia; 7 reported postprandial bloating at 3 months
  - 2 patients required dilation of the wrap

Surgical Treatment of GERD Patients with Pulmonary Fibrosis
Current evidence regarding fundoplication in patients with pulmonary fibrosis (PF) mainly consist of case series\cite{16-18} and review articles, which indicated that silent reflux, or asymptomatic GERD, occurs in about one third of PF patients.\cite{6,8} Only a single case series was identified regarding the efficacy of reflux surgery in patients with idiopathic PF (IPF) and GERD symptoms who were awaiting lung transplant:

In 2006, Linden and colleagues evaluated Laparoscopic fundoplication in patients with GERD symptoms and end-stage lung disease awaiting transplantation.\cite{7} Of 149 patients on the transplant wait list, 19 were identified as having a history of reflux and of those, 14 were diagnosed with IPF. All 14 IPF patients underwent a Nissen fundoplication and were compared to 31 patients with IPF on the transplant list who did not have fundoplication surgery. No perioperative complications or decreases in lung function were reported over a mean 15 month follow-up period. Authors reported that, "patients with idiopathic pulmonary fibrosis treated with fundoplication had stable oxygen requirements, whereas control patients with idiopathic pulmonary fibrosis on the waiting list had a statistically significant deterioration in oxygen requirement."

Overall, the evidence regarding Nissen fundoplication as a treatment of gastrointestinal reflux disease (GERD) in patients with pulmonary fibrosis (PF) is limited; however, treatment of PF is often tailored to treat a patients’ specific condition and symptoms. Potential benefits of fundoplication surgery in PF patients include improved oxygenation and reduction of acid and microaspiration into the lungs. Considering no standardized treatment protocol for patients with PF if available, Nissen fundoplication surgery may be considered in patients with symptomatic or asymptomatic GERD to reduce acid reflux and microaspirations to the lungs.

**Gastrectomy**

Gastrectomy involves a partial or full surgical removal of the stomach and is most often performed to treat cancer, non-cancerous tumors, perforation, polyps, ulcers, or obesity. In order to determine whether the benefits of surgical gastrectomy in patients with chronic GERD outweigh the risks, well-designed RCTs are necessary, comparing gastrectomy to medical therapy and accepted surgical interventions (fundoplication).

**Nonrandomized Studies**

Current evidence regarding the use of distal, partial or complete gastrectomy with or without gastroduodenostomy, gastrojejunostomy, or Roux-en-Y reconstruction as a treatment of gastric reflux disease consists of small case series.\cite{19-21} These studies do not permit conclusions due to the small sample size, lack of a control group, differences in patient characteristics and surgical techniques, and other methodological limitations. In addition, several studies\cite{21-25} were identified which reported on GERD reduction after sleeve gastrectomy in obese patients; however, the primary focus of these studies was on weight reduction and the reduction of GERD symptoms was a secondary outcome. In order to isolate the direct effects of gastrectomy upon chronic GERD symptoms, well-designed RCTs are required which compare health outcomes of patients treated with gastrectomy versus medication or fundoplication.

**Hiatal Hernia Repair without Fundoplication**
Several studies were identified which reported an improvement in GERD symptoms associated with sliding type hernia repair; however, no studies were identified which evaluated the use of hiatal hernia repair as an independent treatment of gastric reflux disease.

**Clinical Practice Guidelines**

Three evidence-based clinical practice guidelines address surgical treatment of GERD. These guidelines offer differing recommendations concerning indications for surgery. No evidence-based clinical practice guidelines were identified which recommend fundoplication surgery as a treatment of GERD in patients with pulmonary fibrosis. In addition, no evidence-based clinical practice guidelines were identified which address the use of gastrectomy or hiatal hernia repair as a treatment of GERD.

**Society of American Gastrointestinal and Endoscopic Surgeons**

The Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) guidelines recommend surgical therapy when the diagnosis of reflux is objectively confirmed, in individuals who:[26]

1) have failed medical management (inadequate symptom control, severe regurgitation not controlled with acid suppression, or medication side effects)  
OR
2) opt for surgery despite successful medical management (due to quality of life considerations, lifelong need for medication intake, expense of medications, etc.)  
OR
3) have complications of GERD (e.g., Barrett's esophagus, peptic stricture)  
OR
4) have extra-esophageal manifestations (asthma, hoarseness, cough, chest pain, aspiration)

“Surgical therapy for GERD is an equally effective alternative to medical therapy and should be offered to appropriately selected patients by appropriately skilled surgeons (Grade A*). Surgical therapy effectively addresses the mechanical issues associated with the disease and results in long-term patient satisfaction (Grade A). For surgery to compete with medical treatment, it has to be associated with minimal morbidity and cost.”

*Definitions*

- Grade A: “Based on high level (Level I or II), well-performed studies with uniform interpretation and conclusions by the expert panels”
- Level I Evidence: “Evidence from properly conducted randomized, controlled trials
- Level II Evidence: “Evidence from controlled trials without randomization; cohort or case-control studies; multiple time series; dramatic uncontrolled experiments

**American Gastroenterological Association (AGA)**

In 2008, the American Gastroenterological Association (AGA) published a guideline regarding the management of gastroesophageal reflux disease which made the following recommendations:[1]

- “When antireflux surgery and PPI therapy are judged to offer similar efficacy in a patient with an esophageal GERD syndrome, PPI therapy should be recommended as initial therapy because of superior safety.” (Grade A**)
• “When a patient with an esophageal GERD syndrome is responsive to, but intolerant of, acid suppressive therapy, antireflux surgery should be recommended as an alternative.” (Grade A)

• Antireflux surgery is recommended “for patients with an esophageal GERD syndrome with persistent troublesome symptoms, especially troublesome regurgitation, despite PPI therapy. The potential benefits of antireflux surgery should be weighed against the deleterious effect of new symptoms consequent from surgery, particularly dysphagia, flatulence, an inability to belch, and postsurgery bowel symptoms.” (Grade B**)

• “Patients with an extraesophageal GERD syndrome with persistent troublesome symptoms despite PPI therapy should be considered for antireflux surgery. The potential benefits of antireflux surgery should be weighed against the deleterious effect of new symptoms consequent from surgery, particularly dysphagia, flatulence, an inability to belch, and postsurgery bowel symptoms.” (Grade C**)

• The AGA recommends against antireflux surgery (Grade D**):
  o “for patients with an esophageal syndrome with or without tissue damage who are symptomatically well controlled on medical therapy.”
  o “as an antineoplastic measure in patients with Barrett's metaplasia.”

**Definitions**

• Grade A: “strongly recommended based on good evidence that it improves important health outcomes.”

• Grade B: “recommended with fair evidence that it improves important outcomes”

• Grade C: “balance of benefits and harms is too close to justify a general recommendation”

• Grade D: “recommend against, fair evidence that it is ineffective or harms outweigh benefits”

American College of Gastroenterology

In 2013, the American College of Gastroenterology (ACG)[27] issued a guideline for the diagnosis and management of gastroesophageal reflux disease and made numerous recommendations regarding the management and surgical options for GERD. The following are some of the major recommendations regarding PPI use and fundoplication:

• In patients with partial response to PPI therapy, increasing the dose to twice daily therapy or switching to a different PPI may provide additional symptom relief. (Conditional recommendation, low level evidence)

• Surgical therapy is a treatment option for long-term therapy in GERD patients. (Strong recommendation, high level of evidence)

• Surgical therapy is generally not recommended in patients who do not respond to PPI therapy. (Strong recommendation, high level of evidence)

• Surgical therapy is as effective as medical therapy for carefully selected patients with chronic GERD when performed by an experienced surgeon. (Strong recommendation, high level of evidence)

**Definitions**

• The strength of a recommendation was graded as "strong" when the desirable effects of an intervention clearly outweigh the undesirable effects and as "conditional" when there is uncertainty about the trade-offs.
The level of evidence could range from "high" (implying that further research was unlikely to change the authors' confidence in the estimate of the effect) to "moderate" (further research would be likely to have an impact on the confidence in the estimate of effect) or "low" (further research would be expected to have an important impact on the confidence in the estimate of the effect and would be likely to change the estimate).

Summary

Esophagogastric Fundoplication

There is enough research to show that initial or repeat esophagogastric fundoplication improves symptomatic gastroesophageal reflux disease (GERD) for most patients with chronic GERD who have tried lifestyle changes and long-term use of proton pump inhibitors (PPIs), or in those with a documented mechanical failure from a previous antireflux procedure. It appears that initial or repeat esophagogastric fundoplication may also improve symptoms in patients with pulmonary fibrosis. When esophagogastric fundoplication is performed with a paraesophageal hiatal hernia repair, patients with a paraesophageal type of hiatal hernia may also benefit. Patients with achalasia may also have improved health outcomes when esophagogastric fundoplication is performed with an esophageal myotomy. Clinical guidelines based on research recommend fundoplication for select patients. Therefore, initial or repeat esophagogastric fundoplication may be considered medically necessary when policy criteria are met. Initial or repeat esophagogastric fundoplication for GERD is not medically necessary when policy criteria are not met.

Gastrectomy

There is not enough research to show that distal, partial or complete gastrectomy with or without gastroduodenostomy, gastrojejunostomy, or Roux-en-Y reconstruction improves health outcomes for people with gastrointestinal reflux disease (GERD). No clinical practice guidelines based on research recommend gastrectomy for people with GERD. Therefore, distal, partial or complete gastrectomy with or without gastroduodenostomy, gastrojejunostomy, or Roux-en-Y reconstruction is considered investigational as a treatment of GERD.

Hiatal Hernia Repair without Fundoplication

There is not enough research to show that hiatal hernia repair without fundoplication, including repair of sliding or paraesophageal hernia, improves health outcomes for people with gastrointestinal reflux disease (GERD). No clinical practice guidelines based on research recommend independent hiatal hernia repair as a treatment for GERD. Therefore hiatal hernia repair without fundoplication is considered investigational as an independent treatment of GERD.

REFERENCES


**CROSS REFERENCES**

*Bariatric Surgery*, Surgery, Policy No. 58

*Transesophageal Endoscopic Therapies for Gastroesophageal Reflux Disease (GERD)*, Surgery, Policy No. 110

*Magnetic Esophageal Ring to Treat Gastroesophageal Reflux Disease (GERD)*, Surgery, Policy No. 190

*Peroral Endoscopic Myotomy for Treatment of Esophageal Achalasia*, Surgery, Policy No. 196

**CODES**

<table>
<thead>
<tr>
<th>CODES</th>
<th>NUMBER</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>43279</td>
<td>Laparoscopy, surgical, esophagomyotomy (Heller type), with fundoplaty, when performed</td>
</tr>
<tr>
<td>CODES</td>
<td>NUMBER</td>
<td>DESCRIPTION</td>
</tr>
<tr>
<td>-------</td>
<td>--------</td>
<td>-------------</td>
</tr>
<tr>
<td></td>
<td>43280</td>
<td>Laparoscopy, surgical, esophagogastric fundoplasty (eg, Nissen, Toupet procedures)</td>
</tr>
<tr>
<td></td>
<td>43281</td>
<td>Laparoscopy, surgical, repair of paraesophageal hernia, includes fundopasty, when performed; without implantation of mesh</td>
</tr>
<tr>
<td></td>
<td>43282</td>
<td>; with implantation of mesh</td>
</tr>
<tr>
<td></td>
<td>43325</td>
<td>Esophagogastric fundoplasty; with fundic patch (Thal-Nissen procedure)</td>
</tr>
<tr>
<td></td>
<td>43327</td>
<td>Esophagogastric fundoplasty partial or complete; laparotomy</td>
</tr>
<tr>
<td></td>
<td>43328</td>
<td>; thoracotomy</td>
</tr>
<tr>
<td></td>
<td>43332</td>
<td>Repair, paraesophageal hiatal hernia (including fundoplication), via laparotomy, except neonatal; without implantation of mesh or other prosthesis</td>
</tr>
<tr>
<td></td>
<td>43333</td>
<td>; with implantation of mesh or other prosthesis</td>
</tr>
<tr>
<td></td>
<td>43334</td>
<td>Repair, paraesophageal hiatal hernia (including fundoplication), via thoracotomy, except neonatal; without implantation of mesh or other prosthesis</td>
</tr>
<tr>
<td></td>
<td>43335</td>
<td>; with implantation of mesh or other prosthesis</td>
</tr>
<tr>
<td></td>
<td>43336</td>
<td>Repair, paraesophageal hiatal hernia (including fundoplication), via thoracoabdominal incision, except neonatal; without implantation of mesh or other prosthesis</td>
</tr>
<tr>
<td></td>
<td>43337</td>
<td>; with implantation of mesh or other prosthesis</td>
</tr>
<tr>
<td></td>
<td>43338</td>
<td>Esophageal lengthening procedure (eg, Collis gastroplasty or wedge gastroplasty) (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td></td>
<td>43631</td>
<td>Gastrectomy, partial, distal; with gastroduodenostomy</td>
</tr>
<tr>
<td></td>
<td>43632</td>
<td>; with gastrojejunostomy</td>
</tr>
<tr>
<td></td>
<td>43633</td>
<td>; with roux-en-Y reconstruction</td>
</tr>
<tr>
<td></td>
<td>43634</td>
<td>; with formation of intestinal pouch</td>
</tr>
<tr>
<td></td>
<td>HCPCS</td>
<td>None</td>
</tr>
</tbody>
</table>

October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage.

Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
Implantable Bone Conduction and Bone-Anchored Hearing Aids

Effective: May 1, 2017

Next Review: March 2018
Last Review: April 2017

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

External bone-conduction hearing aids function by transmitting sound waves through the bone to the ossicles of the middle ear.

MEDICAL POLICY CRITERIA

Notes:

- This policy applies only to implantable bone conduction and bone anchored hearing aid systems, also called osseointegrated implants. It does not apply to cochlear implants which are addressed in a separate medical policy (see Cross References) or to devices with no implantable components such as intraoral bone conduction hearing aids.
- Bone anchored hearing aids (BAHAs) are bone conduction hearing aids. There may be specific member benefit language addressing coverage of hearing aids. Any specific contract language supersedes medical policy. Unless otherwise specified, the contract language addressing coverage of hearing aids applies to both surgically implanted bone conduction hearing aids and externally worn air-conduction hearing aids.

  Unilateral or bilateral fully- or partially- implantable bone-conduction (bone-anchored) hearing aid(s) may be considered medically necessary as an alternative...
to an air-conduction hearing aid in patients 5 years of age and older with a conductive or mixed hearing loss when both of the following criteria (A and B) are met:

A At least one of the following criteria is met:
   1. Congenital or surgically induced malformations (e.g., atresia) of the external ear canal or middle ear;
   2. Chronic external otitis or otitis media;
   3. Tumors of the external canal and/or tympanic cavity;

B One of the following audiologic criteria is met:
   1. A pure tone average bone-conduction threshold measured at 0.5, 1, 2, and 3 kHz of dB lower than or equal to 45 dB (OBC, BP100, Baha4 and Baha5 devices), 55 dB (BP110 and Intenso devices), or 65 dB (Cordele II device) in patients with unilateral hearing loss (see Policy Guidelines below); or
   2. For bilateral implantation, patients should have a symmetrically conductive or mixed hearing loss (measured without augmentation) as defined by a difference between left and right side bone conduction threshold of less than 10 dB on average measured at 0.5, 1, 2 and 3 kHz (4 kHz for OBC, Ponto Pro, and Otomag Alpha 1 [M]), or less than 15 dB at individual frequencies.

II A fully- or partially-implantable bone-conduction (bone-anchored) hearing aid may be considered medically necessary as an alternative to an air-conduction contralateral routing of signals hearing aid in patients 5 years of age and older with single-sided sensorineural deafness and normal hearing in the other ear.

III A transcutaneously worn, non-surgical application of an implantable bone-anchored hearing aid (bone conduction-type hearing aid) utilizing a headband or Softband is considered medically necessary as an alternative to an implantable bone-anchored hearing aid or air-conduction hearing aid in individuals who meet criteria I. or II., above, except for the age limitation of 5 years of age or older which does not apply for a transcutaneously worn bone-anchored hearing aid.

IV Implant replacement with a next-generation device may be considered medically necessary only in the small subset of patients whose response to existing components is inadequate to the point of interfering with activities of daily living, which would include school and work; or when components are no longer functional.

V Replacement parts or upgrades to existing bone-anchored hearing aids and/or components that are currently functional are considered not medically necessary, including but not limited to when requested for convenience or technology upgrade. Replacement parts or upgrades include, but are not limited to batteries, processors, headbands or Softbands.

VI Other uses of fully- or partially-implantable bone-conduction (bone-anchored) hearing aids, including use in patients with bilateral sensorineural hearing loss, are considered investigational.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.
POLICY GUIDELINES

Pure tone hearing tests measure the faintest level (hearing threshold) at which a tone can be heard at selected frequencies approximately 50% of the time. Each ear is tested separately. The pure tone average threshold hearing level is calculated separately for each ear by averaging the hearing levels at each frequency. For example, if a patient’s bone-conduction hearing threshold in the right ear at frequencies 0.5, 1, 2, and 3 kHz is 20, 20, 30, and 40 dB, respectively, the pure tone average for that ear is \((20 + 20 + 30 + 40) \div 4 = 27.5\) dB.

CROSS REFERENCES

1. Cochlear Implant, Surgery Policy No. 8

BACKGROUND

Conventional external hearing aids can be generally subdivided into air-conduction hearing aids and bone-conduction hearing aids. Air-conduction hearing aids require the use of ear molds, which may be problematic in patients with chronic middle ear and ear canal infections, atresia of the external canal, or an ear canal that cannot accommodate an ear mold. In these patients, bone-conduction hearing aids may be an alternative.

External bone-conduction hearing aids must be closely applied to the temporal bone, with either a steel spring over the top of the head or with the use of a spring-loaded arm on a pair of spectacles. These devices may be associated with either pressure headaches or soreness. Partially implantable bone-conduction hearing aids have been investigated as an alternative.

The bone-anchored hearing aid (BAHA) implant systems, also called osseointegrated devices, work by combining a vibrational transducer coupled directly to the skull via a percutaneous abutment that permanently protrudes through the skin from a small titanium implant anchored in the temporal bone. The system is based on the process of "osseointegration" through which living tissue integrates with titanium in the implant over a period of 3 to 6 months, allowing amplified and processed sound to be conducted via the skull bone directly to the cochlea. The lack of intervening skin permits the transmission of vibrations at a lower energy level than required for external bone-conduction hearing aids.

The BAHA device has been used successfully in children younger than 5 years in Europe and the United Kingdom. (The most recent [1999] update of the U.S. Food and Drug Administration [FDA] notification lists age less than 5 years as a contraindication.) A number of reports describe experience with preschool children or children with developmental issues that might interfere with maintenance of the device and skin integrity. A two-stage procedure is used in young children with the fixture placed into the bone at the first stage and, after 3 to 6 months to allow for osseointegration, a second procedure to connect the abutment through the skin to the fixture.

Baha sound processors can also be used with the Baha® Softband™. With this application there is no implantation surgery. The sound processor is attached to the head using either a hard or soft headband. The band can be adjusted to the individual's head size. The amplified sound is transmitted transcutaneously to the bones of the skull for transmission to the cochlea. These devices have been suggested as a bridge to bone anchor implantation in young children who are not eligible for the implant due to young age and/or bone strength/thickness not yet adequate.
Partially implantable magnetic bone conduction hearing systems, also referred to as transcutaneous bone-anchored systems, are an alternative to bone conduction hearing systems connected percutaneously via an abutment. With this technique, acoustic transmission occurs transcutaneously via magnetic coupling of the external sound processor and the internally implanted device components. The bone conduction hearing processor contains a magnet that adheres externally to magnets implanted in shallow bone beds with the bone conduction hearing implant. Since the processor adheres magnetically to the implant, there is no need for a percutaneous abutment. To facilitate greater transmission of acoustics between magnets, skin thickness may be reduced to 4-5 mm over the implant when it is surgically placed.

REGULATORY STATUS

The following *Baha® sound processors, currently marketed by Cochlear™ (formerly called Cochlear™ Americas), have received 510(k) clearance from the U.S. Food and Drug Administration (FDA) for use with the Baha auditory osseointegrated implant (hearing aid) systems (such as the Baha® Connect system):

- Baha® 5 Sound Processor
- Baha® 5 SuperPower Sound Processor
- Baha® 5 Power Sound Processor

The above devices are currently available from Cochlear™. However, predicate devices include the Baha®4, Cordelle II, Divino®, Intenso™ and BP100™.

*Note: These devices may be referred to as Cochlear™ Baha® systems or Cochlear osseointegrated implants, reflecting the manufacturer’s name. These devices are bone conduction hearing aids and should not be confused with cochlear implants which are prostheses that replace a damaged or absent cochlea in the inner ear. Cochlear implants are addressed in a separate medical policy (see Cross References).

The FDA approved the Cochlear™ Baha® system (initially approved under the trade name Branemark Bone-Anchored Hearing Aid [BAHA™] by Entific Medical Systems, Inc.) for use in children aged 5 years and older, and in adults, for the following indications:

- Patients who have conductive or mixed hearing loss and can still benefit from sound amplification;
- Patients with bilaterally symmetric conductive or mixed hearing loss, may be implanted bilaterally;
- Patients with sensorineural deafness in one ear and normal hearing in the other (i.e., single-sided deafness, SSD);
- Patients who are candidates for an air-conduction contralateral routing of signals (AC CROS) hearing aid but who cannot or will not wear an AC CROS device.

Baha sound processors can also be used with the Baha® Softband™. The Baha® Softband™ received FDA clearance in 2002 for use in children under the age of 5 years.

Subsequent bone conduction hearing systems (listed below) share similar indications as the Cochlear™ Baha® devices:

- OBC Bone Anchored Hearing Aid System (Oticon Medical)
- Sophono® (S) (Cochlear) (predicate device was Otomag [Sophono])
• Ponto (Oticon Medical).
• Ponto Pro, Ponto Plus, Ponto Plus Power, Ponto 3, Ponto 3 Power or Ponto 3 SuperPower processors (Oticon Medical), to be used with the Oticon or BAHA devices.

The following partially implantable magnetic bone conduction devices have received FDA 510(k) clearance:

• Sophono® (M) (Cochlear) (predicate device was Otomag Alpha [Sophono])
• Sophono™ Alpha 2 MPO™ (Medtronic)
• Baha® Attract (Cochlear®)

The BoneBridge™ (MedEl) partially implantable bone-conduction hearing aid has not received FDA approval for use in the United States.

**EVIDENCE SUMMARY**

Hearing results of semi-implantable bone-conduction hearing aids may be compared either to 1) external bone-conduction hearing aids in patients with atresias who are unable to use external air-conduction hearing aids, or 2) external air-conduction hearing aids in patients who are unable to tolerate air-conduction hearing aids due to chronic infection. Reported studies have suggested that the bone-anchored hearing aid (BAHA) is associated with improved hearing outcomes compared to external bone-conduction hearing aids and equivalent outcomes compared to conventional air-conduction hearing aids.[1-4] However, given the objectively measured outcomes and the largely invariable natural history of hearing loss in individuals who would be eligible for an implantable bone-conduction device, a within-subjects comparison of hearing before and after device placement may be a reasonable study design.

**UNILATERAL DEVICES**

**Systematic Review**

In 2017 Kim et al. conducted a systematic review on the efficacy of BAHAs in single-sided deafness, including 14 studies (N=296 patients). The reviewers reported that in the six studies that dealt with sound localization, no significant difference was found after the implantation. However, twelve studies showed the benefits of BAHAs for speech discrimination in noise. Regarding subjective outcomes of using the prosthesis in patients with SSD (abbreviated profile of hearing aid benefit [APHAB] and the Glasgow hearing aid benefit profile [GHABP], etc.), improvements in quality of life were reported in the majority of studies.

**Conclusions:**

This systematic review has indicated that BAHAs may successfully rehabilitate patients with SSD by alleviating the hearing handicap to a certain degree, which could improve patients' quality of life. This report has presented additional evidence of effective auditory rehabilitation for SSD and will be helpful to clinicians counseling patients regarding treatment options for SSD.

In a 2015 Peters et al. published a systematic review of the literature through April 7, 2014 on the use of BAHA devices with contralateral routing of sound systems for single-sided deafness (SSD).[5] Five[6-10] of the six studies that met inclusion criteria were rated as moderate to high directness of evidence and low to moderate risk of bias and, thus, were included in the review.
Significant heterogeneity was found in the 91 total patients included. For speech perception in noise there was not consistent improvement with aided hearing over unaided hearing in all environments. All studies reported equal sound localization in the aided and unaided conditions, and quality of life measures were similar for the aided and unaided conditions. Interpretation of these outcomes was limited by the methodological limitations of the included studies, including the lack of RCTs, unclear inclusion criteria, small sample sizes, use in some studies of headband devices which have different bone conduction thresholds in the higher frequencies than implanted devices, clinical heterogeneity of included populations (e.g., duration of deafness, grade of hearing loss), unexplained missing data, and lack of long-term audiometric follow-up. The authors also noted that the lack of recent studies was surprising considering the recent advances in these devices, and recommended high-quality studies on the clinical outcome of current devices.

**Randomized Controlled Trials**

No RCTs of unilateral BAHAs have been published.

**Nonrandomized Studies**

Since publication of the Peters systematic review, one prospective, interventional study compared patient satisfaction with transcutaneous BAHA devices to CROS hearing aids for SSD.

In 2017, Snapp et al. reported a prospective single-center study of 27 patients with unilateral severe-profound sensorineural hearing loss who had either a CROS (n=13) or transcutaneous BAHA (n=14) device.[11] Mean device use was 66 months for the BAHAs and 34 months for CROS devices. Both BAHA and CROS groups had significant improvement in speech-in-noise performance, but neither showed improvement in localization ability. There were no differences between the devices for subjective measures of posttreatment residual disability or satisfaction as measured by the Glasgow Hearing Aid Benefit Profile (GHABP).

Leterme et al. assessed 24 adults with SSD, 18 of whom were evaluated with trials of both hearing aids with CROS and bone conduction–assisted hearing using the Baha Softband.[12] Most patients (72%), after completing trials of both devices, preferred the BAHA device to hearing aid with CROS. Glasgow Benefit Index and Abbreviated Profile of Hearing Aid Benefit (APHAB) scores did not differ significantly between devices. Sixteen of the 18 subjects elected to undergo implantation of a percutaneous BAHA device. In general, hearing improvement with the Baha Softband trial correlated with hearing improvements following device implantation.

**BILATERAL DEVICES**

Use of bilateral devices has been evaluated in nonrandomized studies of patients with conductive or mixed hearing losses. A number of studies, published over several years, have demonstrated a consistent improvement in speech recognition in noise and in sound localization with bilateral devices.

**Systematic Reviews**

A systematic review by the Health Technology Assessment Program was published in 2011 on the use of bone-anchored hearing aids (BAHAs) for bilateral hearing impairment.[13,14] The authors noted that the quality of available studies on the use of BAHAs is weak. No studies with control groups were identified for the review. Cohort pre-post studies and cross-sectional
comparative studies demonstrated improvements in hearing with use of BAHAs over conventional bone-conduction hearing aids or unaided hearing. However, whether improvements in hearing with BAHAs are greater than air-conduction hearing aids is uncertain. Additionally, bilateral use of BAHAs improved hearing outcomes in some patients over unilateral use, but the evidence was uncertain. Implant loss was noted to be between 6.1% and 19.4%. The authors noted hearing-specific quality of life improved, but overall quality of life did not differ.

In 2012 Janssen and colleagues reported similar findings in a systematic review that assessed the outcomes of bilateral versus unilateral BAHA for individuals with bilateral permanent conductive hearing loss (CHL). Their search strategy included studies of all languages published between 1977 and July 2011. Studies were included if subjects of any age had permanent bilateral CHL and bilateral implanted BAHAs. Outcome measures of interest were any subjective or objective audiologic measures, quality of life indicators, or reports of adverse events. Eleven studies met their inclusion criteria. All 11 studies were observational. There were a total of 168 patients in the 11 studies, 155 of whom had BAHAs and 146 of whom had bilateral BAHAs. In most studies, comparisons between unilateral and bilateral BAHA were intra-subject. Patients ranged from 5 to 83 years of age; 46% were male, and 54% were female. Heterogeneity of the methodologies between studies precluded meta-analysis, therefore a qualitative review was performed. Results from three studies were excluded from synthesis because their patients had been included in multiple publications. Adverse events were not an outcome measure of any of the included studies. In general, bilateral BAHA was observed to provide additional objective and subjective benefit compared to unilateral BAHA. For example, the improvement in tone thresholds associated with bilateral BAHA ranged from 2-15dB, the improvement in speech recognition patterns ranged from 4-5.4dB, and the improvement in the Word Recognition Score ranged from 1-8%. However, these results were based on a limited number of small observational studies consisting of heterogeneous patient groups that varied in age, severity of hearing loss, etiology of hearing loss, and previous amplification experience.

Randomized Controlled Trials

No RCTs of bilateral BAHAs have been published.

Nonrandomized Studies

No new studies have been published since the most recent systematic review.

BAHA IN CHILDREN UNDER AGE 5 YEARS

Nonrandomized Studies

The literature on the use of these devices in children consists of a review article and several nonrandomized studies.

The largest series in children under 5 years identified for this review, described by Amonoo-Kuofi et al. in 2015, which included 24 children identified from a single center’s prospectively maintained database. Most patients underwent a 2-stage surgical approach. The largest proportion of patients (52%) received the implant for isolated microtia, followed by Goldenhar syndrome (16%). Following implantation, 13 patients (54%) had grade 2 or 3 local reactions on the Holgers Scale (redness, moistness, and/or granulation tissue) and 7 (29%) had grade 4 local reactions on the Holgers Scale (extensive soft-tissue reaction requiring removal of the
Quality of life scores (Glasgow Children’s Benefit Inventory [GCBI]; scoring range, -100 to 100) were obtained in 18 subjects/parents with a finale mean score change of +40 points. Audiologic testing indicated that the average performance of the device fell within the range of normal auditory perception in noisy and quiet environments.

Marsella et al. reported on their center’s experience with pediatric BAHA in all 47 children implanted, 7 of which were younger than 5 years of age. The functional gain was significantly better with BAHA than with conventional bone-conduction hearing aids. There was no significant difference in terms of functional outcome between the 7 patients younger than age 5 and the rest of the patient cohort. Based on these findings, the study authors suggested that implantation of children at an age younger than 5 years can be conducted safely and effectively in such settings. However, the conclusions from this study were limited by the small number of children younger than 5 years of age and the limited power to detect a difference between younger and older children.

A 2008 review article noted that for children younger than age 5 years, other solutions (such as a bone conductor with transcutaneous coupling) should be utilized. This recommendation is in agreement with the FDA clearance of the osseointegration implant only for children 5 years of age and older, and adults.

McDermott reported on the role of BAHAs in children with Down syndrome in a retrospective case analysis and postal survey of complication rates and quality of life outcomes for 15 children aged 2 to 15 years. All patients were using their BAHA devices after a follow-up of 14 months. No fixtures were lost, and skin problems were encountered in 3 patients. All 15 patients had improved social and physical functioning as a result of better hearing.

Davids and colleagues at the University of Toronto provided BAHA devices to children less than 5 years of age for auditory and speech-language development and retrospectively compared surgical outcomes for a study group of 20 children 5 years or younger and a control group of 20 older children. Children with cortical bone thickness greater than 4 mm underwent a single-stage procedure. The interstage interval for children having 2-stage procedures was significantly longer in the study group to allow implantation in younger patients without increasing surgical or postoperative morbidity. Two traumatic fractures occurred in the study group versus 4 in the older children. Three younger children required skin site revision. All children were wearing their BAHA devices at the time of writing.

**BAHA SOFTBAND USE IN CHILDREN**

**Nonrandomized Studies**

The current evidence consists of small retrospective studies and comparative studies. In children under age five years, externally worn AOD sound processors appears to consistently be beneficial for children under age five years with bilateral aural atresia who are too young to receive an implantable device.

A 2014 report compared use of the Softband in 16 children (ages ranging from 3 months to 6 years) with bilateral aural atresia to 29 normal-hearing children (ages ranging from 8 months to 6 years). Auditory development was assessed at baseline, 6 months, and 12 months. The full text of the article was not available and the abstract did not provide data from the normal-hearing children for comparison. The authors concluded that the Softband was a suitable bridge to surgical implantation in infants and young children with bilateral atresia.
Ramakrishnan and colleagues used the Glasgow Benefit Inventory (GBI) and Listening Situation Questionnaire to report quality of life findings in a retrospective cross-sectional survey administered to parents of 22 children (n=109 total participants), some with skull and congenital/chromosomal abnormalities from inherited syndromes that involve unilateral (hemifocal microsomia) or bilateral hearing impairment (Treacher-Collins Syndrome, n=4 of 22) due to microtia or aural atresia. The youngest child utilizing an externally worn BAHA with Softband was 6 months of age. Overall, parents reported short-term satisfaction in the mean GBI scores for the children after 3 months of implanted BAHA or externally worn BAHA with Softband use. Despite the heterogeneous etiology of children in the study population, the authors suggest that the utility of BAHAs for children with syndromes and craniofacial anomalies is poorly recognized, resulting in delays in aid fitting and therefore in early hearing rehabilitation. In such cases, surgical reconstruction of the ear canal and middle-ear defects is not only technically challenging but also plagued by poor results (with a high rate of ear canal restenosis and limited functional hearing benefit). Hence, alternative treatment options such as Softband and BAHA may be of considerable benefit.

In 2010 Christensen et al. reported on a retrospective chart review of 10 children (ages 6 months to 16 years) with bilateral conductive hearing loss. Participants had been initially fit with a traditional bone-conduction hearing aid, then progressed first to the externally worn AOS with the Softband, then to the implanted BAHA. Functional gain was measured at 500 Hz, 1000 Hz, 2000 Hz, and 4000 Hz for each device. Both the external AOS and the implanted BAHA provided statistically significantly higher functional gain than the conventional BCHAs.

A number of the same authors for the Christensen et al. study also reported the results of a retrospective chart review of 25 children aged 6 months to 18 years with craniofacial disorders and bilateral conductive hearing loss.

It is unknown whether some of the children in the 2010 study were also included in these results. The focus of this study was on functional as measure by comparison of aided (using the Baha Softband) and unaided soundfield audiometric thresholds. Soundfield thresholds were improved with the Baha amplification, with over 80% of the thresholds meeting significant target levels. The authors concluded that this demonstrated the benefit of the Baha for children with bilateral congenital conductive hearing loss.

Hol and colleagues evaluated the validity of a BAHA with Softband (fitted unilaterally and bilaterally) in 2 young children with severe bilateral conductive hearing loss due to CAA. In a small multicenter comparative study, 12 children (including the 2 children in the Hol, 2005 study) with bilateral CAA with a pure conductive hearing loss of around 60 dB HL were fitted with the BAHA with Softband. These children were retrospectively compared to a reference group of 8 children selected from a database of those who had a conventional bone conduction hearing aid for bilateral CAA. The authors reported the mean aided hearing threshold of the children with the BAHA with Softband compared to the reference group was 27 dB HL, ± 6 dB HL to 25 dB HL ± 6 dB HL, respectively. Further results compared psychological and language development in 5 of the 12 children available from the BAHA with Softband group.

ADVERSE EFFECTS OF BAHAS

Systematic Reviews
In 2016, Verheij et al. published a systematic review on complications of tissue preservation surgical techniques with percutaneous BAHA devices including 18 studies with 381 devices.[29] The implantation techniques reported in the studies were as follows: punch method, four studies (81 implants); linear incision technique without soft tissue reduction, 13 studies (288 implants); and Weber technique, one study (12 implants). Indications for surgery were SSD (n=68), sensorineural hearing loss (n=4), mixed hearing loss (n=65), or CHL (n=66). The Holgers classification was used to grade soft tissue reactions (grade 0, no reaction; grade 2, red and moist tissue; grade 3, granulation tissue; grade 4, removal of skin-penetrating implant necessary due to infection). The incidence of Holgers 3 was 2.5% with the punch technique, 5.9% with the linear incision technique, and 0% with the Weber technique. Holgers 4 was reported in one patient implanted with the linear incision technique.

In 2014 Mohamad et al. performed a systematic review focusing on the association between surgical technique and skin complications following BAHA implantation. Thirty randomized controlled trials and retrospective studies were included, which highlighted that the most common surgical techniques identified were full-thickness skin graft, dermatome and linear incision. The investigators reported that dermatome technique is associated with higher rate of skin complications and the use of a linear incision technique is associated with lower skin complications. However, the investigators concluded that the data to support these conclusions in limited and that higher quality studies are needed.[30]

In 2103 Kiringoda et al. reported on a meta-analysis of complications related to BAHA devices. Included in the meta-analysis were 20 studies that evaluated complication in 2134 adult and pediatric patients who received a total of 2310 BAHA devices.[31] The quality of available studies was considered poor and lacking in uniformity. The most common complications related to BAHA devices were minor skin reactions. Holgers Grade 2 to 4 skin reactions were reported to occur from 2.4% to 38.1% in all studies. Zero to 18% of implants failed osseointegration in adult and mixed population studies while 0% to 14.3% failed osseointegration in pediatric population studies. Adult and mixed population studies reported revision surgery was required in 1.7% to 34.5% of cases while pediatric population studies reported required revision surgery in 0.0% to 44.4% of cases. Implant loss occurred in 1.6% to 17.4% in adult and mixed population studies and from 0.0% to 25% in pediatric studies.

Nonrandomized Studies

In 2016, Roplekar et al. compared skin-related complications of the traditional skin flap method to the linear incision method performed by a single surgeon in 117 patients with at least 1 year of follow-up.[32] Twenty-one (24%) patients experienced skin-related complications in the skin flap group (12 skin overgrowths, eight wound infections, one numbness) and three (10%) patients experienced complications in the linear incision group (three wound infections).

Four 2014 retrospective studies reported specific complication rates related to BAHA implants. The rate of skin reaction (e.g., skin overgrowth, inflammation) ranged from 6% to 22%. Implant loss was 10-18% and were spontaneous while others required removal; the primary reasons for implant loss were loss of osseointegration, trauma, and soft tissue reactions or discomfort. In addition, a number of small studies reported the safety outcomes of various techniques for surgically implanting BAHA devices. These included skin flap versus full-thickness skin graft implantation,[33] non-skin-thinning technique versus either flap or dermatome implantation,[34] and techniques related to implant size[35,36].
**Section Summary: Safety and Adverse Events Related to BAHA Devices**

The quality of available data for adverse events is generally poor with high heterogeneity. The most frequently reported complication from surgical procedures for BAHA insertion are adverse skin reactions, with an incidence of Holgers grade 2 to 4 reactions ranging from less than 2% to more than 34%, and implant loss ranging from less than 2% to more than 17%. There is some evidence of improvement in complication rates and severity with newer surgical techniques such as linear incision.

**PARTIALLY IMPLANTABLE MAGNETIC BONE CONDUCTION HEARING AIDS**

A small body of literature addresses outcomes associated with transcutaneous, partially implantable bone-anchored devices. The majority of studies use a within-subjects comparison of hearing thresholds with and without the device. The indications for partially implantable systems are the same as those for transcutaneous bone-anchored devices.

**Systematic Reviews**

In 2016, Dimitriadis et al. reported on a systematic review of observational studies of the BAHA Attract device including 10 studies (total N=89 patients; range, 1-27 patients). Seventeen (19%) of the patients were children, of whom five had unilateral sensorineural hearing loss and 4 had CHL. Of the 27 (45%) adults, 22 had unilateral sensorineural hearing loss and 11 (18%) had bilateral mixed hearing loss. Audiologic and functional outcome measures and the timing of testing varied greatly in the studies. Summary measures were not reported. In general, audiologic and functional outcomes measured pre- and postimplantation showed improvement, although statistical comparisons were lacking in some studies.

**Nonrandomized Studies**

Iseri et al. described a retrospective, single-center study from Turkey comparing 21 patients treated with a transcutaneous, fully implantable BAHA with 16 patients treated with a percutaneous device (the BAHA Attract). Groups were generally similar at baseline, with most individuals undergoing BAHA placement for chronic otitis media. Operating time was longer in patients treated with the transcutaneous partially implantable devices (46 minutes vs 26 minutes, p<0.05). Three patients treated with percutaneous devices had Holger grade 2 skin reactions, and two had stopped using their devices. Mean thresholds for frequencies 0.5 to 4.0 kHz were 64.4 dB without the BAHA and 31.6 dB with the BAHA in the percutaneous device group, and 58.3 dB without the BAHA and 27.2 dB with the BAHA in the transcutaneous device group. Frequency-specific threshold hearing gains did not differ significantly between groups. Mean hearing gain measured by speech reception threshold was statistically significantly smaller in the percutaneous group (24 dB vs 36.7 dB, p=0.02).

There have been other, small nonrandomized studies that have assessed the outcomes of the BAHA Attract device, in comparison with other devices, or in single-center observational studies. In addition, one case series of 34 patients has reported on complications of the BAHA Attract device, where only three patients reported moderate to severe complications, two of which required removal of the magnet.

In 2015, Denoyelle et al. reported on a prospective trial of the Sophono device in children ages 5 to 18 years with uni- or bilateral congenital aural atresia with complete absence of the external auditory canal with pure CHL. The study included a within-subject comparison of
hearing results with the Sophono devices to those obtained with the Baha Softband preoperatively. All 15 patients enrolled were implanted (median age, 97 months). At 6-month follow-up, mean aided AC pure-tone audiometry was 33.49 (mean gain, 35.53 dB), with a mean aided sound reception threshold of 38.2 (mean gain, 33.47 dB). The difference in AC PTA between the Baha Softband and the Sophono device was 0.6 dB (confidence interval upper limit, 4.42 dB), which met the study’s prespecified noninferiority margin. Adverse effects were generally mild, including skin erythema in two patients, which improved by using a weaker magnet, and brief episodes of pain or tingling in three patients.

The Otomag Sophono system has been studied in a number of very small (n=5-12) nonrandomized studies in pediatric patients.[39,40,44-51]

Similarly, the Bonebridge partially implantable system has also been studied in a number of small (n=5-44) case series.[52-58] Preliminary results showed hearing gains. However, conclusions based on these studies are limited by the small sample size, and lack of treatment randomization or appropriate control group.

Section Summary: Partially Implantable Magnetic BAHA Devices

Studies of transcutaneous, partially implantable BAHAAs have typically used a retrospective within-subjects comparison of hearing thresholds with and without the device, although there have been 2 small (27 and 15 participants) prospective studies. There was heterogeneity in the audiologic and functional outcome measures used in the studies and the timing of testing. Studies of partially implantable BAHAAs have generally demonstrated within-subjects improvements in hearing.

PRACTICE GUIDELINE SUMMARY

No evidence-based clinical practice guidelines were identified for these devices.

AMERICAN ACADEMY OF OTOLARYNGOLOGY-HEAD AND NECK SURGERY (AAO-HNS)[59]

In 2016, the American Academy of Otolaryngology – Head and Neck Surgery updated its consensus-based position statement on the use of implantable hearing devices. It specifies that active middle ear implants are appropriate for adults with moderate to severe hearing loss who may benefit from amplification but are unable to benefit from the amplification provided by conventional hearing aids. The statement indicates that the procedure should be performed by a qualified otolaryngologist-head and neck surgeon with devices which have been Food and Drug Administration (FDA)-approved, and “should adhere to the restrictions and guidelines specified by the appropriate governing agency, such as the Food and Drug Administration in the United States”.

SUMMARY

There is enough research to show that unilateral or bilateral partially- and fully-implantable (bone-anchored) bone-conduction hearing aid(s) improve net health outcomes when used as an alternative to air-conduction hearing aids in select patients aged five years and older. In addition, a binaural hearing benefit may be provided for patients with single-sided sensorineural deafness by the routing of signals to the hearing ear. Therefore, use of these
devices is considered medically necessary for patients who meet the policy criteria. These devices are considered investigational for patients who do not meet the policy criteria due to a lack of research showing improvement in health outcomes, including but not limited to children younger than five years and patients with bilateral sensorineural hearing loss.

The research on externally worn, nonimplanted transcutaneous auditory osseointegrated devices held in place by a headband is limited. However, despite these limitations, there appears to be benefit of these devices in patients who have been unable to benefit from conventional bone-anchored hearing aids but who are not eligible to receive the implantable devices due to young age or other contraindications. Therefore, the use of externally worn, nonimplanted transcutaneous auditory osseointegrated devices held in place by a headband may be considered medically necessary for patients of any age when the policy criteria (other than the age restriction) for an implantable bone anchored hearing aid device are met.

Implant replacement with a next-generation device may be considered medically necessary only in the small subset of patients whose response to existing components is inadequate to the point of interfering with activities of daily living, which would include school and work; or when components are no longer functional.

Replacement parts or upgrades to existing bone-anchored hearing aid components (for example, batteries, processor, headband or Softband) are considered not medically necessary when requested for convenience or to upgrade to newer technology when the current components remain functional.

### REFERENCES

8. Hol, MK, Kunst, SJ, Snik, AF, Cremers, CW. Pilot study on the effectiveness of the conventional CROS, the transcranial CROS and the BAHA transcranial CROS in adults with unilateral inner ear deafness. Eur Arch Otorhinolaryngol. 2010 Jun;267(6):889-96. PMID: 19904546


60. BlueCross BlueShield Association Medical Policy Reference Manual "Implantable Bone-Conduction and Bone-Anchored Hearing Aids." Policy No. 7.01.03

### CODES

<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>The following CPT codes describe semi-implantable electromagnetic bone conduction hearing aids:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPT</td>
<td>69710</td>
<td>Implantation or replacement of electromagnetic bone conduction hearing device in temporal bone*</td>
</tr>
<tr>
<td></td>
<td>69711</td>
<td>Removal or repair of electromagnetic bone conduction hearing device in temporal bone</td>
</tr>
</tbody>
</table>

*The Audiant™ bone conductor is a type of electromagnetic bone conduction hearing device. While this product is no longer actively marketed, patients with existing Audiant devices may require replacement, removal, or repair.|

| | 69714 | Implantation, osseointegrated implant, temporal bone, with percutaneous attachment to external speech processor/cochlear stimulator; without mastoidectomy** |
| | 69715 | ; with mastoidectomy** |
| | 69716 | Replacement (including removal of existing device), osseointegrated implant, temporal bone, with percutaneous attachment to external speech processor/cochlear stimulator; without mastoidectomy |
| | 69717 | ; with mastoidectomy |

**These codes describe implantation of the Baha®, Ponto™, and similar devices.**

<table>
<thead>
<tr>
<th>HCPCS</th>
<th>L8690</th>
<th>Auditory osseointegrated device, includes all internal and external components***</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>L8691</td>
<td>Auditory osseointegrated device, external sound processor, replacement</td>
</tr>
<tr>
<td></td>
<td>L8692</td>
<td>Auditory osseointegrated device, external sound processor, used without osseointegration, body worn, includes headband or other means of external attachment</td>
</tr>
<tr>
<td></td>
<td>L8693</td>
<td>Auditory osseointegrated device abutment, any length, replacement only</td>
</tr>
</tbody>
</table>

***These codes describe the Baha®, Ponto™, and similar devices.**

*Date of Origin: July 2003*
Implantable Cardioverter Defibrillator

Effective: August 1, 2017

Next Review: April 2018
Last Review: April 2017

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

The automatic implantable cardioverter defibrillator (ICD) is a device designed to monitor a patient’s heart rate, recognize ventricular fibrillation (VF) or ventricular tachycardia (VT), and deliver an electric shock to terminate these arrhythmias to reduce the risk of sudden cardiac death. Indications for ICD implantation can be broadly subdivided into 1) primary prevention, i.e., their use in patients who are considered at high risk for sudden cardiac death but who have not yet experienced life-threatening VT or VF; and 2) secondary prevention, i.e., their use in patients who have experienced a potentially life-threatening episode of VT (near sudden cardiac death).

MEDICAL POLICY CRITERIA

Note:

- This policy addresses only initial ICD implantation; it does not address ICD removal or replacement.
- This policy does not address ICD implantation in pediatric patients less than 18 years of age, which may be considered medically necessary.

Transvenous Implantable Cardioverter Defibrillator (ICD)
A The use of the *transvenous* automatic implantable cardioverter defibrillator (ICD) may be considered *medically necessary* in patients who are not candidates for a cardiac revascularization procedure (coronary artery bypass graft [CABG] or percutaneous transluminal coronary angioplasty [PTCA]) and who meet one of the following criteria (1 or 2):

1. For *primary* prevention when at least one of the following criteria (a.-i.) are met:
   a. Ischemic cardiomyopathy with New York Heart Association (NYHA) functional *Class I* symptoms when both of the following criteria (i and ii) are met:
      i. History of myocardial infarction at least 40 days before ICD treatment; and
      ii. Left ventricular ejection fraction of 30% or less
   *NYHA Class I = No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, or dyspnea (shortness of breath).
   b. Ischemic cardiomyopathy with NYHA functional *Class II* symptoms when both of the following criteria (i and ii) are met:
      i. History of myocardial infarction at least 40 days before ICD treatment; and
      ii. Left ventricular ejection fraction of 35% or less
   **NYHA Class II = Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in fatigue, palpitation, or dyspnea.**
   ***NYHA Class III = Marked limitation of physical activity; less than ordinary activity leads to symptoms
   c. Nonischemic dilated cardiomyopathy when all of the following criteria (i - iii) are met:
      i. Left ventricular ejection fraction of 35% or less; and
      ii. Reversible causes have been excluded; and
      iii. Response to optimal medical therapy has been adequately determined
   d. Hypertrophic cardiomyopathy (HCM) at high risk for sudden cardiac death with at least one of the following major risk factors:
      i. History of premature HCM-related sudden death in one or more first-degree relatives younger than 50 years; or
      ii. Left ventricular hypertrophy greater than 30 mm; or
      iii. One or more runs of nonsustained ventricular tachycardia at heart rates of 120 beats per minute or greater on 24-hour holter monitoring; or

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
iv. Prior unexplained syncope inconsistent with neurocardiogenic origin

e. Documented LMNA gene mutations (lamin A/C deficiency) in patients with at least one of the following conditions:
   i. Cardiomyopathy; or
   ii. Symptomatic cardiac arrhythmias

f. Diagnosis of long QT syndrome (LQTS) with at least one of the following:
   i. Prior cardiac arrest; or
   ii. Recurrent syncopal events while on beta blocker therapy

g. Diagnosis of Brugada syndrome (BrS) with at least one of the following:
   i. Prior cardiac arrest; or
   ii. Spontaneous sustained ventricular tachycardia (VT) with or without syncope; or
   iii. Spontaneous diagnostic type 1 ECG with a history of syncope, seizure, or nocturnal agonal respiration after noncardiac causes have been excluded; or
   iv. Development of ventricular fibrillation (VF) during programmed electrical stimulation

h. Diagnosis of catecholaminergic polymorphic ventricular tachycardia (CPVT) with at least one of the following:
   i. Prior cardiac arrest; or
   ii. Recurrent syncope; or
   iii. Polymorphic/bidirectional VT that is nonresponsive to medical management, or left cardiac sympathetic denervation

i. Diagnosis of short QT syndrome (SQTS) with at least one of the following:
   i. Prior cardiac arrest; or
   ii. Symptomatic and have documented spontaneous VT with or without syncope; or
   iii. Family history of sudden cardiac death

2. For secondary prevention in patients with a history of a life-threatening clinical event associated with ventricular arrhythmic events such as sustained ventricular tachyarrhythmia, after reversible causes (e.g., acute ischemia) have been excluded.

B The use of the transvenous ICD is considered investigational when Criteria I.A. are not met and including, but not limited to, patients with any of the following:
1. Have had an acute myocardial infarction (i.e., less than 40 days before ICD treatment); or

2. Have New York Heart Association (NYHA) **Class IV** congestive heart failure (unless patient is eligible to receive a combination cardiac resynchronization therapy ICD device); or

****NYHA Class IV = inability to carry on any activity without symptoms; symptoms may be present at rest

3. Have had a cardiac revascularization procedure in the past 3 months (coronary artery bypass graft [CABG] or percutaneous transluminal coronary angioplasty [PTCA]) or are candidates for a cardiac revascularization procedure; or

4. Have noncardiac disease that would be associated with life expectancy less than 1 year

II **Subcutaneous Implantable Cardioverter Defibrillator (ICD)**

A The use of the subcutaneous ICD may be considered **medically necessary** in patients who meet all of the following criteria (1-4):

1. Applicable medical necessity criteria for transvenous ICD is met (Criteria I.); and

2. Have a contraindication to a transvenous ICD due to at least one of the following (a-c):
   a. Lack of adequate vascular access; or
   b. The need to preserve existing vascular access due to chronic dialysis; or
   c. Repeat transvenous ICD placement not indicated due to complications with previous transvenous ICD placement;

3. Have no indication for antibradycardia pacing; and

4. Do not have ventricular arrhythmias that are known or anticipated to respond to antitachycardia pacing

B The use of the subcutaneous ICD is considered **investigational** when the above criteria (II. A.) are not met.

III The use of ICDs with an ST-segment monitoring feature in patients is considered **investigational** for all indications.

**NOTE:** A summary of the supporting rationale for the policy criteria is at the end of the policy.

CROSS REFERENCES

1. Wearable Cardioverter-Defibrillators as a Bridge to Implantable Cardioverter-Defibrillator Placement, Durable Medical Equipment, Policy No 61.
2. Genetic Testing for Predisposition to Inherited Hypertrophic Cardiomyopathy, Genetic Testing, Policy No. 72

BACKGROUND

October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage.

Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
The standard ICD involves placement of a generator in the subcutaneous tissue of the chest wall. Transvenous leads are attached to the generator and threaded intravenously into the endocardium. The leads sense and transmit information on cardiac rhythm to the generator which analyzes the rhythm information and produces an electrical shock when a malignant arrhythmia is recognized.

A totally subcutaneous ICD (S-ICD®) has also been developed. This device does not employ transvenous leads, and thus avoids the need for venous access and complications associated with the venous leads. Rather, a subcutaneous electrode is implanted adjacent to the left sternum. The electrodes sense the cardiac rhythm and deliver countershocks through the subcutaneous tissue of the chest wall.

ICDs with a built-in ST-segment monitoring feature, also called ICD-based ischemia monitors, are currently being studied. ST segment monitoring may also be referred to as intracardiac ischemia monitoring. The continuous ST-segment monitoring provided by this added feature is intended to detect changes in the patient’s ST-segment as a possible indicator of an ischemic cardiac event. If an ST segment shift meets or exceeds a preprogrammed threshold, the device stores the event data (e.g., date, time, heart rate, maximum ST shift, duration of the event). The device has a patient notifier feature that vibrates to alert the patient that an ST episode has occurred.

REGULATORY STATUS

The U.S. Food and Drug Administration (FDA) has approved a number of ICDs through the premarket approval (PMA) process. The FDA-labeled indications generally include patients who have experienced life-threatening ventricular tachyarrhythmia associated with cardiac arrest or ventricular tachyarrhythmia associated with hemodynamic compromise and resistance to pharmacologic treatment.

The following are examples of FDA-approved transvenous ICDs:

- Devices manufactured by Boston Scientific include Dynagen, Inogen, Origen, and Teligen.
- Medtronic produces the Evera Family of devices (originally: Virtuosos/Entrust/Maximo/Intrinsic/Marquis family).
- St. Jude Medical, Inc. devices include the Ellipse / Fortify Assura Family and the Current Plus ICD (originally: Cadence Tiered Therapy Defibrillation System).
- Other devices with similar approval language include devices from Biotronik, Boston Scientific, and Sorin Crm USA.

The following are examples of FDA-approved subcutaneous ICDs:

- The Subcutaneous Implantable Defibrillator (S-ICD®) System (Cameron Health, Inc., acquired by Boston Scientific, Inc.) received FDA approval on September 28, 2012 for “defibrillation therapy for the treatment of life-threatening ventricular tachyarrhythmias in patients who do not have symptomatic bradycardia, incessant ventricular tachycardia, or spontaneous frequently recurring ventricular tachycardia that is reliably terminated with antitachycardia pacing.” The electrode is called the Q-TRAK® and the electrode insertion tool is called the Q-Guide™.
- The Fortify™ ST ICD (St. Jude Medical, Inc.) has received investigational device exemption (IDE) clearance from the FDA for use only in the clinical trial setting.

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
The Emblem S-ICD™ (Boston Scientific, Inc.), which is smaller and longer-lasting than the original S-ICD, was cleared for marketing through a PMA supplement.

Note: This policy addresses only initial ICD implantation; it does not address ICD removal or replacement.

### EVIDENCE SUMMARY

**TRANSVENOUS IMPLANTABLE CARDIAC DEFIBRILLATOR (ICD)**

The scientific evidence evaluating the use of automatic ICDs on health outcomes consists of several technology assessments and clinical trials. Evidence from well-conducted randomized controlled trials (RCTs) shows consistent associations between use of ICDs and improved health outcomes among specific groups of patients with symptomatic ischemic or nonischemic dilated cardiomyopathy and those with history of prior arrhythmogenic events.

#### Systematic Reviews

In 2016, results from the Danish Study were published. This was a multi-center RCT comparing ICD to standard management in patients with non-ischemic heart failure, described in more detail below.[1] While the trial demonstrated a significantly lower risk of sudden cardiac death with ICD, there was no difference seen in overall mortality. After this article was published, several systematic reviews evaluated the evidence from RCTs on ICD use in patients with nonischemic cardiomyopathy. Wolff et al. meta-analyzed five RCTs with a total of 2992 dilated cardiomyopathy patients that compared ICD therapy with medical therapy for primary prevention.[2] They found a significant reduction in mortality and sudden cardiac death with ICD therapy (odds ratio [OR], 0.77; 95% CI, 0.64-0.93; p = 0.006 and OR, 0.43; 95% CI, 0.27-0.69; p = 0.0004, respectively). Similarly, Luni et al. performed a meta-analysis of six RCTs evaluating ICD use for primary prevention in patients with nonischemic cardiomyopathy.[3] While they reported a significant survival benefit with ICD therapy, this benefit was no longer significant when the analysis was restricted to trials which had adequate beta blocker, ACE/ARB and aldosterone receptor blocker use. A meta-analysis by Al-Khatib et al. included only four RCTs, as they included only trials that compared ICD to medical therapy that included at least 100 nonischemic cardiomyopathy patients and had follow-up periods of at least 12 months.[4] This analysis also reported a significant mortality reduction with ICD therapy (hazard ratio [HR], 0.75; 95% CI, 0.61-0.93; P = .008).

In 2014 Gracieux et al. published the results of a systematic review of nine RCTs of adults aged 19 years or older with ischemic cardiomyopathy to determine the incidence and predictors of appropriate ICD therapy delivery.[5] Only four of the nine RCTs that met inclusion criteria reported the clinical characteristics of patients who received appropriate shocks. These characteristics included male sex, advanced NYHA class, nonsustained ventricular tachycardia, and lower serum creatinine. These patients were also less likely to be on beta-blocker medications. LVEF was not a significant factor. The authors noted that predictors of appropriate shocks were not adequately studied in large trials and recommended further large prospective studies.

A 2013 technology assessment from the Agency for Healthcare Research and Quality (AHRQ) assessed the evidence published through December 4, 2012 for ICDs for primary prevention of sudden cardiac death.[6] Included studies were RCTs or comparative cohort studies comparing ICD to no ICD or to different ICD interventions, a minimum of 10 participants per study group,
and concurrent controls in the cohort studies. Patients in the ICD groups must have been followed from the time of ICD implantation. Key questions were well defined and focused on the following:

- Outcomes of 1) ICD vs. no ICD, 2) ICD with antitachycardia pacing (ATP) vs. ICD alone, and 3) ICD with CRT vs. ICD alone
- Variations in outcomes and adverse events among subgroups of participants, ICD devices, clinicians, and facilities
- Eligibility criteria and methods for evaluation of participants in comparative trials
- Likelihood of SCD or ventricular tachyarrhythmia (VT) as measured by total shocks in patients with ICDs or SCD episodes in patients without ICDs.

Ten RCTs (18 articles[7-23]) and four cohort studies[24-27] of adults met inclusion criteria; no studies of ICDs in children met inclusion criteria. All included studies conducted intention-to-treat analyses. In studies comparing ICD to no ICD the strength of evidence for all-cause mortality and sudden cardiac death (SCD) was rated as high. These studies found reduced risk of all-cause mortality 3-7 years after ICD implantation and SCD 2-6 years after implantation (HR 0.69 and 0.37, respectively). There was indirect evidence across studies that ICD provided no benefit for patients with recent myocardial infarction (MI), defined as <30-40 days. No significant difference was found for all-cause mortality or SCD across subgroups by patient sex or age or by the facilities in which the ICDs were placed. The evidence for quality of life in these studies was rated as low and failed to show consistent effects of ICD placement. No studies reported the effect of adding ATP in ICD patients. Four RCTs[28-31] that compared ICD alone to ICD with CRT (CRT-D) met inclusion criteria, but the strength of evidence was rated as insufficient due to discordant findings.

Eligibility criteria for ICD implantation in 13 of the 14 studies included both ischemic or nonischemic dilated cardiomyopathy (DCM) and left ventricular ejection fraction (LVEF) ≤35%. Most of the studies excluded adults over 70-80 years of age. Heart failure (HF) class varied between studies. While most RCTs tested ICD patients for nonsustained VT, different diagnostic tools were used. Only one RCT used electrophysiology studies (EPS) in all participants. Coronary angiography or exercise testing for coronary stenosis was tested in four of the RCTs. Limitations of the included studies were high attrition rates (>20%), differential attrition and/or crossover rates between study groups, and between-group differences in concurrent beta blocker use and control treatments. In addition, outcome assessors were not blinded. The authors concluded that there was high strength evidence in favor of ICD therapy compared to no ICD therapy for primary prevention of SCD in certain patients with reduced LVEF and ischemic or NICM.

Chen et al. (2013) analyzed eight RCTs[28,32-50] that compared the safety and effectiveness of ICD alone with cardiac resynchronization therapy and ICD (CRT-D) in patients with heart failure.[51] The study quality was rate as high in four RCTs with follow-up of more than six months. The quality of the other four RCTs was down-graded slightly due to short-term follow-up of less than 6 months. CRT-D showed significantly superior outcomes compared to ICD alone for cardiac function, improved clinical condition, fewer hospitalizations, and lower all-cause mortality 12 months or more after implantation, though not during the initial 3-6 months after implantation. However, CRT-D had a significantly higher rate of serious adverse events (e.g., pneumothorax, hemothorax, lead dislodgement, coronary sinus dissection). There were a number of methodological limitations of the meta-analysis and the included RCTs. The limitations included the between-study differences in follow-up duration noted above. In
addition, some studies included primarily NYHA class I and II heart failure patients while others focused on class III and IV patients. The authors also noted that the enrolled patients were younger than the general population of candidates for ICD or CRT-D which could result in an overestimation of benefit since older patients would be expected to have more comorbidities that could negatively impact clinical outcomes.

In a 2012 Shinkel et al. reported the results of a systematic review and meta-analysis of 16 studies\(^52-54\) of patients with ICDs for hypertrophic cardiomyopathy (HCM)\(^55\). Mean age was 42 years and mean follow-up was 3.7 years. The majority of the studies were for primary prevention ICDs. Risk factors for SCD included left ventricular wall thickness \(\geq 30\) mm, family history of SCD, nonsustained ventricular tachycardia, syncope, and abnormal blood pressure response. The rate of appropriate ICD therapy was 14%, with annualized rate of 3.3%. Inappropriate shocks occurred in 20% of the 1966 patients in the 13 studies that reported this outcome. The annualized rate of inappropriate therapy was 4.8%. Mortality rates were reported in 13 studies and included 3% from cardiac death and 2% from noncardiac death. Nine studies reported adverse events which occurred in 15% of patients. The most frequent complications were lead malfunction (7%) or displacement (3%) and infection (3%). Limitations of the meta-analysis was the use of data from observational studies and the potential risk of heterogeneity of participant clinical characteristics and SCD risk profiles when pooling data from different studies. Limitations of the included studies were lack of clear information on the clinical decision strategy and risk factors for ICD placement, lack of long-term data on ICD-related complications in the general practice setting, younger age of participants than would be expected in the general clinical setting, and insufficient consideration of the psychological and behavioral aspects of ICD therapy in HCM patients. This latter limitation is important because many HCM patients who are candidates for ICD are otherwise healthy, asymptomatic young individuals.

**Randomized Controlled Trials (RCTs)**

Kober et al. reported results from the Danish Study in 2016,\(^1\) which was included in several of the recent systematic reviews described above. This unblinded trial included 556 patients with NICM, enrolled between 2008 and 2014 from multiple centers in Denmark, to compare ICD therapy to usual clinical care. As many patients with heart failure are not treated with cardiac resynchronization therapy (CRT), the randomization of patients was stratified such that both ICD and control groups had a similar proportion of CRT patients (58%). The primary outcome of the study was death from any cause, and secondary outcomes included sudden cardiac death, cardiovascular death and non-fatal MIs. The median follow-up time was 67.6 months (interquartile range, 49-85 months). There were 120 patients (21.6%) in the ICD group and 131 patients in the control group that died during follow-up (4.4 and 5.0 deaths/100 person-years, respectively), which was not significantly different. Subgroup analysis showed no difference in ICD effect between patients receiving CRT and those who did not, but younger patients (< age 59) did demonstrate a survival benefit with ICD (HR, 0.51; 95% CI, 0.29-0.92). The risk for cardiovascular death was also not significantly different between groups (hazard ratio [HR] for ICD group vs. control, 0.77; 95% CI, 0.57 to 1.05; \(P = 0.10\)). However, sudden cardiac death was far less frequent in the ICD group than in controls (HR, 0.50; 95% CI, 0.31-0.82). The lack of benefit with IDC therapy for overall survival seen in this study differs from previous findings. The authors concluded that recent advances in heart failure treatment, including CRT, have reduced the potential benefit from ICD therapy, except in select patients.

**Non-randomized Studies**
Nonischemic Dilated Cardiomyopathy

Amara et al. (2017) compared ICD therapy for the prevention of sudden cardiac death in patients with nonischemic (NICM) and ischemic (ICM) cardiomyopathy enrolled in the multicenter Défibrillateur Automatique Implantable-Prévention Primaire (DAI-PP) study.[56] A total of 5485 patients participated in the study, 2181 (39.8%) with NICM and 3304 (60.2%) with ICM. The mean follow-up was 3.1 ± 2.2 years. Patients with ICM were significantly older (63.7 ± 10.3 vs. 60.6 ± 12.2 years, P < 0.0001) and had a higher prevalence of sinus rhythm (77.3% vs. 74.0%, P = 0.009), a higher ejection fraction (27% vs. 25% P < 0.0001), and a narrower QRS (37.3% vs. 21.4% with QRS <120, P < 0.0001) than those with NICM. Mortality during follow-up was significantly higher in ICM patients, at 52.3 events/1000 person-years vs. 48.6 events/1000 person-years for NICM patients (p=0.008). This difference was primarily due to increased non-cardiovascular mortality, as cardiovascular mortality rates were similar between groups. The authors noted that inappropriate therapies were more frequent in those with NICM (7.94 vs. 5.96%; P = 0.005).

Results from subjects with nonischemic dilated cardiomyopathy (NIDCM) included in SCD-HeFT and DEFINITE studies suggested a mortality benefit from ICD therapy, although statistical significance that was not achieved in these studies was likely related to insufficient power.

A meta-analysis of five trials including nonischemic subjects reported a statistically significant reduction in mortality associated with ICD therapy. Furthermore, when the body of evidence for ICD therapy in both ischemic and nonischemic populations is considered together, the preponderance of evidence suggests that ICD therapy improves health outcomes compared with medical management alone with a relative risk reduction in all-cause mortality between 21% and 35%. While the risk of adverse events (AEs) is not well-reported in studies of patients without prior MI, it seems reasonable to expect similar low rates of device-related AEs as seen in studies of patients with prior MI.

Hypertrophic Cardiomyopathy

In 2015, Magnusson et al. reported outcomes for 321 patients with HCM treated with an ICD enrolled in a Swedish registry.[57] Over a mean 5.4 years of follow-up, appropriate ICD discharges in response to ventricular tachycardia or fibrillation occurred in 77 patients (24%), corresponding to an annual rate of appropriate discharges of 5.3%. At least 1 inappropriate shock occurred in 46 patients (14.3%), corresponding to an annualized event rate of 3.0%. Ninety-two patients (28.7%) required at least one surgical intervention for an ICD-related complication, with a total of 150 ICD-related reinterventions. Most reinterventions (n=105, 70%) were related to lead dysfunction.

Adverse Effects

Ezzat et al. (2015) published a systematic review and meta-analysis of adverse events (AEs) following ICD implantation, comparing rates of AEs reported in clinical trials of ICDs with those reported in the U.S. National Cardiovascular Data Registry.[58] The review included 18 RCTs with a total of 6796 patients. In pooled analysis, the overall AE rate was 9.1% (95% CI 6.4 to 12.6%). Rates of access-related complications, lead-related complications, generator-related complications, and infection were 2.1% (91% CI 1.3 to 3.3%), 5.8% (95% CI 3.3 to 9.8%), 2.7% (95% CI 1.3 to 5.7%), and 1.5% (95% CI 0.8 to 2.6%), respectively. Complication rates in the RCTs were higher than those in the U.S. registry, which reports only in-hospital
complications (9.1% in the RCTs vs 3.08%, p<0.01). The overall complication rate was similar to that reported by Kirkfelt et al., in a population-based cohort study including all Danish patients who underwent a cardiac implantable electronic device procedure from 2010-2011 (562/5918 patients [9.5%] with at least 1 complication).[59]

Persson et al. (2014) published a systematic review and meta-analysis of AEs following ICD implantation.[60] The authors included data from 35 cohort studies, reported in 53 articles. In-hospital serious AE rates ranged from 1.2% to 1.4%, most frequently pneumothorax (0.4%-0.5%) and cardiac arrest (0.3%). Posthospitalization complication rates were variable: device-related complications occurred in 0.1% to 6.4%; lead-related complications in 0.1% to 3.9%; infection in 0.2% to 3.7%; thrombosis in 0.2% to 2.9%; and inappropriate shock in 3% to 21%.

The 2013 AHRQ technology assessment summarized above identified 14, 33, and 22 studies that reported early (up to 30 days after ICD implantation) AEs, late AEs, and inappropriate ICD shock, respectively.[6] The rate of early adverse events was 2.8-3.6% during hospitalization, of which 1.2-1.35% were considered serious events (strength of evidence high). The most common early AEs were lead dislodgement and hematoma. Higher early AE rates were found with dual chamber ICDs, in older patients, in women, and in patients with end-stage renal disease (ESRD). The most common late AEs were device-related AEs that occurred in <0.1-6.4% of ICD patients during follow-up ranging from 2 to 49 months (strength of evidence low). Lead malfunction, infection, and thrombosis were also reported. Inappropriate shocks at 1-5 years follow-up occurred in 3-21% of patients, with more occurring in younger patients. There was inconsistent evidence related to the rate of inappropriate shocks for single and dual chamber ICDs.

A systematic review and meta-analysis by Auricchio et al. (2017) focused on inappropriate shocks from both single chamber ICDs (VR-ICDs) and subcutaneous ICDs (S-ICDs).[61] The review included 16 articles, which showed that an average of 6.4% (95% CI, 5.1-7.9%) of patients with these ICDs received an inappropriate shock per year. There was evidence that this proportion was lower in more recent studies and in studies with longer follow-up.

ICDS IN PATIENTS WITH LMNA GENE MUTATION

In a systematic review for GeneReviews®, Hershberger et al. concluded, “Because risk for sudden cardiac death in LMNA-related DCM accompanies heart block and bradyarrhythmias, ICD use (rather than just pacemaker use) has been recommended for all indications.”[62]

Pasotti et al. conducted a retrospective longitudinal study with 94 individuals with mutations in the LMNA gene.[63] Subjects were observed for a median follow-up time of 57 months. During follow-up, 20 patients received a pacemaker and 16 received an ICD implantation. Twelve appropriate ICD interventions detected by the device (eight ventricular fibrillation and four sustained ventricular tachycardia). None of the subjects with ICDs died from sudden cardiac death, whereas the pacemaker did not appear to protect from SCD.

ICDS IN PATIENTS WITH CARDIAC ION CANNELOPATHIES

ICDs have been used for both primary and secondary prevention in patients with a number of disorders that predispose to ventricular arrhythmias and sudden cardiac death, including long QT syndrome (LQTS), Brugada syndrome (BrS), short QT syndrome (SQTS), and catecholaminergic polymorphic ventricular tachycardia (CPVT). Some of these conditions are
extremely rare, but the use of ICDs has been described in small cohorts of patients with BrS, LQTS, and SQTS. These small cohort studies are listed below:

**Long QT Syndrome**

In 2010, Horner et al. reported on outcomes for 51 patients with genetically confirmed LQTS treated with an ICD from 2000 to 2010 who were included in a single-center retrospective analysis of 459 patients with genetically confirmed LQTS.[64] Of the patients treated with ICDs, 43 (84%) received the device as primary prevention. Twelve patients (24%) received appropriate ventricular fibrillation or torsades de pointes- terminated ICD shocks. Factors associated with appropriate shocks included secondary prevention indications (p=0.008), QT corrected (QTc) duration greater than 500 ms (p=0.0008), non-LQT3 genotype (p=0.02), documented syncope (p=0.05), documented torsades de pointes (p=0.003), and a negative sudden family death history (p=0.0001). Inappropriate shocks were delivered in 15 patients (29%). Patients with the LQT3 genotype had only received inappropriate shocks.

**Brugada Syndrome**

Conte et al. described outcomes for a cohort of 176 patients with spontaneous or drug-induced Brugada type 1 electrocardiographic findings who received an ICD at a single institution and were followed for at least six months.[65] Before ICD implantation, 14.2% of subjects had a history of aborted sudden cardiac death (SCD) due to sustained spontaneous ventricular arrhythmias, 59.7% had at least one episode of syncope, and 25.1% were asymptomatic. Over a mean follow up of 83.8 months, 30 patients (17%) had spontaneous sustained ventricular arrhythmias detected. Sustained ventricular arrhythmias were terminated by ICD shocks or antitachycardia pacing in 28 patients (15.9%) and two patients (1.1%), respectively. However, 33 patients (18.7%) experienced inappropriate shocks. Eight patients (4.5%) died during follow up, three of whom died of cardiac causes.

Dores et al. reported results of a Portuguese registry that included 55 patients with Brugada syndrome, 36 of whom were treated with ICDs for either primary or secondary prevention.[66] Before ICD implantation, 52.8% of subjects were asymptomatic, 30.6% had a history of syncope with suspected arrhythmic cause, and 16.7% had a history of aborted SCD. Over a mean follow up of 74 months, 7 patients experienced appropriate shocks, corresponding to an incidence of 19.4% and an annual event rate of 2.8%. In multivariate analysis, predictors of appropriate shocks were a history of aborted SCD (HR 7.87, 95% CI 1.27 to 49.6, p=0.027) and nonsustained ventricular tachycardia during follow up (HR 6.73, 95% CI 1.27 to 35.7, p=0.025). In data from a US cohort of 33 patients with Brugada syndrome treated with ICDs, Steven et al. reported that 2/3 patients with a prior history of aborted SCD received appropriate shocks over a mean 7.9 years of follow up, while none of the 30 patients without a history of aborted SCD had an arrhythmia detected.[67] In a smaller registry that included 25 patients with Brugada syndrome treated with ICDs, over an average follow up of 41.2 months, appropriate shocks were delivered in 3 patients, all of whom had prior cardiac arrest.[68]

**Catecholaminergic Polymorphic Ventricular Tachycardia**

Roston et al. reported results of a multicenter retrospective cohort study that included 226 patients with catecholaminergic polymorphic ventricular tachycardia.[69] Implantable cardioverter defibrillators were placed in 121 (54%) most often for history of cardiac arrest (67 patients [55%]). One or more treatment failure events while on beta blockers were documented in 42 patients (35%). Appropriate shocks were experienced by 56 patients (46%) and
inappropriate shocks occurred in 21 patients (22%). Arrhythmia was terminated after appropriate shock in 31 patients (55%), but 9 (16%) had poor response to appropriate shocks. Electrical storm occurred in 22 patients (18%). ICD-related complications occurred in 28 patients (23%), usually manifesting as lead problems in 16 (57%). There were no differences in number of appropriate shocks, success of shocks, or incidence of electrical storm between patients with and without history of cardiac arrest. Death occurred in 3 patients (2%) despite ICD placement, one of which was associated with electrical storm. Fifty-eight patients (48%) were asymptomatic after ICD placement; however, 30 (25%) had persistent ventricular ectopy, 13 (11%) experienced syncope, and 13 (11%) had subsequent cardiac arrest.

Roses-Noguer et al. reported results of a small retrospective study of 13 patients with CPVT who received an ICD.[70] The indication for ICD therapy was syncope despite maximal beta-blocker therapy in 6 patients (46%) and aborted SCD in 7 patients (54%). Over a median follow-up of 4.0 years, 10 patients (77%) received a median 4 shocks. For 96 shocks, 87 electrocardiograms (ECGs) were available for review; of those, 63 (72%) were appropriate and 24 (28%) were inappropriate. Among appropriate shocks, 20 (32%) were effective in restoring sinus rhythm.

Adverse Effects

In contrast to patients requiring ICDs for secondary prevention or for primary prevention after acute MI, patients with hereditary arrhythmia syndromes are more likely to potentially require ICDs for primary prevention.

In 2016, Olde Nordkamp et al. reported on a systematic review and meta-analysis of studies reporting on ICD complications in individuals with inherited arrhythmia syndromes.[71] The review included 63 cohort studies with a total of 4916 patients (710 [10%] with arrhythmogenic right ventricular tachycardia; 1037 [21%] with BrS; 28 [0.6%] with CPVT; 2466 [50%] with hypertrophic cardiomyopathy; 162 [3.3%] with lamin A/C gene mutations; 462 [9.4%] with LQTS; and 51 [1.0%] with SQTS). Overall, inappropriate shocks occurred in 20% over a mean follow up of 51 months, corresponding to an inappropriate shock rate of 4.7% per year (95% CI 4.2 to 5.3%). Over a mean follow up of 55 months, ICD-related complications occurred in 22%, most commonly lead malfunction (10.3% of patients). The pooled rate of ICD-related complications was 4.4% per year (95% CI 3.6 to 5.2%).

SUBCUTANEOUS ICDs

Totally subcutaneous ICDs (S-ICDs) are a less invasive alternative to the conventional transvenous ICD, and are intended for patients who do have standard indications for an ICD, but who do not require pacing for bradycardia or antitachycardia overdrive pacing for VT. The S-ICD has also been proposed to be of particular benefit for patients with limited vascular access, including patients undergoing renal dialysis or children; or those who have had complications with transvenous ICDs. Evaluating the safety and efficacy of S-ICDs requires comparisons with transvenous ICDs in large, long-term, randomized, controlled trials. These comparisons are necessary to determine whether any benefits of S-ICDs outweigh risks and whether they offer advantages over transvenous ICDs with respect to the rate of adverse effects, successful termination of life-threatening arrhythmias, and unnecessary shocks.

Randomized Controlled Trials

No randomized controlled trials of S-ICDs have been published.
Nonrandomized Studies

Comparative Studies

In 2013, Kobe et al. prospectively followed 69 patients who received S-ICD.[72] These were compared with a group of 69 sex- and age-matched patients with conventional ICD who were randomly selected from an ICD database. Fifty-four patients were followed-up over a minimum of two years. The successful conversion rate was 89.5% for S-ICD and 90.8% for transvenous ICD (p=0.81). The rate of perioperative adverse events were similar between the two groups, as were the rate of inappropriate shocks (p=0.745) during short-term follow-up.

The Subcutaneous versus Transvenous Arrhythmia Recognition Testing (START) study compared the performance of a subcutaneous ICD with a transvenous ICD for detecting arrhythmias in the electrophysiology lab.[73] The patient population included 64 patients who were scheduled for ICD implantation. All patients had a transvenous ICD placed as well as subcutaneous electrodes attached to a subcutaneous ICD. Arrhythmias were induced and the sensitivity and specificity of detection by each device was compared. For ventricular arrhythmias, sensitivity of detection was 100% for the subcutaneous ICD and 99% for the transvenous ICD. Specificity was 98.0% for the subcutaneous ICD device compared to 76.7% for the transvenous device (p<0.001).

Non-comparative Studies

In 2016, Lambiase et al. evaluated the use of the S-ICD in patients with hypertrophic cardiomyopathy in the S-ICD IDE study and the EFFORTLESS registry, reporting on 99 patients with hypertrophic cardiomyopathy, who were compared with 773 non-hypertrophic cardiomyopathy patients.[74] At the time of reporting, three episodes of ventricular arrhythmias had been identified in the hypertrophic cardiomyopathy cohort, all of which were successfully terminated. In the hypertrophic cardiomyopathy group, 12.5% of subjects had experienced an inappropriate shock at a mean follow up of 22.0 months, which did not differ significantly from the rate in non-hypertrophic cardiomyopathy patients (10.7%; p=NS).

In 2015, Boersma et al. reported outcomes for patients in the S-ICD IDE study and the EFFORTLESS registry stratified by whether patients had been previously treated with a transvenous ICD.[75] At the time of analysis, 866 patients were available for inclusion. Of those, 75 (8.7%) were implanted with an S-ICD following transvenous ICD extraction for a system-related infection and 44 (5.1%) were implanted following transvenous ICD extraction for reasons other than a system-related infection, while the remaining 747 (86.3%) were de novo implants. Patients explanted for infection were older than patients whose transvenous ICD was explanted for non-infection related events and the de novo implant patients (55.5, 47.8, and 49.9 years, respectively; p=0.01), were more likely to have an ICD for secondary prevention (42.7%, 37.2%, and 25.6%, respectively; p<0.0001), and had a higher incidence of comorbidities. There were no significant differences in the rates of system- or procedure-related complications between patients whose transvenous ICDs were explanted for infection, those whose transvenous ICDs were explanted for non-infectious reasons, and the de novo S-ICD patients (10.7%, 6.8%, and 9.6%, respectively; p=0.078).

Another subanalysis of the pooled S-ICD IDE study and EFFORTLESS registry data, which included 882 patients at the time of analysis, evaluated the effect of learning curves on implant time, procedure complications, and inappropriate shocks.[76] Rates of complications were...
significantly lower in patients treated by the least experienced providers than those treated with the most experienced (9.8% vs 5.4%, p=0.02).

In 2015, Theuns et al. reported long term follow up of the Bardy cohort.[77] Over a median follow up of 5.8 years, 26 devices (47%) were replaced and 5 (9%) were explanted. Four patients (7%) required S-ICD explantation and replacement with a transvenous system, 2 due to a requirement for cardiac resynchronization therapy, 1 due to a requirement for bradycardia pacing, and 1 due to ineffective defibrillation testing. Most devices (81%) were replaced due to an elective replacement indication, at a median time to replacement of 5.0 years. Event-free rates for device replacement after 2, 4, and 6 years were 94%, 89%, and 30%, respectively. A total of 119 delivered shocks in 16 patients (29%) were recorded).

El-Chami et al. reported on a single-center study of outcomes after S-ICD placement in patients with endstage renal disease (ESRD) undergoing chronic dialysis, which included 79 patients who underwent SICD placement, 27 of whom were on chronic dialysis.[78] This research was prompted by prior studies that suggested higher mortality rates for ESRD patients implanted with transvenous ICDs. The composite outcome (frequency of death, heart failure hospitalization, or appropriate S-ICD shocks) was nonsignificantly higher in the ESRD group (23.8%/year vs 10.9%/year, p=0.317), a difference that was primarily driven by a significantly higher incidence of appropriate S-ICD shocks in the ESRD group (17.9%/year vs 1.4%/year, p=0.021).

In 2015 Burke et al. published a pooled analysis of patients from the S-ICD IDE study and the EFFORTLESS registry, which included 882 patients.[79] The poolability of data across the two studies was assessed by analysis of complications, appropriate and inappropriate shocks, conversion efficacy, and mortality by study, with additional analyses for outcomes that differed by study. Patients were followed for a mean of 651 (±345) days. Most patients (63%) presented with a history of previous transvenous ICDs that required extraction due to infection. Within 30 days of the procedure, 4.5% of subjects experienced a complication, while 11.1% of subjects experienced a complication within 3 years of the procedure. The most common complication was infection requiring device removal/revision (17 events in 14 patients [1.7%]). Mortality was low: the annual mortality rate was 1.6% and the 2 –year mortality rate was 3.2%. The Kaplan-Meier incidence of time to first therapy for VT or VF was 5.3% at 1 year, 7.9% at 2 years, and 10.5% at 3 years. Excluding VT/VF storms, 111 discrete VT/VF events were treated, with 100 (90.1%) terminated with the first shock, and 109 (98.2%) terminated within the 5 shocks available. The Kaplan-Meier incidence of time to first inappropriate shock was 13.1% at 3 years. In patients with dual zone programming at the index procedure, the Kaplan-Meier incidence of inappropriate shock at 3 years was 11.7% compared with 20.5% with single-zone programming. A significant study effect was observed for inappropriate shocks (p=0.0209), with a smaller proportion of inappropriate shocks in the EFFORTLESS group, but this effect was negated after correction for initially-programmed number of zones, shock zone rate, and conditional zone rate.

Gold et al. published a subanalysis of patients in the S-ICD IDE study to evaluate a discrimination algorithm to reduce inappropriate shocks.[80] Patients in the study could receive 1 of 2 shock detection algorithms, a single- or double-zone configuration. In the single-zone configuration, shocks are delivered for detected heart rates above the programmed rate threshold. In the dual-zone configuration, arrhythmia discrimination algorithms are active in a lower rate zone up to a shockable heart rate threshold. At hospital discharge, dual-zone programming was used in 226 subjects (72%) and single-zone programming was used in the
remaining 88 subjects (28%). Inappropriate shocks occurred on 23 of 226 (10.2%) subjects with dual-zone programming and 23 of 88 (26.1%; p<0.001) subjects with single-zone programming. Freedom from appropriate shocks did not differ between groups.

A large study was reported by Lambiase et al. who described patients in the EFFORTLESS-ICD registry, a multicenter European registry to report outcomes for patients treated with S-ICD. At the time of analysis, the registry included 472 patients, 241 of whom (51%) were enrolled prospectively, at a median follow-up time of 498 days. Nine patients (2%) died during the reported period, none of the deaths, which were known to occur in the perioperative period, although the cause of death was unknown for 1 patient. A total of 317 spontaneous episodes in 85 patients were recorded during the follow-up, of which 169 episodes received therapy in 59 patients. Of the 145 classified untreated episodes, 93 were adjudicated as inappropriate sensing, 37 were nonsustained VT/VF, 12 were nonsustained SVT above discrimination zone, and 3 were unclassified. Of the VT/VF episodes, the first shock conversion efficacy was 88%, with 100% overall successful clinical conversion after a maximum of five shocks. A total of 73 inappropriate shocks were recorded in 32 patients over an average follow-up of 18 months (360 day inappropriate shock rate of 7%).

A large series was a multicenter study 330 patients from several countries, the S-ICD System Clinical Investigation (S-ICD IDE Study). The S-ICD was successfully implanted in 314 of 330 patients (95.1%). Laboratory-induced VF was successfully terminated in more than 90% of patients, which was one of the primary outcomes of the study. The second primary outcome, greater than 99% freedom from complications at 180 days, was also met. Patients were followed for a mean duration of 11 months. There were 38 spontaneous episodes of VT in 21 patients (6.7%), and all were successfully terminated. Inappropriate shocks were received by 41 patients (13.1%).

A series of 118 patients from 4 centers in the Netherlands was published in 2013. Patients were followed for a mean of 18±7 months. Device-related complications occurred in 14% of patients, including infection (5.9%), dislodgement of the device or leads (3.3%), skin erosion (1.7%), and battery failure (1.7%). In 1 patient, the S-ICD was replaced with a transvenous ICD because of the need for antitachycardia pacing. Over the entire follow-up period, 8 patients experienced 45 appropriate shocks, with a first-shock conversion efficacy of 98%. Fifteen patients (13%) received a total of 33 inappropriate shocks. Two patients died, 1 due to cancer and 1 to progressive heart failure.

Aydin et al. reported outcomes for 40 consecutive patients implanted with SICDs at 3 German centers. Patients were considered for S-ICD if they met criteria for ICD implantation for primary or secondary prevention specified by the American College of Cardiology/American Heart Association/European Society of Cardiology, did not have symptomatic bradycardia, incessant ventricular tachycardia, or documented spontaneous, frequently-recurring ventricular tachycardia that was reliably terminated with antitachycardia pacing, and did not have pacemakers. Of the cohort, 25.0% had a prior transvenous ICD, and 57.5% received the S-ICD for secondary prevention. Over a median follow-up of 229 days, S-ICD activity was recorded in 10.0% of the patients, for whom a total of 25 episodes were retrieved. Of these, 21 shock episodes were correctly identified as ventricular tachyarrhythmia. The overall S-ICD shock efficacy was 96.4% (95% CI 12.8% to 100%).

Bardy et al. described the development and testing of the device, including empiric evidence for the optimal placement of the subcutaneous electrode, in 2010. A total of 55 patients were
tested in the electrophysiology lab for termination of induced arrhythmias and subsequently followed for a mean of 10.1 months for successful termination of detected arrhythmias and clinical outcomes. In the electrophysiology lab study, intraoperative VF was induced in 53 of 55. All episodes were correctly detected by the S-ICD. In 52 of 53 patients, 2 consecutive episodes of ventricular arrhythmia were successfully terminated. In the final patient, the arrhythmia was terminated on 1 occasion but not on the other. In the cohort portion of this study, 54 of 55 patients were alive at last follow-up. The 1 death was due to renal failure, and this patient requested removal of the S-ICD before death. An infection at the generator site occurred in 2 patients, necessitating a revision procedure. Another 3 patients had lead dislodgement requiring repositioning. There were a total of 12 episodes of VT that were detected by the S-ICD; all 12 episodes were successfully terminated by countershock.

**Adverse Effects**

The systematic review and meta-analysis by Auricchio et al. evaluated inappropriate shocks in patients with single-chamber ICDs (VR-ICDs) and S-ICDs using data from 16 articles. They found an overall rate of 6.4% of patients per year received an inappropriate shock, and this risk was no significant difference associated with the use of S-ICDs or ventricular tachycardia zone programming. The authors noted that one of the included studies had an anomalously low reported rate of inappropriate shocks (1.9%), which was not explained by the study design or covariates.

Olde Nordkamp et al. used data from the EFFORTLESS-ICD registry to evaluate rates of inappropriate shocks associated with the S-ICD. The patient population at the time of publication included 581 S-ICD recipients, 48 of whom (8.3%) experienced a total of 101 inappropriate shocks over a follow up period of 21.4 months. Most inappropriate shocks (73%) were related to T-wave oversensing.

Brisben et al. described the development of an algorithm designed to reduce T-wave oversensing by S-ICDs. The algorithm was developed using 133 episodes of T-wave oversensing and 70 episodes of appropriately treated VT or VF collected from S-ICD log files and 174 VT/VF recordings from an ECG signal library. It was validated using 164 episodes of T-wave oversensing from S-ICD log files and 137 and 328 recorded episodes, respectively, of VT/VF and supraventricular tachycardia from an ECG signal library. The revised algorithm was associated with a reduction in T-wave oversensing of 39.8% (95% CI, 28.4% to 51.2%; p=0.001 vs baseline.) Patient outcomes after the use of this algorithm have not been reported yet.

Groh et al. evaluated an ECG screening test to determine patients who are potential S-ICD candidates who are at risk for T wave oversensing. One hundred patients who had previously undergone transvenous ICD implantation and who were not receiving bradycardia pacing and did not have an indication for pacing were included. ECGs were obtained with lead placement to mimic the sensing vectors available on the S-ICD, and a patient was considered to qualify for S-ICD if the screening ECG template passed in any same lead supine and standing, at any gain, and without significant morphologic changes in QRS complexes. Of the included subjects who were potentially eligible for S-ICD, 8% were considered to fail based the ECG screening.

Kooiman et al. reported inappropriate shock rates among 69 patients treated at a single center with an S-ICD between February 2009 and July 2012 who were not enrolled in 1 of 2 other concurrent trials. Over a total follow-up of 1316 months (median per patient, 21 months), the
annual incidence of inappropriate shocks was 10.8%. In 8 patients, inappropriate shocks were related to T wave oversensing. After patients underwent adjustment of the sensing vector, no further inappropriate shocks occurred in 87.5% of patients with T wave oversensing.

ICDS WITH ST SEGMENT MONITORING

The intent of ICDs with the capability for continuous ST segment monitoring is to detect possible myocardial ischemic events. Thus, the validation of this additional feature in ICDs focuses on evidence demonstrating the following:

- Technical performance of ICD-based ischemic monitoring compared with intermittent monitoring with conventional external ECG
- Diagnostic performance (i.e., sensitivity, specificity, and positive and negative predictive value), particularly the rate of false positive detections that could lead to unnecessary testing or invasive procedures
- Clinical utility, specifically evidence that demonstrates the ability of this monitoring to improve patient health outcomes.

There are currently no randomized controlled trials for ICD-based ischemia monitoring. Two preliminary nonrandomized comparative trials have been published. In 2006, Baron et al. compared surface ECG (SECG) with intrathoracic ECG (IT-ECG) in 22 patient undergoing PTCA.[90] IT-ECG was reported to be significantly more sensitive than SECG in early and overall ischemia assessment, with highest sensitivity of 85%. However, this study did not indicate how these tests results were used in patient management to improve health outcomes. More recently, Forleo et al. compared ICDs with (n=53) versus without (n=50) ST-segment monitoring capability.[91] After at least 6 months follow-up, one patient in the ST monitoring group had an ST elevation myocardial infarction 3 weeks after implantation, but the algorithm had not yet been activated. Seven patients in the ST monitoring group had at least one episode (range 1-90) of false-positive ST events; the programmable features of the device helped overcome the problem in six patients. Unscheduled outpatient visits were significantly increased in ST monitored patients with a remote monitoring system (17 vs. 4 p=0.032). The authors concluded that ICD-based ST monitoring failed to provide a benefit over ICD alone and increased unscheduled evaluations in patients with remote follow-up.

PRACTICE GUIDELINE SUMMARY

The following section includes the current evidence-based clinical practice guidelines for use of ICDs. Consensus statements are not included.

THE AMERICAN COLLEGE OF CARDIOLOGY/AMERICAN HEART ASSOCIATION/HEART RHYTHM SOCIETY (ACC/AHA/HRS) GUIDELINES

The 2012[92] ACC/AHA/HRS Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities updates the 2008[93] Guideline for Implantation of Cardiac Pacemakers and Antiarrhythmic Devices. Guideline recommendations are classified into three levels: Classes I, II, and III. Class I is defined as “conditions for which there is evidence for and/or general agreement that the procedure or treatment is useful and effective.” Only Class I recommendations are listed here. Each recommendation is further classified as either A, B, or C, based on the weight of the evidence available. Level A is applied when data are from multiple, randomized clinical trials; level B is when data are from a limited number of
randomized trials; and level C is when the recommendation is primarily based on expert consensus.

The 2008 guidelines of the ACC/AHA/HRS for implantation of cardiac pacemakers and antiarrhythmia devices include the following Class I indications for ICDs:

1. ICD therapy is indicated in patients who are survivors of cardiac arrest due to ventricular fibrillation (VF) or hemodynamically unstable sustained ventricular tachycardia (VT) after evaluation to define the cause of the event and to exclude any completely reversible causes. (Level of Evidence: A)
2. ICD therapy is indicated in patients with structural heart disease and spontaneous sustained VT, whether hemodynamically stable or unstable. (Level of Evidence: B)
3. ICD therapy is indicated in patients with syncope of undetermined origin with clinically relevant, hemodynamically significant sustained VT or VF induced at electrophysiological study. (Level of Evidence: B)
4. ICD therapy is indicated in patients with LVEF less than 35% due to prior MI who are at least 40 days post-MI and are in NYHA functional Class II or III. (Level of Evidence: A)
5. ICD therapy is indicated in patients with NIDCM who have an LVEF less than or equal to 35% and who are in NYHA functional Class II or III. (Level of Evidence: B)
6. ICD therapy is indicated in patients with LV dysfunction due to prior MI who are at least 40 days post-MI, have an LVEF less than 30%, and are in NYHA functional Class I. (Level of Evidence: A)
7. ICD therapy is indicated in patients with nonsustained VT due to prior MI, LVEF less than 40%, and inducible VF or sustained VT at electrophysiological study. (Level of Evidence: B)

ACC/AHA GUIDELINES ON THE DIAGNOSIS AND MANAGEMENT OF HEART FAILURE

In 2013 the ACC/AHA issued practice guidelines on the management of heart failure which made the recommendations below about the use of ICDs as primary prevention. The following guideline recommendations are classified into three levels: Classes I, IIa, IIb, and III.

- Class I: Procedure/treatment is considered useful/effective and is recommended.
- Class IIa: Procedure is reasonable to perform but additional studies are needed
- Class IIb: Procedure may be considered; usefulness is unknown or not well established
- Class III No Benefit: Procedure is not recommended/indicated.
- Class III Harm: Procedure should not be performed; potentially harmful or associated with excess morbidity/mortality.

Each recommendation is further classified as either A, B, or C, based on the weight of the evidence available.

- Level A is applied when data are from multiple, randomized clinical trials;
- Level B indicates data are from a limited number of randomized trials; and
- Level C is applied when the recommendation is primarily based on expert consensus.

For patients with stage B heart failure, an ICD is reasonable in patients with asymptomatic ischemic cardiomyopathy who are at least 40 days post-MI, have an LVEF ≤30%, are on appropriate medical therapy, and have reasonable expectation of survival with a good functional status for > 1 year. (Class of recommendation: IIa; Level of Evidence: B)

For patients with stage C heart failure, ICD therapy is recommended for:
• Primary prevention of SCD in select patients with NIDCM or ischemic heart disease at least 40 days post-MI with LVEF ≤ 35%, and NYHA Class II or III symptoms for > 1 year. (Class of recommendation: I; Level of Evidence: A)

• Primary prevention of SCD to reduce total mortality in selected patients at least 40 days post-MI with LVEF < 30%, and NYHA class I symptoms while receiving guideline-directed medical therapy (GDMT), who have reasonable expectation of (Class of recommendation: I; Level of Evidence: B)

• An ICD is of uncertain benefit to prolong meaningful survival in patients with a high risk of non-sudden death such as frequent hospitalizations, advanced frailty, or comorbidities such as systemic malignancy or severe renal dysfunction. (Class of recommendation: IIb; Level of Evidence: B)

AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION/AMERICAN HEART ASSOCIATION

In 2011, ACCF/AHA guidelines were published on the management of patients with hypertrophic cardiomyopathy. These guidelines contained the following statements about the use of ICDs in patients with HCM:

• Class I Recommendations
  o The decision to place an ICD in patients with HCM should include application of individual clinical judgment, as well as a thorough discussion of the strength of evidence, benefits, and risks to allow the informed patient’s active participation in decision making. (Level of Evidence: C)
  o ICD placement is recommended for patients with HCM with prior documented cardiac arrest, ventricular fibrillation, or hemodynamically significant VT. (Level of Evidence: B)

• Class IIa Recommendations
  o It is reasonable to recommend an ICD for patients with HCM with:
    ▪ Sudden death presumably caused by HCM in 1 or more first-degree relatives. (Level of Evidence: C)
    ▪ A maximum LV wall thickness greater than or equal to 30 mm. (Level of Evidence: C)
    ▪ One or more recent, unexplained syncopal episodes. (Level of Evidence: C)
  o An ICD can be useful in select patients with NSVT [non-sustained VT] (particularly those <30 years of age) in the presence of other SCD risk factors or modifiers. (Level of Evidence: C)
  o An ICD can be useful in select patients with HCM with an abnormal blood pressure response with exercise in the presence of other SCD risk factors or modifiers. (Level of Evidence: C)

• Class IIb Recommendations
  o The usefulness of an ICD is uncertain in patients with HCM with isolated bursts of NSVT when in the absence of any other SCD risk factors or modifiers. (Level of Evidence: C)
  o The usefulness of an ICD is uncertain in patients with HCM with an abnormal blood pressure response with exercise when in the absence of any other SCD risk factors or
modifiers, particularly in the presence of significant outflow obstruction. (Level of Evidence: C)

- **Class III Recommendations: Harm**
  - ICD placement as a routine strategy in patients with HCM without an indication of increased risk is potentially harmful. (Level of Evidence: C)
  - ICD placement as a strategy to permit patients with HCM to participate in competitive athletics is potentially harmful. (Level of Evidence: C)
  - ICD placement in patients who have an identified HCM genotype in the absence of clinical manifestations of HCM is potentially harmful. (Level of Evidence: C)

**THE HEART FAILURE SOCIETY OF AMERICA/HEART RHYTHM SOCIETY/EUROPEAN HEART RHYTHM ASSOCIATION**

In 2009 the HFSA, HRS and EHRA published a guideline for the management of genetic cardiomyopathies that included specific mention of LMNA-related DCM:[96]

- In patients with cardiomyopathy and significant arrhythmia or known risk of arrhythmia an ICD may be considered before the left ventricular ejection fraction falls below 35%. (Level of Evidence = C)

The guideline states: “In this setting of lamin A/C cardiomyopathy requiring pacemaker placement, the use of an ICD rather than a pacemaker has been recommended. Patients with a dilated cardiomyopathy but with ejection fraction >30% to 35% may be considered for an ICD if the family history is positive for SCD or for patients with LMNA mutations.”

**PEDIATRIC AND CONGENITAL ELECTROPHYSIOLOGY SOCIETY (PACES)/ HEART RHYTHM SOCIETY (HRS)**

In 2014, PACES and HRS issued an expert consensus statement on the recognition and management of arrhythmias in adult congenital heart disease (CHD) which made the following recommendations on the use of ICD therapy in adults with CHD:[97]

- **Class I Recommendations:**
  - ICD therapy is indicated in adults with CHD who are survivors of cardiac arrest due to ventricular fibrillation or hemodynamically unstable ventricular tachycardia after evaluation to define the cause of the event and exclude any completely reversible etiology (Level of evidence: B).
  - ICD therapy is indicated in adults with CHD and spontaneous sustained ventricular tachycardia who have undergone hemodynamic and electrophysiologic evaluation (Level of evidence: B).
  - ICD therapy is indicated in adults with CHD and a systemic left ventricular ejection fraction <35%, biventricular physiology, and New York Heart Association (NYHA) class II or III symptoms (Level of evidence: B).

- **Class IIa Recommendations:**
  - ICD therapy is reasonable in selected adults with tetralogy of Fallot and multiple risk factors for sudden cardiac death, such as left ventricular systolic or diastolic dysfunction, nonsustained ventricular tachycardia, QRS duration>180 ms, extensive...
right ventricular scarring, or inducible sustained ventricular tachycardia at electrophysiologic study (Level of evidence: B).

- **Class IIb Recommendations:**
  - ICD therapy may be reasonable in adults with a single or systemic right ventricular ejection fraction <35%, particularly in the presence of additional risk factors such as complex ventricular arrhythmias, unexplained syncope, NYHA functional class II or III symptoms, QRS duration >140 ms, or severe systemic AV valve regurgitation (Level of evidence: C).
  - ICD therapy may be considered in adults with CHD and a systemic ventricular ejection fraction <35% in the absence of overt symptoms (NYHA class I) or other known risk factors (Level of evidence: C).
  - ICD therapy may be considered in adults with CHD and syncope of unknown origin with hemodynamically significant sustained ventricular tachycardia or fibrillation inducible at electrophysiologic study (Level of evidence: B).
  - ICD therapy may be considered for nonhospitalized adults with CHD awaiting heart transplantation (Level of evidence: C).
  - ICD therapy may be considered for adults with syncope and moderate or complex CHD in whom there is a high clinical suspicion of ventricular arrhythmia and in whom thorough invasive and noninvasive investigations have failed to define a cause (Level of evidence: C).

- **Class III Recommendations:**
  - All Class III recommendations listed in current ACC/AHA/HRS guidelines apply to adults with CHD (Level of evidence: C).
  - Adults with CHD and advanced pulmonary vascular disease (Eisenmenger syndrome) are generally not considered candidates for ICD therapy (Level of evidence: B).
  - Endocardial leads are generally avoided in adults with CHD and intracardiac shunts. Risk assessment regarding hemodynamic circumstances, concomitant anticoagulation, shunt closure prior to endocardial lead placement, or alternative approaches for lead access should be individualized (Level of Evidence: B).

HEART RHYTHM SOCIETY/EUROPEAN HEART RHYTHM ASSOCIATION/ASIA-PACIFIC HEART RHYTHM SOCIETY

In 2013, the Heart Rhythm Society (HRS), European Heart Rhythm Association (EHRA), and the Asia-Pacific Heart Rhythm Society (APHRS) issued a consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes, which included a number of recommendations related to ICD use in patients with long QT syndrome (LQTS), Brugada syndrome (BrS), catecholaminergic polymorphic ventricular tachycardia (CPVT), and short QT syndrome (SQTS).

**Long QT Syndrome**

- **Class I Recommendations**
  - ICD implantation is recommended for patients with a diagnosis of LQTS who are survivors of a cardiac arrest.

- **Class IIa Recommendations**
ICD implantation can be useful in patients with a diagnosis of LQTS who experience recurrent syncopal events while on beta-blocker therapy.

- **Class III Recommendations: Harm**
  - Except under special circumstances, ICD implantation is not indicated in asymptomatic LQTS patients who have not been tried on beta-blocker therapy.

**Brugada Syndrome**

- **Class I Recommendations:**
  - ICD implantation is recommended in patients with a diagnosis of BrS who:
    - Are survivors of a cardiac arrest and/or
    - Have documented spontaneous sustained VT with or without syncope.

- **Class IIa Recommendations:**
  - ICD implantation can be useful in patients with a spontaneous diagnostic type I ECG who have a history of syncope judged to be likely caused by ventricular arrhythmias.

- **Class IIb Recommendations:**
  - ICD implantation may be considered in patients with a diagnosis of BrS who develop VF during programmed electrical stimulation (inducible patients).

- **Class III Recommendations: Harm**
  - ICD implantation is not indicated in asymptomatic BrS patients with a drug-induced type I ECG and on the basis of a family history of SCD alone.

**Catecholaminergic Polymorphic Ventricular Tachycardia**

- **Class I Recommendations:**
  - ICD implantation is recommended for patients with a diagnosis of CPVT who experience cardiac arrest, recurrent syncope or polymorphic/bidirectional VT despite optimal medical management, and/or left cardiac sympathetic denervation.

- **Class III Recommendations: Harm**
  - ICD as a standalone therapy is not indicated in an asymptomatic patient with a diagnosis of CPVT.

**Short QT Syndrome**

- **Class I Recommendations:**
  - ICD implantation is recommended in symptomatic patients with a diagnosis of SQTS who:
    - Are survivors of cardiac arrest and/or
    - Have documented spontaneous VT with or without syncope.
• Class IIb Recommendations:
  o ICD implantation may be considered in asymptomatic patients with a diagnosis of SQTS and a family history of sudden cardiac death.

HEART RHYTHM SOCIETY/EUROPEAN HEART RHYTHM ASSOCIATION[99]

In a consensus report from the second consensus conference on Brugada syndrome, held in September 2003, HRS/EHRA addressed diagnostic criteria, risk stratification schemes, and device- and pharmacologic-based therapy for Brugada syndrome. This report was published in 2005 and makes the following recommendations for ICD implantation in Brugada syndrome:

• Symptomatic patients displaying the type 1 Brugada ECG (either spontaneously or after sodium channel blockade) who present with aborted sudden death should receive an ICD without additional need for electrophysiologic studies.
• Symptomatic patients displaying the type 1 Brugada ECG (either spontaneously or after sodium channel blockade) who present with syncope, seizure, or nocturnal agonal respiration should undergo ICD implantation after noncardiac causes of these symptoms have been ruled out.
• Asymptomatic patients displaying a type 1 Brugada ECG (either spontaneously or after sodium channel blockade) should undergo EPS if a family history of sudden cardiac death is suspected to be the result of Brugada syndrome. EPS is justified when the family history is negative for sudden cardiac death if the type 1 ECG occurs spontaneously. If inducible for ventricular arrhythmia, then the patient should receive an ICD.
• Asymptomatic patients who have no family history and who develop a type 1 ECG only after sodium channel blockade should be closely followed up.

SUMMARY

TRANSVENOUS IMPLANTABLE CARDIOVERTER DEFIBRILLATORS (ICDS)

ICDs in Patients with Prior Arrhythmogenic Events and Ischemic Cardiomyopathy

There is enough research to show that transvenous implantable cardioverter defibrillators (ICDs) can improve survival for certain patients that have had arrhythmogenic events and ischemic cardiomyopathy. A number of clinical guidelines based on research recommend these ICDs for patients meeting specific criteria. Therefore, the use of ICDs is considered medically necessary for patients that meet the policy criteria.

There is not enough research to show that transvenous implantable cardioverter defibrillators (ICDs) can improve health outcomes for patients with ischemic cardiomyopathy that do not meet the policy criteria. This includes people who have had a myocardial infarction (heart attack) in the past 40 days, people with a relatively high level of heart function. Therefore, the use of ICDs in ischemic cardiomyopathy patients that do not meet the policy criteria is considered investigational

ICDs for Nonischemic Dilated Cardiomyopathy (NIDCM)

There is enough research to show that transvenous implantable cardioverter defibrillators (ICDs) can improve survival for certain patients with nonischemic dilated cardiomyopathy (NIDCM). Also, clinical guidelines based on research recommend ICD use for some
patients with NIDCM. Therefore, ICD implantation among patients with NIDCM that meet the policy criteria may be considered medically necessary.

There is not enough research to show that transvenous implantable cardioverter defibrillators (ICDs) can improve survival for patients with nonischemic dilated cardiomyopathy (NIDCM) that do not meet policy criteria, including patients that have a treatable cause for their NIDCM. Therefore, ICD use in these patients is considered investigational.

**Hypertrophic Cardiomyopathy**

There is enough research to show that implantable cardioverter defibrillators (ICDs) can improve survival in some patients with hypertrophic cardiomyopathy (HCM). There are also clinical guidelines based on research that recommend ICDs for certain patients with HCM. Therefore, ICD implantation among patients with HCM that meet policy criteria is considered medically necessary.

There is not enough research to show that implantable cardioverter defibrillators (ICDs) can improve health outcomes for people with hypertrophic cardiomyopathy (HCM) that do not have major risk factors for sudden cardiac death. Therefore, ICD use is considered investigational for patients with HCM that do not meet the policy criteria.

**LMNA-related Cardiac Arrhythmia or Cardiomyopathy**

There is enough research to show that implantable cardioverter defibrillators (ICDs) can improve health outcomes compared with pacemakers or medical treatment in patients with LMNA-related cardiac arrhythmias or cardiomyopathy. Because of the high risk for sudden cardiac death, ICDs may be considered medically necessary in patients with LMNA gene mutations that have cardiomyopathy or symptomatic arrhythmias.

There is not enough research to show that implantable cardioverter defibrillators (ICDs) can improve health outcomes in patients with LMNA gene mutations that do not have cardiomyopathy or symptomatic arrhythmias, and therefore, the use of ICDs among these patients is considered investigational.

**ICDs for Patients with Cardiac Ion Channelopathies**

There is enough research to show that implantable cardioverter defibrillators (ICDs) can reduce sudden cardiac death in certain patients with long QT syndrome, short QT syndrome, Brugada syndrome, or catecholaminergic polymorphic ventricular tachycardia. Clinical guidelines based on research also recommend ICD therapy in patients with these conditions that have other cardiac risk factors. Therefore, ICDs are considered medically necessary in select patients with cardiac ion channelopathies.

There is not enough research to show that implantable cardioverter defibrillators (ICDs) can improve health outcomes in patients with cardiac ion channelopathies that do not have certain cardiac risk factors, and therefore, the use of ICDs among these patients is considered investigational.

**ICDs for Secondary Prevention**

October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
There is enough research to show that implantable cardioverter defibrillators (ICDs) can be effective for *secondary* prevention in patients that have had life-threatening ventricular arrhythmia not caused by a reversible condition. Therefore, ICD use may be considered medically necessary for secondary prevention in these patients.

There is not enough research to show that implantable cardioverter defibrillators (ICDs) can improve health outcomes in patients that have had arrhythmia events caused by reversible conditions, and ICD use is therefore considered investigational for these patients.

**SUBCUTANEOUS ICDs**

There is enough research to show that subcutaneous implantable cardioverter defibrillators (S-ICDs) can improve health outcomes in patients that may benefit from ICD use, but for whom transvenous ICD placement is not recommended for medical reasons. Therefore, the use of S-ICDs is considered medically necessary for the same indications as transvenous ICDs.

There is not enough research to show that subcutaneous implantable cardioverter defibrillators (S-ICDs) use can improve health outcomes compared with transvenous ICD use. Therefore, S-ICD placement is considered investigational for patients that do not meet policy criteria for ICD placement and patients that are candidates for transvenous ICD placement.

**ICDS WITH ST SEGMENT MONITORING CAPABILITY**

There is not enough research to show that implantable cardioverter defibrillators (ICDs) with ST segment monitoring capability can improve health outcomes compared to traditional transvenous ICDs. Also, there are no ICDS with segment monitoring capabilities that have received U.S. Food and Drug Administration (FDA) approval for marketing in the U.S. Therefore, the use of implantable cardioverter defibrillators with ST segment monitoring capability is considered investigational for all indications.

**REFERENCES**


5. Gracieux, J, Sanders, GD, Pokorney, SD, Lopes, RD, Thomas, K, Al-Khatib, SM. Incidence and predictors of appropriate therapies delivered by the implantable


51. Chen, S, Ling, Z, Kiuchi, MG, Yin, Y, Krucoff, MW. The efficacy and safety of cardiac resynchronization therapy combined with implantable cardioverter defibrillator for heart


97. Khairy, P, Van Hare, GF, Balaji, S, et al. PACES/HRS expert consensus statement on the recognition and management of arrhythmias in adult congenital heart disease: developed in partnership between the Pediatric and Congenital Electrophysiology Society (PACES) and the Heart Rhythm Society (HRS). Endorsed by the governing bodies of PACES, HRS, the American College of Cardiology (ACC), the American Heart Association (AHA), the European Heart Rhythm Association (EHRA), the Canadian Heart Rhythm Society (CHR), and the International Society for Adult Congenital Heart Disease (ISACHD). *The Canadian journal of cardiology.* 2014 Oct;30(10):e1-e63. PMID: 25262867


100. BlueCross BlueShield Association Medical Policy Reference Manual "Implantable Cardioverter Defibrillator (ICD)." Policy No. 7.01.44

**CODES**

<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>33216</td>
<td>Insertion of a single transvenous electrode, permanent pacemaker or cardioverter-defibrillator</td>
</tr>
<tr>
<td></td>
<td>33217</td>
<td>Insertion of 2 transvenous electrodes, permanent pacemaker or cardioverter-defibrillator</td>
</tr>
<tr>
<td></td>
<td>33218</td>
<td>Repair of single transvenous electrode for a single chamber, permanent pacemaker or single chamber pacing cardioverter-defibrillator</td>
</tr>
<tr>
<td></td>
<td>33220</td>
<td>Repair of 2 transvenous electrodes for a dual chamber permanent pacemaker or dual chamber pacing cardioverter-defibrillator</td>
</tr>
<tr>
<td></td>
<td>33223</td>
<td>Relocation of skin pocket for cardioverter-defibrillator</td>
</tr>
<tr>
<td></td>
<td>33230</td>
<td>Insertion of pacing cardioverter-defibrillator pulse generator only; with existing dual leads</td>
</tr>
</tbody>
</table>

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>33231</td>
<td>Insertion of pacing cardioverter-defibrillator pulse generator only; with existing multiple leads</td>
</tr>
<tr>
<td></td>
<td>33240</td>
<td>Insertion of single or dual chamber pacing cardioverter-defibrillator pulse generator</td>
</tr>
<tr>
<td></td>
<td>33241</td>
<td>Removal of implantable defibrillator pulse generator only</td>
</tr>
<tr>
<td></td>
<td>33243</td>
<td>Removal of single or dual chamber implantable defibrillator electrode(s); by thoracotomy</td>
</tr>
<tr>
<td></td>
<td>33244</td>
<td>;by transvenous extraction</td>
</tr>
<tr>
<td></td>
<td>33249</td>
<td>Insertion or repositioning of electrode lead(s) for single or dual chamber pacing cardioverter-defibrillator and insertion of pulse generator</td>
</tr>
<tr>
<td></td>
<td>33262</td>
<td>Removal of implantable defibrillator pulse generator with replacement of implantable defibrillator pulse generator; single lead system; dual lead system</td>
</tr>
<tr>
<td></td>
<td>33263</td>
<td>;multiple lead system</td>
</tr>
<tr>
<td></td>
<td>33264</td>
<td></td>
</tr>
<tr>
<td></td>
<td>33270</td>
<td>Insertion or replacement of permanent subcutaneous implantable defibrillator system, with subcutaneous electrode, including defibrillation threshold evaluation, induction of arrhythmia, evaluation of sensing for arrhythmia termination, and programming or reprogramming of sensing or therapeutic parameters, when performed</td>
</tr>
<tr>
<td></td>
<td>33271</td>
<td>Insertion of subcutaneous implantable defibrillator electrode</td>
</tr>
<tr>
<td></td>
<td>33272</td>
<td>Removal of subcutaneous implantable defibrillator electrode</td>
</tr>
<tr>
<td></td>
<td>33273</td>
<td>Repositioning of previously implanted subcutaneous implantable defibrillator electrode</td>
</tr>
<tr>
<td></td>
<td>93260</td>
<td>Programming device evaluation (in person) with iterative adjustment of the implantable device to test the function of the device and select optimal permanent programmed values with analysis, review and report by a physician or other qualified health care professional; implantable subcutaneous lead defibrillator system</td>
</tr>
<tr>
<td></td>
<td>93261</td>
<td>Interrogation device evaluation (in person) with analysis, review and report by a physician or other qualified health care professional, includes connection, recording and disconnection per patient encounter; implantable subcutaneous lead defibrillator system</td>
</tr>
<tr>
<td></td>
<td>93644</td>
<td>Electrophysiologic evaluation of subcutaneous implantable defibrillator (includes defibrillation threshold evaluation, induction of arrhythmia, evaluation of sensing for arrhythmia termination, and programming or reprogramming of sensing or therapeutic parameters)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCPCS</td>
<td>C1721</td>
<td>Cardioverter-defibrillator, dual chamber (implantable)</td>
</tr>
<tr>
<td></td>
<td>C1722</td>
<td>Cardioverter-defibrillator, single chamber (implantable)</td>
</tr>
<tr>
<td></td>
<td>C1882</td>
<td>Cardioverter-defibrillator, other than single or dual chamber (implantable)</td>
</tr>
</tbody>
</table>

Date of Origin: April 2012
Medical Policy Manual

Topic: Mechanical Embolectomy for Treatment of Acute Stroke  
Date of Origin: February 6, 2007

Section: Surgery  
Last Reviewed Date: November 2016

Policy No: 158  
Effective Date: December 1, 2016

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Mechanical embolectomy devices are being studied as an alternative, or adjunct to intravenous tPA therapy, and, among patients contraindicated for tPA, as a primary therapy for the treatment of ischemic stroke.

Background

The majority of strokes are caused by thrombotic or embolic occlusion, and these frequently present as acute neurologic emergencies. Standard treatment options for acute stroke include thrombolysis with intravenous tissue plasminogen activator (tPA) if patients present early (within 4.5 hours of stroke symptom onset), and supportive medical care if patients present late or do not otherwise meet criteria for thrombolysis. Endovascular interventions, including mechanical embolectomy/thrombectomy, are another method of acute stroke treatment. Mechanical embolectomy/thrombectomy is an endovascular technique to physically remove or disrupt an intracranial occlusion with a device inserted via percutaneous catheter to the site of the occlusion.

Mechanical embolectomy devices, also known as thrombectomy or neurothrombectomy devices, are being studied as an alternative, or adjunct to intravenous tPA therapy and, among patients contraindicated for tPA, as a primary therapy for the treatment of ischemic stroke. Mechanical
Embolectomy devices used to extract clots in ischemic stroke can be categorized into one of the following types: clot retriever, aspiration or suction device, snare, ultrasound technology, or laser.\textsuperscript{[1]}

**Regulatory Status**

The following devices have received 510(k) clearance from the US Food and Drug Administration (FDA) for mechanical embolectomy in acute stroke. Marketing clearance via the 510(k) process does not require data regarding clinical efficacy.

In August 2004, the Merci Retriever\textsuperscript{®} (Concentric Medical) was cleared by the FDA. With the Merci\textsuperscript{®} device, a microcatheter is passed through the thrombus from a larger, percutaneous catheter positioned proximal to the occlusion. A helical snare is deployed, and the catheter and clot are withdrawn together.

A modified Merci Retriever, also manufactured by Concentric Medical, Inc., received 510(k) clearance from the FDA in May 2006. The clearance notes that the Modified Merci Retriever is intended to restore blood flow in the neurovasculature by removing thrombus in patients experiencing ischemic stroke. Patients who are ineligible for intravenous tPA, or who fail intravenous tPA therapy, are candidates for treatment. The device also has clearance for retrieval of foreign bodies misplaced during interventional radiological procedures in the neuro-, peripheral, and coronary vasculature.

In December 2007, the Penumbra System\textsuperscript{®} (Penumbra Inc.) was cleared through the 510(k) process. With the Penumbra device, an opening at the tip of a percutaneous catheter utilizes suction to extract the clot. The Penumbra System is intended for use in the revascularization of patients with acute ischemic stroke secondary to intracranial large vessel occlusive disease (in the internal carotid, middle cerebral – first (M1) and second (M2) segments, basilar, and vertebral arteries) within 8 hours of symptom onset.

In March 2012, the Solitaire\textsuperscript{™} FR device was cleared for marketing by the FDA through the 510(k) process. The FDA determined that this device was substantially equivalent to the Merci Retriever device, based on a randomized controlled trial (RCT) of 113 patients submitted to the FDA comparing the Merci and Solitaire devices. Indications for the device are patients with ischemic stroke due to large intracranial vessel occlusion who are ineligible for intravenous tPA, or who fail intravenous tPA.

The Trevo\textsuperscript{®} Pro Retriever\textsuperscript{™} device (Stryker\textsuperscript{®} Neurovascular) along with later versions, the Modified Trevo\textsuperscript{®} Retriever and the Trevo\textsuperscript{®} XP ProVue Retriever, have been cleared for marketing by the FDA through the 510(k) process. The FDA determined that this device was substantially equivalent to the Merci Retriever device, based on an RCT of 178 patients from 27 centers in the U.S. and Europe that compared the Trevo device with the Merci device. Indications for the device are patients with acute ischemic stroke due to large intracranial vessel occlusion who are ineligible for or fail intravenous tPA.

**MEDICAL POLICY CRITERIA**

I. Use of endovascular mechanical embolectomy with a device that is approved by the U.S. Food and Drug Administration for the treatment of acute ischemic stroke may be considered medically necessary for the treatment of acute ischemic stroke when clinical records document all of the following criteria (I. A-E) are met:

A. Arterial occlusion is demonstrated; AND
B. Endovascular mechanical embolectomy can be received within an estimated 12 hours of symptom onset; AND

C. Evidence of clinically significant neurological deficit (see Policy Guidelines); AND

D. Salvageable brain tissue is present in the affected vascular territory; AND

E. There is no evidence of intracranial hemorrhage on CT or MRI.

II. Mechanical Embolectomy is considered **not medically necessary** for the treatment of acute stroke when the above criteria are not met.

**POLICY GUIDELINES**

**Stroke Assessment Scales**

Stroke assessment scales\(^2\) may be used to measure neurological deficit, which may include, but are not limited to the following:

- National Institutes of Health Stroke Scale (NIHSS)
- Face Arm Speech Test (FAST)
- Cincinnati Prehospital Stroke Scale (CPSS)
- Los Angeles Prehospital Stroke Screen (LAPSS)
- Recognition of Stoke in the Emergency Room (ROSIER) scale

**SCIENTIFIC EVIDENCE\(^3,4\)**

The principal outcomes associated with treatment of acute ischemic stroke are clinically relevant improvements in short and long-term neurological outcomes, as measured by a validated instrument (such as the National Institutes of Health Stroke Scale [NIHSS]). Measures of disability, such as those provided by the Rankin Scale or modified Rankin Scale (mRS), may also be reported. Mechanical embolectomy devices are proposed as an alternative or adjunct to tPA or as a primary therapy for patients in whom tPA is contraindicated.

Assessment of the safety and efficacy for mechanical embolectomy involves a determination of whether the intervention improves health outcomes compared to standard treatment. The optimal study design for this purpose is a randomized controlled trial (RCT) that includes clinically relevant measures of health outcomes. Randomization controls for baseline differences between groups which may impact findings. In addition, a controlled study design reduces the influence of confounding factors on observed results.

**Literature Appraisal**

The review of evidence below focuses on systematic reviews and RCTs.

**Systematic Reviews**
In 2015, Badhiwala et al reported results of a meta-analysis of RCTs evaluating mechanical embolectomy after acute ischemic stroke.[5] Eligible studies were RCTs comparing endovascular therapy with standard care, including the use of intravenous (IV) plasminogen activator (tPA), in adult participants with acute stroke. Eight trials were included (Ciccone et al,[6] Kidwell et al,[7] Broderick et al,[8] Berkhemer et al,[9] Goyal et al,[10] Campbell et al,[11] Saver et al,[12] Jovin et al[13]), with a total of 2423 patients. Studies were assessed as having low risk of bias overall with the Cochrane Collaboration’s tool. In a meta-analysis, the use of endovascular intervention lead to proportional treatment benefit across modified Rankin Scale (mRS) scores (odds ratio [OR], 1.56; 95% confidence interval [CI], 1.14 to 2.13; p=0.005). Patients treated with endovascular intervention were more likely than standard care patients to have functional independence at 90 days (44.6% for endovascular treatment [95% CI, 36.6% to 52.8%]; 31.8% for standard treatment [95% CI, 24.6% to 40.0%]), with an associated absolute risk difference of 12.0% (95% CI, 3.8% to 20.3%; OR=1.71; 95% CI, 1.18 to 2.49; p=0.005). However, there was significant heterogeneity ($I^2=75.4\%$) in the analysis of functional improvement outcomes. The authors conducted a number of sensitivity analyses around predictors of functional outcomes, and found that the following factors were associated with functional outcomes:

- Use of angiographic imaging confirming proximal arterial occlusion (OR=2.24; 95% CI, 1.72 to 2.9; p<0.001 for interaction).
- Use of IV tPA and endovascular therapy (OR=2.07; 95% CI, 1.46 to 2.92; p=0.018 for interaction).
- Use of stent retriever for mechanical thrombectomy (OR=2.39; 95% CI, 1.88 to 3.04; p<0.001 for interaction).

There were no significant differences between endovascular intervention group and standard care group patients in rates of symptomatic intracranial hemorrhage or death at 90 days. In a meta-analysis including the same 8 trials included in the Badhiwala study, Chen et al[14] reported a similar OR for 90 day functional independence as Badhiwala.

In 2015, Prabhakaran et al. published results from a systematic review of studies evaluating thrombolysis and mechanical thrombectomy in acute stroke.[15] The authors included 68 articles with a total of 108,082 patients, including RCTs, observational studies, guideline statements, and review articles. Six RCTs comparing endovascular therapy with standard management were included. Although pooled results of the trial results are not presented, the authors do report that, across the available RCTs, rates of substantial reperfusion (thrombolysis in cerebral infarction [TICI] score 2b or 3) were positively associated with the proportion of patients with a good clinical outcome (mRS 0-2) at 90 days, while time to reperfusion was negatively associated with the proportion of patients with a good clinical outcome at 90 days.

A number of systematic reviews have been published which have incorporated some of the RCTs comparing endovascular therapies and standard therapy.

In 2014, Fargen et al[16] published a meta-analysis of prospective RCTs evaluating endovascular therapies for acute stroke, which included 4 previously identified RCTs (Broderick et al.,[17] Ciccone et al.,[18] Kidwell et al.[7] and Berkhemer et al.[19]) but not the more recently published RCTs by Campbell et al.,[11] Goyal et al.,[20] Saver et al.,[21] and Jovin et al.[22] In a pooled analysis of the subgroup of patients with large vessel occlusion, patients randomized to endovascular therapy were more likely to have a mRS score of 0-2 at 90 days than patients randomized to standard of care (38.3% vs 25.8%; OR 1.67, 95% CI 1.29 to 2.16; P=0.0001).
In 2015, Kappelhof et al. published results of a systematic review and meta-analysis of studies comparing outcomes for mechanical therapy and intra-arterial thrombolysis for acute ischemic stroke due to intracranial internal carotid artery (ICA) occlusion, with separate results reported for intracranial and extracranial occlusions.\[23\] The overall review included 32 studies, 6 of which (N=95) reported outcomes for intracranial occlusion treated by intraarterial thrombolysis and 8 of which (N=115) reported outcomes for intracranial occlusion treated by mechanical thrombectomy. None of the recently-published RCTs of endovascular therapy were included in the review, which included studies published through July 2013 and specifically reported outcomes for ICA occlusions. In the subset of studies reporting on intracranial occlusions, overall outcome rates were 55% recanalization, 12% symptomatic intracranial hemorrhage, 34% mortality, and 25% favorable outcome. Compared with intra-arterial fibrinolysis, mechanical thrombectomy was associated with a higher recanalization rate (69% vs 38%; P<0.001), a higher rate of favorable outcomes (34% vs 14%; P<0.001), with nonsignificantly different rates of death (29% vs 40%; P=0.085) and symptomatic intracranial hemorrhage (12.2% vs 11.7%; P=0.085).

In 2014, a Blue Cross and Blue Shield Association (BCBSA) Technology Evaluation Center (TEC) Assessment evaluated endovascular therapy for acute ischemic stroke in adults.\[24\] The Assessment identified 5 multicenter randomized controlled trials (RCTs) meeting selection criteria, 3 of which compared endovascular treatment with standard stroke care (Broderick et al.\[17\], Ciccone et al.\[18\], and Kidwell et al.\[7\] [summarized in more detail below]) and 2 of which compared newer and older endovascular treatments (Saver et al.\[25\] and Nogueira et al.\[26\]). The TEC Assessment made the following overall observations and conclusions: “The 3 RCTs published in early 2013 concluded that endovascular treatment is no more effective than IV tPA in reducing disability among patients with acute ischemic stroke treated 3 to 8 hours after symptom onset. Although specific aspects of these trials have been criticized, we identified no RCTs that demonstrate endovascular treatments produce better health outcomes. Use of newer FDA-cleared endovascular devices was allowed. A major limitation in generalizing from these studies is that the number of patients treated with each of these newer devices was small. Therefore, as noted by critics of the trials, evidence on the newest devices may not substantively impact the overall outcomes. If the newer devices are more effective than the older ones, the results might be dominated by the performance of the less effective, older device(s).”

In 2015, BCBSA issued a special report to update the literature of the previous 2014 TEC Assessment. The updated Assessment focused on 4 RCTs published from 2014-2015 comparing endovascular mechanical embolectomy with medical therapy. The Assessment concluded that the use of endovascular treatment with mechanical embolectomy in adults with radiologically confirmed large-vessel, anterior circulation acute ischemic stroke meets the BCBSA Technology Evaluation Center (TEC) criteria. The specific RCTs are described in more detail below.

In a 2013 systematic review and meta-analysis, Singh and others consolidated the evidence from 5 RCTs for the use of endovascular therapy (ET) in patients with acute ischemic stroke (N=1197).\[27\] One of the reviewed studies did not include mechanical embolectomy devices in the trial.\[28\] In addition, a trial included in the review defined endovascular therapy as intraarterial thrombolysis with recombinant tissue plasminogen activator [tPA], mechanical clot disruption or retrieval, or a combination of these approaches.\[18\] Seven hundred eleven patients received ET, and 486 received intravenous (IV) tPA. There was no significant improvement in any of the outcomes in patients receiving ET compared with those receiving IV tPA. On subgroup analysis, ET was found to have better outcomes in patients with severe stroke (National Institutes of Health Stroke Scale score ≥20),
showing a dose-response gradient and improving excellent, good, and fair outcomes by an additional 4%, 7%, and 13%, respectively, compared with IV thrombolysis. Authors concluded that ET was not superior to IV thrombolysis for acute ischemic strokes (level B recommendation).

Several systematic reviews were published prior to the publication of several recent RCTs and as a result will not be summarized. These systematic reviews include Mokin et al.[29] (2012), Almekhlafi et al.[30] (2012), Baker et al.[31] (2011), and Stead et al.[32] (2008).

**Randomized Controlled Trials**

From 2012 to 2015, results from 8 large RCTs comparing endovascular therapies with standard of care for acute ischemic stroke were published. Five prospective, open-label, blinded end point (PROBE design) RCTs comparing endovascular therapy with standard care in the treatment of acute stroke were published from 2014 to 2015 and are the focus of this section. These most recent studies are of particular importance as they are well-designed, primarily assessed newer devices and addressed the methodological limitations noted in previous RCTs.

**REVASCAT Trial**

In 2015, Jovin et al., reported results of the REVASCAT trial, which compared endovascular therapy with the Solitaire stent-retriever device with medical therapy, including IV tPA when indicated, within 8 hours of stroke onset among 206 patients.[22] Eligible patients had an occlusion within the proximal anterior circulation which could be treated within 8 hours of stroke onset and a prestroke mRS score of 0-1, and a baseline National Institutes of Health Stroke Scale (NIHSS) score of at least 6 points (NIHSS score range 0-42; higher scores associated with greater deficit). Intravenous tPA was administered before randomization. Patients were excluded if they had imaging-based evidence of a large ischemic core, indicated by an Alberta Stroke Program Early Computed Tomography Score of less than 7 on non-contrast CT imaging or a score of less than 6 on diffusion-weighted MRI. The trial was halted early for loss of equipoise given the results of the EXTEND-IA, ESCAPE, and MR CLEAN trials (described below) after the first planned interim analysis after the first 25% of patients (n=174) reached 90-day of follow up.

One hundred and three patients were randomized to mechanical embolectomy, of whom 98 successfully underwent thrombectomy. Rates of tPA use between the groups did not differ significantly (68.0% in the mechanical embolectomy group and 77.7% in the control group). For the study’s primary outcome, the odds ratio (OR) for improvement in the distribution of the mRS score was 1.7 (95% confidence interval [CI] 1.05 to 2.8), favoring mechanical embolectomy. A greater proportion of patients in the mechanical embolectomy group were functionally independent (mRS score 0-2; 43.7% vs 28.2% in the control group; absolute risk difference 15.5%; adjusted OR 2.1, 95% CI 1.1 to 4.0). There were no significant differences between the mechanical embolectomy and control groups in 90-day mortality (18.4% vs 15.5%; P=0.60) or 90-day rates of symptomatic intracranial hemorrhage (1.9% in each group; P=1.00).

**EXTEND-IA Trial**

In 2015, Campbell et al., reported results of the EXTEND-IA trial comparing endovascular therapy with tPA alone.[11] This trial enrolled patients with ischemic stroke who were receiving IV tPA within 4.5 hours after stroke onset. Eligible patients had an occlusion of the intracranial anterior (ICA) or M1 or M2 segments of the middle cerebral artery (MCA) on CTA, were able to receive
endovascular therapy within 6 hours of stroke onset, and were functionally independent prior to the stroke. Patients were evaluated prior to enrollment with computed tomography (CT) perfusion imaging, and were required to have evidence of salvageable brain tissue and an ischemic core with a volume of less than 70 mL. CT perfusion imaging was analyzed with an operator-independent post-processing software. Enrollment was planned for 100 patients. The trial’s data safety and monitoring board reviewed data for the first 70 enrolled patients after the results of the MR CLEAN trial were published and stopped EXTEND-IA for efficacy based on prespecified criteria. The first 70 patients were randomized to either IV tPA plus endovascular therapy with the Solitaire FR retrievable stent (n=35) or no further therapy (IV tPA only; n=35). The study used 2 co-primary end points: reperfusion (measured as the percentage reduction in perfusion-lesion volume between the initial imaging and imaging at 24 hours) and early neurologic improvement (defined as a reduction of ≥ 8 points on the NIHSS or a score of 0 or 1 at day 3).

The demographics of the randomized groups were similar at baseline. About 25% of clinically eligible patients were excluded on the basis of perfusion imaging criteria. In the endovascular group, 8 (22.9%) of 35 patients did not undergo mechanical embolectomy, most commonly because most of the thrombus was lysed before angiography (n=4). Endovascular therapy subjects had increased reperfusion at 24 hours, with a median reperfusion of 100% (percentage reduction in perfusion-lesion volume), compared with 37% for the tPA-only group (adjusted OR=4.7; 95% CI, 2.5 to 9.0; p<0.001). Of the endovascular therapy subjects, 28 (80%) of 35 had early neurologic improvement compared with 13 (37%) of 35 of the tPA-only subjects (adjusted OR=6.0; 95% CI, 2.0 to 18.0; p=0.002). Rates of reperfusion of at least 90% at 24 hours without symptomatic intracerebral hemorrhage were higher in endovascular therapy patients (89% vs 34%; adjusted OR=27.0; 95% CI, 5.5 to 135.0; p<0.001). Safety outcomes, including death, symptomatic intracerebral hemorrhage, and parenchymal hematoma, did not differ significantly between groups.

**ESCAPE Trial**

Also in 2015, Goyal et al., reported results of the ESCAPE trial that compared endovascular therapy with guideline-based stroke care, including IV tPA if indicated.[20] Patients with acute stroke were eligible if they presented within 12 hours of stroke onset, had a proximal intracranial occlusion in the anterior circulation, and had noncontrast CT or CTA with the following findings: (1) small infarct core; (2) proximal artery occlusion, defined by occlusion of the MCA trunk and its immediate branches, with or without intracranial occlusion of the ICA; and (3) moderate-to-good collateral circulation, as defined as filling of 50% or more of the MCA pial artery circulation on CTA. A small infarct core was defined as a score of 6 to 10 on the Alberta Stroke Program Early Computed Tomography Score (ASPECTS), which is a 10-point scoring system designed to quantify the extent of ischemic changes in the MCA territory. Patients received IV tPA if they met local guidelines. Patients were randomized to endovascular treatment (n=165), which could include any FDA-approved stent retriever or aspiration device, balloon angioplasty, guidewire manipulation, and/or IA tPA, or guideline-based stroke care (n=150). Use of retrievable stents was recommended. Enrollment was planned for 316 subjects. The trial was stopped early on the advice of its data safety monitoring board, after an unplanned interim analysis following publication of MR CLEAN trial results, because ESCAPE’s prespecified efficacy boundary had been crossed.

Of the 165 patients randomized to the intervention group, 151 (91.5%) underwent endovascular therapy, most commonly with a retrievable stent (130/151 [86.1%] of those who underwent an endovascular procedure), most often with the Solitaire stent (100/130 [77.0%] of those who received a retrievable stent). In the intervention group, 120 (72.7%) also received IV tPA. Of the 150 control
group subjects, 118 (78.6%) received IV tPA. The study’s primary end point was the 90-day mRS score. Compared to the control group, the relative odds of improving 1 point on the mRS was 2.6 (95% CI, 1.7 to 3.8) in the endovascular treatment group. Endovascular treatment group subjects compared with control group subject also had lower 90-day mRS scores (median, 2 vs. 4, respectively; p<0.001) and were more likely to have 90-day mRS scores of 0 to 2 (53% vs 29.3%; rate ratio [RR], 1.8; 95% CI, 1.4 to 2.4; p<0.001). Ninety-day mortality was 10.4% among endovascular treatment group subjects and 19.0% in control group subjects (RR=0.5; 95% CI, 0.3 to 1.0; p=0.04).

**SWIFT-PRIME Trial**

In 2015, Saver et al., reported results of the SWIFT-PRIME trial comparing IV tPA followed by mechanical embolectomy using a stent retriever device with IV tPA alone in patients presenting with acute ischemic stroke.31 Eligible patients had moderate-to-severe neurologic deficits, imaging-confirmed occlusion of the intracranial ICA and/or the first segment of the MCA, were receiving or had received IV tPA, and were able to undergo endovascular treatment within 6 hours of symptom onset. In addition, eligible patients were required to have ischemic penumbral imaging analysis showing a small-to-moderate core infarct. For the first 71 patients enrolled, the infarct core size was defined based on CT perfusion imaging analyzed with an operator-independent postprocessing software; for the remainder of the study, infarct core size could be determined by CT perfusion imaging or noncontrast CT with a small-to-moderate core infarct based on ASPECTS score. Patients were randomized to mechanical embolectomy with the Solitaire 2 or the Solitaire FR device (n=98) or to ongoing IV tPA (n=98). Enrollment was planned for a maximum of 833 subjects, but stopped at 196 subjects after an interim analysis, following publication of the results of the MR CLEAN and ESCAPE trials, showed that results met SWIFT-PRIME’s prespecified efficacy criteria.

In the intervention group, a stent retriever was successfully deployed in 87 patients (89%). At 90 days, 60% of endovascular therapy group patients were functionally independent (mRS score, 0-2) compared with 35% of control subjects (absolute risk reduction, 25%; OR=1.70; 95% CI, 1.23 to 2.33; p<0.001). Endovascular therapy group patients compared with controls were more likely to have successful (≥90%) reperfusion at 27 hours (83% vs 40%, respectively; OR=2.05; 95% CI, 1.45 to 2.91; p<0.001). Rates of death and serious adverse events did not differ significantly between groups.

**MR CLEAN Trial**

In 2014, Berkhermer et al., reported initial results of the MR CLEAN trial (Multicenter Randomized Clinical trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands), an open-label, blinded end-point RCT with 500 subjects conducted at 16 centers in the Netherlands.[19] Eligible patients had acute ischemic stroke caused by an intracranial occlusion of the distal intracranial carotid artery, middle cerebral artery (M1 or M2), or anterior cerebral artery (A1 or A2), and a score of 2 or higher on the National Institutes of Health Stroke Scale (NIHSS). Initiation of intra-arterial treatment had to be possible within 6 hours of stroke onset. Patients were randomly assigned to standard stroke treatment (n=267 [53.4%]) or intra-arterial treatment (n=233 [46.6%]). Most patients in both groups (87.1% in the intervention group and 90.6% in the control group) received IV alteplase, at a median of 85 and 87 minutes after stroke onset, respectively. Patients in the intra-arterial group underwent arterial catheterization with a microcatheter to the level of the occlusion. Specific treatment options included delivery of a thrombolytic agent, mechanical thrombectomy, or both, at the discretion of the local interventionist. Intra-arterial thrombolytic...
agents were either alteplase or urokinase. Mechanical treatment could involve thrombus retraction, aspiration, wire disruption, or use of a retrievable stent. Analysis was intention-to-treat. One control group patient received intra-arterial treatment, and 17 patients (7.3%) in the intervention group did not receive intra-arterial therapy, most commonly (n=8) due to clinical improvement before the start of the intervention. Among the 233 patients randomize to intra-arterial therapy, 195 (83.7%) received mechanical therapies, with retrievable stents used in 190 patients (81.5%) and other devices in 5 patients (2.1%). Twenty-four patients (10.3%) received additional intra-arterial thrombolytic agents.

For the study’s primary outcome (mRS score at 90 days), the median score was 3 (interquartile range [IQR], 2-5) among intervention subjects, compared with a median score of 4 (IQR, 3-5) among control subjects, with an unadjusted common odds ratio (OR) of 1.66 (95% confidence interval [CI], 1.21 to 2.28; favors intervention). Twenty-seven (11.6%) intervention subjects had a mRS score of 0 or 1 at 90 days, compared with 16 (6.0%) control subjects (unadjusted OR=2.06; 95% CI, 1.08 to 3.92). Follow-up computed tomography (CT) angiography was available for 187 control subjects, of whom 141 had no intracranial occlusion (75.4%), compared with 68/207 (32.9%) of control subjects with follow-up CT angiography available (unadjusted OR=6.27; 95% CI, 4.03 to 9.74). The thirty-day mortality rate was 18.9% in the intervention group, compared with 18.4% in the control group (p=NS). Rates of serious adverse events (AEs) during the 90-day follow-up period did not differ significantly between groups (p=0.31). Symptomatic intracerebral hemorrhage occurred in 7.7% of intervention subjects compared with 6.4% of control subjects, which was not a significant difference. However, intervention subjects were more likely to demonstrate a new ischemic stroke in different vascular territory (5.6% vs 0.4%; p<0.001).

**MR RESCUE Trial**

Kidwell and colleagues reported on the MR RESCUE (Mechanical Retrieval and Recanalization of Stroke Clots Using Embolectomy) trial in 2013.[7] MR RESCUE was a randomized, controlled, open-label, blinded outcome trial of 118 patients from 22 North American sites. All patients had large vessel, anterior circulation ischemic strokes and were stratified by penumbral pattern as determined by pretreatment computed tomography (CT) or magnetic resonance imaging (MRI) of the brain. Patients were randomly assigned to standard stroke treatment (n=54) or mechanical embolectomy (n=64) using the Merci Retriever or Penumbra System within 8 hours after presentation of symptoms. Eight patients in the embolectomy group also received tissue plasminogen activator (tPA). The primary hypothesis of the study was that patients with favorable penumbral patterns (at-risk area of viable ischemic cerebral tissue of 70% or less and a small, 90 ml or less, area of predicted core infarct) would benefit more from mechanical embolectomy than patients with nonpenumbral patterns (large infarct area and small or absent penumbra [viable ischemic cerebral tissue]) as determined by the 90-day mRS, ranging from a score of 0 (no symptoms) to 6 (dead). In the embolectomy group, 67% achieved revascularization but this was not superior to standard care. Mean mRS scores were the same (3.9) in both groups and pretreatment imaging patterns did not show any relationship to treatment outcomes in any group. Overall mortality (21% at 90 days) and symptomatic intracranial hemorrhage (4%) did not differ across groups.

**SYNTHESIS Expansion Trial**

In 2013, Ciccone et al., reported on the SYNTHESIS Expansion trial of 362 patients randomized within 4.5 hours of the onset of various types of acute ischemic strokes to receive endovascular
therapy (n=181) or IV tPA (n=181).\[18\] Endovascular therapy consisted of intraarterial tPA, mechanical embolectomy (using the Solitaire, Penumbra, Trevo, or Merci devices) or a combination of these treatments. Endovascular treatment was completed in 163 of the 181 patients randomized to endovascular therapy. No significant differences in 90-day survival without disability (modified Rankin score 0-1) occurred between the endovascular therapy group and TPA group (30.4% vs. 34.8%, respectively, 0.71; 95% confidence interval (CI), 0.44 to 1.14; p=0.16). Within 7 days, fatal or nonfatal symptomatic intracranial hemorrhage occurred in each group at a rate of 6%. Rates of other serious adverse events were also not significantly different between groups. While there were different treatment approaches in the endovascular group, these results suggest endovascular therapy is not superior to tPA.

IMS-III Trial

In 2013, Broderick et al., reported the results of the IMS III trial, an open-label RCT that compared IV thrombolysis with either mechanical thrombectomy or endovascular tPA at the site of the occlusion. In the latter group, the treatment choice was made at the discretion of the treating physician.[17] The study had a planned enrollment of 900 patients, but was halted prematurely in April 2012 for futility when an interim analysis of the 656 enrolled patients showed no significant between-group differences in outcomes. In a predefined subgroup analysis of the IMS III RCT (summarized below), the authors reported that for the subgroup of patients with ICA, middle cerebral artery, first branch (M1), or basilar artery occlusion who received tPA within 120 minutes of stroke onset (N-124), the relative risk (RR) for a modified Rankin score of 2 or less at 90 days was not statistically significant: RR 1.18 (95% CI 0.66 to 2.1).

In 2014, Tomsick et al., published a subgroup analysis of the IMS-III trial focusing on subjects with ICA or M1 occlusion.[33] This analysis included 200 subjects, 65 with intracranial ICA and 135 with M1 segments as the target vessel for revascularization. Of these, at angiography, 82% had an arterial occlusive lesion (AOL) score of 2-3 and 76% had a modified Thrombolysis in Cerebral Infarction (mTICI) score of 2-3 (partial or full perfusion) after IV-tPA, which may have limited the potential benefit for device-related revascularization. Ninety-day Rankin scale scores were higher with higher mTICI scores: of 32 subjects with an mTICI score of 0, 3.1% had a modified Rankin scale score of 0-2 at 90 days, compared with 12.5%, 19.4%, 46.3%, and 80% for subjects with mTICI scores of 1 (total N=16), 2a (total N=67), 2b (total N=80) and 3 (N=5), respectively. To account for potential bias in the choice of endovascular therapy, propensity score analysis was used to compare subjects with different endovascular therapy modalities for the primary study outcomes. After propensity score adjustment, the authors found no clear differences in clinical or revascularization outcomes across revascularization methods, which included standard microcatheter thrombolysis (N=51), the Ekos catheter (N=14), the Merci retriever (N=77), the Penumbra device (N=39), the Solitaire device (N=4), and other methods (N=15).

Demchuck et al., evaluated the association between baseline CT or magnetic resonance (MR) angiography findings and outcomes among 306 (47% of 656) who had baseline CT or MR angiographic imaging available.[34] Ninety-two percent of those with angiography available had arterial occlusions demonstrated, 220 of which were proximal occlusions. Endovascular therapy group subjects with proximal occlusions had higher 24-hour recanalization rates than those with IV tPA only (84.3% of endovascular therapy subjects vs 56% of controls; P<0.001). However, no difference in the primary outcome, 90-day modified Rankin scale score of 0-2, was seen with proximal occlusions between groups (41.3% of endovascular therapy subjects vs 38% of controls; relative risk [RR] 1.07 [99% CI 0.67 to 1.70]).
A number of RCTs have compared endovascular therapies with noninterventional care for acute stroke, with the 5 recent (2014-2015) studies consistently reporting a significant benefit associated with endovascular care. The later-published RCTs addressed some of the limitations of previous studies. In the IMS III and SYNTHESIS Expansion trials, sizable proportions of the endovascular therapy groups did not receive an endovascular device. All 3 of the 2013 trials (Broderick et al., Kidwell et al., Ciccone et al.) had relatively low utilization of the newer generation retrievable stents (Solitaire FR and Trevo devices). In addition, IMS III and the Ciccone et al. study did not require a radiologically-proven intracranial occlusion for study eligibility. In contrast, the 2014-2015 trials which demonstrated a benefit to endovascular therapy either exclusively used stent retriever devices or allowed the treating physician to select a device, mostly a stent retriever device, and had high rates of mechanical embolectomy device use in patients randomized to endovascular therapy.

A number of studies compared different mechanical embolization devices including the following RCTs. These RCTs documented the improvements in the most recent generation of these devices.

In the SWIFT (Solitaire FR With the Intention for Thrombectomy) study, recanalization rates with Solitaire were compared with the Merci Retrieval System in a randomized, prospective, noninferiority trial of 113 patients with moderate or severe large vessel occlusion strokes.[25] Treatment was initiated within 8 hours of symptom onset in patients who had unsuccessful IV tPA or were ineligible for IV tPA. This trial was halted early after an interim analysis found revascularization without symptomatic intracranial hemorrhage occurred in 61% of Solitaire patients compared with 24% of Merci patients. Mortality rates at 90 days were 17% with Solitaire versus 38% with Merci (p=0.001).

A follow up analysis of complications of endovascular procedures using the SWIFT study data was published in 2013.[35] This analysis included 144 patients with acute ischemic stroke (31 patients treated with the Solitaire FR device during the SWIFT trial roll-in period and 113 patients randomly assigned to the Solitaire FR or Merci device). Major periprocedural complications, including symptomatic intracranial hemorrhage, air emboli, vessel dissection, major groin complications, and emboli to new vascular territories, were seen in 18/144 (12.5%) of all patients. Complication rates were similar for patients receiving the Solitaire FR and Merci devices, with the exception of symptomatic cerebral hemorrhage, which was significantly less common in the Solitaire FR group (10.9% vs 1.1%, p=0.013).

In the TREVO 2 (Thrombectomy Revascularization of large Vessel Occlusions) Study, 178 patients were randomized to receive mechanical embolectomy with either the Trevo Retriever or the Merci Retriever for large vessel occlusion strokes.[26] Revascularization rates were 86% in the Trevo group versus 60% in the MERCI group (p<0.001). Procedure-related adverse events occurred in 15% of the Trevo group and 23% in the Merci group; (p=0.183). Mortality rates at 90 days were 33% versus 24% (p=0.18), respectively.

Nonrandomized Studies

A number of nonrandomized[36-44], comparative and noncomparative studies, were published. Results from these studies are limited by a lack of comparison group,[45] small sample size,[39,46-61] lack of short
and long-term follow-up, and the retrospective nature of the study design which limit conclusions concerning the use of this treatment for a broad patient population.

Other case series have compared outcomes of different devices or studied only intermediate outcomes such as vessel recanalization.\[62-75\]

**Clinical Practice Guidelines**

**The American Heart Association and American Stroke Association**\[76\]

The updated 2015 American Heart Association and American Stroke Association (AHA/ASA) guidelines for the Early Management of Patients with Acute Ischemic Stroke included the following conclusions related to mechanical thrombectomy:

“Patients should receive endovascular therapy with a stent retriever if they meet all the following criteria (Class I; Level of Evidence A, indicating a strong recommendation based on high-quality evidence.):

- Prestroke mRS score 0 to 1,
- Acute ischemic stroke receiving intravenous r-tPA [recombinant tissue plasminogen activator] within 4.5 hours of onset according to guidelines from professional medical societies,
- Causative occlusion of the internal carotid artery or proximal MCA (M1),
- Age ≥18 years,
- NIHSS score of ≥6,
- ASPECTS of ≥6, and
- Treatment can be initiated (groin puncture) within 6 hours of symptom onset.

As with intravenous r-tPA, reduced time from symptom onset to reperfusion with endovascular therapies is highly associated with better clinical outcomes. To ensure benefit, reperfusion to TICI grade 2b/3 should be achieved as early as possible and within 6 hours of stroke onset (Class I; Level of Evidence B-R, indicating a strong recommendation based on moderate evidence.).

When treatment is initiated beyond 6 hours from symptom onset, the effectiveness of endovascular therapy is uncertain for patients with acute ischemic stroke who have causative occlusion of the internal carotid artery or proximal MCA (M1) (Class IIb; Level of Evidence C, indicating a weak recommendation based on evidence with methodological limitations.). Additional randomized trial data are needed.

In carefully selected patients with anterior circulation occlusion who have contraindications to intravenous r-tPA, endovascular therapy with stent retrievers completed within 6 hours of stroke onset is reasonable (Class IIa; Level of Evidence C, indicating a moderate recommendation based on evidence with methodological limitations.). There are inadequate data available at this time to determine the clinical efficacy of endovascular therapy with stent retrievers for those patients whose contraindications are time-based or non-time based (e.g., prior stroke, serious head trauma, hemorrhagic coagulopathy, or receiving anticoagulant medications).
Although the benefits are uncertain, use of endovascular therapy with stent retrievers may be reasonable for carefully selected patients with acute ischemic stroke in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset and who have causative occlusion of the M2 or M3 portion of the MCAs, anterior cerebral arteries, vertebral arteries, basilar artery, or posterior cerebral arteries (Class IIb; Level of Evidence C, indicating a weak recommendation based on evidence with methodological limitations.).

Endovascular therapy with stent retrievers may be reasonable for some patients <18 years of age with acute ischemic stroke who have demonstrated large vessel occlusion in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset, but the benefits are not established in this age group (Class IIb; Level of Evidence C, indicating a weak recommendation based on evidence with methodological limitations.).

Although the benefits are uncertain, use of endovascular therapy with stent retrievers may be reasonable for patients with acute ischemic stroke in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset and who have prestroke mRS score of >1, ASPECTS <6, or NIHSS score <6 and causative occlusion of the internal carotid artery or proximal MCA (M1) (Class IIb; Level of Evidence B-R, indicating a weak recommendation based on moderate evidence.). Additional randomized trial data are needed.

Observing patients after intravenous r-tPA to assess for clinical response before pursuing endovascular therapy is not required to achieve beneficial outcomes and is not recommended. (Class III; Level of Evidence B-R, indicating observation has no benefit based on moderate evidence).

Use of stent retrievers is indicated in preference to the MERCI device. (Class I; Level of Evidence A). The use of mechanical thrombectomy devices other than stent retrievers may be reasonable in some circumstances (Class IIb, Level B-NR, indicating a weak recommendation based on moderate evidence).”

Society of Interventional Radiology[77]

In a 2013 position statement the Society of Interventional Radiology (SIR) indicated that rapid treatment with mechanical thrombectomy devices improves outcomes for occlusions in large vessels. However, this statement was not based on a systematic review of the published evidence. Three references were provided to support the SIR position.[7,17,18] The SIR statement included the following conclusions:

1) Intraarterial stroke revascularization is beneficial to patients in whom IV tPA fails or who are not eligible for IV tPA;  
2) Patients with a large vessel occlusion who are treated rapidly (even with first-generation techniques) have improved outcomes compared those treated with IV tPA alone;  
3) Second-generation mechanical thrombectomy devices are the most effective therapy for large vessel occlusion;  
4) Randomized trials of second-generation mechanical thrombectomy devices compared with IV tPA alone need to be performed and/or a national registry needs to be established;  
5) Participation in research is critically important, but reimbursement for IA stroke revascularization should not be restricted to clinical trials; and  
6) All IA cases should be contributed to a trial or national registry, including 90-day clinical outcomes.
Summary

The research for the use of endovascular mechanical embolectomy in individuals with acute ischemic stroke due to occlusion report a significant benefit in terms of reduced disability at 90-days post-treatment. The recent trials which demonstrated a benefit of endovascular therapy primarily used stent retriever devices. In addition, the benefit of mechanical embolectomy was limited by the time-to-treatment, with an increased benefit observed in patients with reduced time frame from symptom onset to embolectomy. Lastly, the American Heart Association and American Stroke Association recently updated their clinical practice guidelines regarding management of acute stroke to recommend endovascular therapy when specific criteria are met. Therefore, the use of endovascular mechanical embolectomy may be considered medically necessary in carefully selected patients with ischemic stroke when criteria are met.

The current research has not demonstrated mechanical embolectomy offers any additional benefit compared with standard treatments for acute stroke when the above criteria are not met. In addition, no clinical practice guidelines were identified which recommend endovascular mechanical embolectomy in patients who fall outside of the defined appropriateness criteria. Therefore, the use of mechanical embolectomy devices for acute stroke is considered not medically necessary when criteria are not met.

REFERENCES

4. BlueCross BlueShield Association Medical Policy Reference Manual "Endovascular Procedures for Intracranial Arterial Disease (Atherosclerosis and Aneurysms)." Policy No. 2.01.54


24. TEC Assessment 2014. "Endovascular Treatments for Acute Ischemic Stroke in Adults " BlueCross and BlueShield Association Technology Evaluation Center, Volume 29 Tab. 11.


October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage.
Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.


43. Shi, ZS, Loh, Y, Walker, G, Duckwiler, GR. Clinical outcomes in middle cerebral artery trunk occlusions versus secondary division occlusions after mechanical thrombectomy: pooled analysis
of the Mechanical Embolus Removal in Cerebral Ischemia (MERCI) and Multi MERCI trials. *Stroke.* 2010 May;41(5):953-60. PMID: 20378867


59. Cohen, JE, Rabinstein, AA, Ramirez-de-Noriega, F, et al. Excellent rates of recanalization and good functional outcome after stent-based thrombectomy for acute middle cerebral artery...


63. Abou-Chebl, A. Endovascular treatment of acute ischemic stroke may be safely performed with no time window limit in appropriately selected patients. *Stroke.* 2010 Sep;41(9):1996-2000. PMID: 20651271


**CROSS REFERENCES**

*Endovascular Angioplasty and/or Stenting for Intracranial Arterial Disease (Atherosclerotic and Aneurysms)*, Surgery, Policy No. 141

<table>
<thead>
<tr>
<th>CODES</th>
<th>NUMBER</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>37184</td>
<td>Primary percutaneous transluminal mechanical thrombectomy, noncoronary, arterial or arterial bypass graft, including fluoroscopic guidance and intraprocedural pharmacological thrombolytic injection(s); initial vessel</td>
</tr>
<tr>
<td></td>
<td>37185</td>
<td>second and all subsequent vessel(s) within the same vascular family (List separately in addition to code for primary mechanical thrombectomy procedure)</td>
</tr>
<tr>
<td></td>
<td>61645</td>
<td>Percutaneous arterial transluminal mechanical thrombectomy and/or infusion for thrombolysis, intracranial, any method, including diagnostic angiography, fluoroscopic guidance, catheter placement, and intraprocedural pharmacological thrombolytic injection(s)</td>
</tr>
<tr>
<td>HCPCS</td>
<td>None</td>
<td></td>
</tr>
</tbody>
</table>
**Microwave Tumor Ablation**

**Effective:** July 1, 2017

**Next Review:** November 2018
**Last Review:** June 2017

**IMPORTANT REMINDER**

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

**DESCRIPTION**

Microwave ablation (MWA) uses microwave thermal energy to create thermal coagulation and localized tissue necrosis. MWA is proposed as a treatment of tumors, palliate symptoms.

**MEDICAL POLICY CRITERIA**

**Note:** This policy does not address liver tumors (primary or metastatic). See Cross References.

Microwave ablation is considered **investigational** as a treatment of primary and metastatic tumors, including but not limited to tumors of the breast, lung, and kidney.

**NOTE:** A summary of the supporting rationale for the policy criteria is at the end of the policy.

**CROSS REFERENCES**

1. [Radioembolization for Primary and Metastatic Tumors of the Liver](#), Medicine, Policy No. 140
2. [Radiofrequency Ablation of Tumors (RFA)](#), Surgery, Policy No. 92
3. [Cryosurgical Ablation of Miscellaneous Solid Organ and Breast Tumors](#), Surgery, Policy No. 132
4. [Magnetic Resonance (MR) Guided Focused Ultrasound (MRgFUS) and High Intensity Focused Ultrasound (HIFU) Ablation](#), Surgery, Policy No. 139
5. [Ablation of Primary and Metastatic Liver Tumors](#), Surgery, Policy No. 204
MICROWAVE ABLATION (MWA)

MWA is a technique in which the use of microwave energy induces an ultra-high speed, 915 MHz or 2.450 MHz (2.45 GHz), alternating electric field which causes water molecule rotation and the creation of heat. This results in thermal coagulation and localized tissue necrosis. In MWA, a single microwave antenna or multiple antennas connected to a generator are inserted directly into the tumor or tissue to be ablated; energy from the antennas generates friction and heat. The local heat coagulates the tissue adjacent to the probe, resulting in a small, approximately 2-3 cm elliptical area (5 x 3 cm) of tissue ablation. In tumors greater than 2 cm in diameter, 2-3 antennas may be used simultaneously to increase the targeted area of MWA and shorten operative time. Multiple antennas may also be used simultaneously to ablate multiple tumors. Tissue ablation occurs quickly, within 1 minute after a pulse of energy, and multiple pulses may be delivered within a treatment session depending on the size of the tumor. The cells killed by MWA are typically not removed but are gradually replaced by fibrosis and scar tissue. If there is local recurrence, it occurs at the edges. Treatment may be repeated as needed. MWA may be used to: 1) control local tumor growth and prevent recurrence; 2) palliate symptoms; and 3) extend survival duration.

Complications from MWA are usually considered mild and may include pain and fever. Other potential complications associated with MWA include those caused by heat damage to normal tissue adjacent to the tumor (e.g., intestinal damage during MWA of the kidney or liver), structural damage along the probe track (e.g., pneumothorax as a consequence of procedures on the lung), liver enzyme elevation, liver abscess, ascites, pleural effusion, diaphragm injury or secondary tumors if cells seed during probe removal. MWA should be avoided in pregnant patients since potential risks to the patient and/or fetus have not been established and in patients with implanted electronic devices such as implantable pacemakers that may be adversely affected by microwave power output.

MWA is an ablative technique similar to radiofrequency or cryosurgical ablation; however, MWA may have some advantages. In MWA, the heating process is active, which produces higher temperatures than the passive heating of radiofrequency ablation and should allow for more complete thermal ablation in a shorter period of time. The higher temperatures reached with MWA (over 100° C) can overcome the "heat sink" effect in which tissue cooling occurs from nearby blood flow in large vessels potentially resulting in incomplete tumor ablation. MWA does not rely on the conduction of electricity for heating, and therefore, does not have electrical current flow through patients and does not require grounding pads be used during the procedure to prevent skin burns. Unlike radiofrequency ablation, MWA does not produce electric noise, which allows ultrasound guidance to occur during the procedure without interference. Finally, MWA can be completed in less time than radiofrequency ablation since multiple antennas can be used simultaneously.

MWA was first used percutaneously in 1986 as an adjunct to liver biopsy. Since that time, MWA has been used for ablation of tumors and tissue for the treatment of many conditions including: hepatocellular carcinoma, colorectal cancer metastatic to the liver, renal cell carcinoma, renal hamartoma, adrenal malignant carcinoma, non-small cell lung cancer, intrahepatic primary cholangiocarcinoma, secondary splenomegaly and hypersplenism, abdominal tumors and other tumors not amenable to resection. Well-established local or systemic treatment alternatives are available for each of these malignancies. The
hypothesized advantages of MWA for these cancers include improved local control and those common to any minimally invasive procedure (e.g., preserving normal organ tissue, decreasing morbidity, decreasing length of hospitalization).

RENAAL CELL CARCINOMA

Radical nephrectomy remains the principal treatment of renal cell carcinoma; however, partial nephrectomy or nephron-sparing surgery has been shown to be as effective as radical nephrectomy, with comparable long-term recurrence-free survival rates, in a select group of patients. Prognosis drops precipitously if the tumor extends outside the kidney capsule, since chemotherapy is relatively ineffective against metastatic renal cell carcinoma. Alternative therapies such as MWA are of interest in patients with small renal tumors when preservation of renal function is necessary (e.g., in patients with marginal renal function, a solitary kidney, bilateral tumors) and in patients with comorbidities that would render them unfit for surgery. Another consideration would be in patients at high risk of developing additional renal cancers (as in von Hippel-Lindau disease).

REGULATORY STATUS

There are several devices cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process for MWA. Covidien’s (a subsidiary of Tyco Healthcare) Evident Microwave Ablation System has 510(k) clearance for soft tissue ablation, including partial or complete ablation of non-resectable liver tumors. The following devices have 510(k) clearance for MWA of (unspecified) soft tissue:

- BSD Medical Corporation’s MicroThermX® Microwave Ablation System (MTX-180);
- Valleylab’s (a subsidiary of Covidien) VivaWave® Microwave Ablation System;
- Vivant’s (acquired by Valleylab in 2005) Tri-Loop™ Microwave Ablation Probe;
- MicroSurgeon Microwave Soft Tissue Ablation Device;
- Microsulis Medical’s Acculis Accu2i; and
- NeuWave Medical’s Certus 140™

FDA determined that these devices were substantially equivalent to existing radiofrequency and MWA devices. FDA product code: NEY.

EVIDENCE SUMMARY

The principal health outcomes associated with treatment of malignancies are typically measured in units of survival past treatment: disease-free survival (DFS), a period of time following treatment where the disease is undetectable; progression-free survival (PFS), the duration of time after treatment before the advancement or progression of disease; and overall survival (OS), the period of time the patient remains alive following treatment.

In order to understand the impact of microwave ablation (MWA) on these outcomes, well-designed randomized controlled trials (RCTs) are needed that compare this therapy with standard medical and/or surgical treatment of primary and metastatic tumors.

BREAST

SYSTEMATIC REVIEW
A 2010 review of ablation techniques by Zhao et al., for breast cancer found only 0-8% of breast tumors were completely ablated with microwave ablation (MWA).\[1\] The authors noted that studies identified for the review were mostly feasibility and pilot studies conducted in research settings.

**NONRANDOMIZED STUDIES**

In 2012, W. Zhou and colleagues reported on 41 patients treated with MWA directly followed by mastectomy for single breast tumors with a mean volume of 5.26 cm $^3$ + 3.8 (range, 0.09 to 14.14 cm).\[2\] Complete tumor ablation was found by microscopic evaluation in 37 of the 41 tumors ablated (90%; 95% confidence interval [CI]: 76.9-97.3%). Reversible thermal injuries to the skin and pectoralis major muscle occurred in 3 patients. Results from this study should be met with caution due to its small sample size and lack of comparison group.

**LUNG**

**NONRANDOMIZED STUDIES**

In 2016, Vogl et al. evaluated local tumor control, time to tumor progression, and survival rates among patients with lung metastatic colorectal cancer who underwent ablation therapy (N=109) performed using laser-induced thermotherapy (LITT), radiofrequency ablation (RFA), or microwave ablation (MWA).\[3\] Twenty-one patients underwent LITT (31 ablations), 41 patients underwent RFA (75 ablations), and 47 patients underwent MWA (125 ablations). Local tumor control was achieved in 17 of 25 lesions (68.0%) treated with LITT, 45 of 65 lesions (69.2%) treated with RFA, and 91 of 103 lesions (88.3%) treated with MWA. The progression-free survival rate at 1, 2, 3, and 4 years was 96.8%, 52.7%, 24.0%, and 19.1%, respectively, for patients who underwent LITT; 77.3%, 50.2%, 30.8%, and 16.4%, respectively, for patients who underwent RFA; and 54.6%, 29.1%, 10.0%, and 1.0%, respectively, for patients who underwent MWA, with no statistically significant difference noted among the three ablation methods.

In 2015, Acksteiner and Steinke reported a retrospective study that evaluated the safety, effectiveness, and follow-up imaging of MWA in 10 patients (age range, ≥75 years) with early-stage non-small-cell lung cancer (NSCLC).\[4\] Follow-up with CT and 18-fluorodeoxyglucose-positron emission tomography (FDG-PET) extended for 30 months (median, 12 months). No periprocedural deaths or major complications were reported. Seven patients were disease-free. Three patients showed growth of the treated lesions, 1 patient died (age 90) due to unknown cause 18 months postsurgery. One patient still living presented with local progression and disseminated metastatic disease at 12 months. One patient showed increasing soft tissue mass at the ablation site 15 months posttreatment, but 3 consecutive core biopsies over 2 months failed to confirm tumor recurrence.

A 2015 observational study evaluated the clinical efficacy and utility of percutaneous microwave ablation therapy (PMAT) for lung cancer without surgical treatment.\[5\] Thirty-nine lesions in 29 patients with peripheral lung cancer were treated by PMAT under local anesthesia. Treatments were completed in 29 patients. Average surgical time was 8 minutes (range, 5-12 minutes). Eight, 14, 4, and 3 patients achieved complete remission, partial remission, stable status, and progression, respectively, for an effectiveness rate of 76%. Complications included 5, 2, and 15 cases of pneumothorax, pleural effusion, and fever, respectively. No complications from needle track insertion were observed. Mean progression-free survival was 15 months. One- and 2-year OS rates were 91% and 83%, respectively.
Other evidence regarding MWA for lung tumors is limited to several nonrandomized retrospective studies. These studies are all limited by lack of comparison group and small sample size. One study was also limited by short-term follow-up. In addition, one small comparative study was published by Wei and colleagues in 2015, which compared MWA with chemotherapy (n=46) to chemotherapy alone (n=28) in patients with untreated stage IIIB or IV NSCLC. PFS was reported to be significantly longer in the MWA/chemo group 10.9 months vs. 4.8 months (p=0.001). Overall survival tended to favor the MWA/chemo group although results were not statistically significant. Adverse events associated with MWA were observed in 67.4% of patients. Larger studies with a randomized design are needed to isolate the effect of MWA upon PFS and OS in patients with lung cancer.

PRIMARY RENAL TUMORS

SYSTEMATIC REVIEWS

In a 2014 systematic review and meta-analysis, Katsanos et al. compared thermal ablation (MWA and RFA) with surgical nephrectomy for small renal tumors (mean size 2.5 cm). Included in the analysis were 1 randomized study on MWA and 5 cohort studies on RFA with a total of 587 patients. In the ablation group, the complication rates and renal function decline were significantly lower than in the nephrectomy group (p=0.04 and p=0.03, respectively). The local recurrence rate was 3.6% in both groups (risk ratio=0.92, 95% CI, 0.4 to 2.14, p=0.79) and disease-free survival up to 5 years was not significantly different between groups (hazard ratio=1.04, 95% CI, 0.48 to 2.24, p=0.92). The authors indicated additional RCTs were needed to compare MWA to nephrectomy and other ablative techniques.

Martin et al. reported on a meta-analysis of MWA versus cryoablation for small renal tumors in 2013. Included in the analysis were 7 MWA studies (n=164) and 44 cryoablation studies (n=2989). The studies were prospective or retrospective, nonrandomized, noncomparative studies. The mean follow-up duration was shorter for MWA than cryoablation (17.86 months vs 30.22 months, p=0.07). While the mean tumor size was significantly larger in the MWA studies than the cryoablation studies (2.58 cm vs 3.13 cm, respectively, p=0.04), local tumor progression (4.07% vs 2.53%, respectively; p=0.46), and progression to metastatic disease (0.8% vs 0%, respectively; p=0.12) were not significantly different.

RANDOMIZED CONTROLLED TRIALS (RCTS)

In 2012, Guan and colleagues reported on a prospective randomized study to compare the use of MWA to partial nephrectomy (the gold standard of nephron-sparing surgical resection) for solitary renal tumors less than 4 cm. Forty-eight patients received MWA and 54 had partial nephrectomy. Patients in the MWA group had significantly fewer postoperative complications than the partial nephrectomy group (6 [23.5%] vs. 18 [33.3%]; p=0.0187). MWA patients also had significantly less postoperative renal function declines (p=0.0092) and estimated perioperative blood loss (p=0.0002) than partial nephrectomy patients. At last follow-up, estimated glomerular filtration rate declines in both groups were similar (p=1.0000). Disease-specific deaths did not occur and overall local recurrence-free survival by Kaplan-Meier estimates at 3 years were 91.3% for MWA and 96.0% for partial nephrectomy (p= 0.5414). Studies with longer follow-up are needed in order to assess the benefits of MWA compared to nephrectomy.

NONRANDOMIZED STUDIES
Evidence regarding MWA treatment in patients with primary renal tumors primarily consists of several nonrandomized case studies, all of which are limited by lack of comparison and small sample size.[19-24] In addition, one study was also limited by short-term follow-up.[20]

OTHER TUMORS OR CONDITIONS

Nonrandomized studies of MWA for other indications are limited by lack of comparison group. Examples of other indications include adrenal carcinoma,[25] benign thyroid tumors,[26] pancreatic cancer,[27] and other non-oncologic conditions (e.g., bleeding peptic ulcers, esophageal varices, secondary hypersplenism).

PRACTICE GUIDELINE SUMMARY

NATIONAL COMPREHENSIVE CANCER NETWORK (NCCN)

Neuroendocrine Tumors

In the NCCN guidelines on neuroendocrine tumors, MWA is listed as one treatment option (along with radiofrequency ablation or cryoablation) for liver metastases as hepatic regional therapy in carcinoid tumors and pancreatic endocrine (islet cell) tumors when there is unresectable disease and/or distant metastases.[28] These guidelines note, currently, there are limited prospective data and no randomized clinical trials on ablative therapies (including MWA), and data on these ablative techniques are emerging. Additionally, the 2 articles cited in the guideline on ablative techniques are not specific to MWA [category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate].

AMERICAN COLLEGE OF CHEST PHYSICIANS (ACCP)

The ACCP evidence-based guidelines on the treatment of non-small cell lung cancer note the role of ablative therapies in the treatment of high-risk patients with stage I non-small cell lung cancer (NSCLC) is evolving. However, the ACCP does not recommend MWA for patients with NSCLC.[29]

AMERICAN COLLEGE OF RADIOLOGY (ACR)

The ACR radiologic management of hepatic malignancy (2015) rates appropriateness of thermal ablation treatment for seven clinical scenarios.[30] Thermal ablation typically refers to RFA, though may include cryoablation and microwave ablation. Only two studies were cited in the discussion regarding the potential benefits of MWA.

SUMMARY

For patients with tumors, it appears that microwave ablation (MWA) may improve health outcomes, though more research is needed to know for sure. Clinical practice guidelines based on research make recommendations for thermal ablative therapies without specifically specifying MWA over other options. Therefore, MWA is considered investigational as a treatment of tumors.

REFERENCES


### CODES

<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>19499</td>
<td>Unlisted procedure, breast</td>
</tr>
<tr>
<td></td>
<td>32998</td>
<td>Ablation therapy for reduction or eradication of 1 or more pulmonary tumor(s) including pleura or chest wall when involved by tumor extension, percutaneous, radiofrequency, unilateral</td>
</tr>
<tr>
<td></td>
<td>32999</td>
<td>Unlisted procedure, lungs and pleura</td>
</tr>
<tr>
<td></td>
<td>38589</td>
<td>Unlisted laparoscopy procedure, lymphatic system</td>
</tr>
<tr>
<td></td>
<td>49999</td>
<td>Unlisted procedure, abdomen, peritoneum and omentum</td>
</tr>
<tr>
<td></td>
<td>50592</td>
<td>Ablation, renal tumor(s), unilateral, percutaneous, radiofrequency</td>
</tr>
<tr>
<td></td>
<td>53899</td>
<td>Unlisted procedure, urinary system</td>
</tr>
<tr>
<td></td>
<td>60699</td>
<td>Unlisted procedure, endocrine system</td>
</tr>
<tr>
<td>HCPCS</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

*Date of Origin: October 2013*
**Occipital Nerve Stimulation**

**Effective:** June 1, 2017

**Next Review:** February 2018  
**Last Review:** May 2017

---

**DESCRIPTION**

Occipital nerve stimulation (ONS) delivers a small electrical charge to the occipital nerve in an attempt to prevent migraines and other headaches in patients who have not responded to medications. The device consists of a subcutaneously implanted pulse generator (in the chest wall or abdomen) attached to extension leads that are tunneled to join electrodes placed across one or both occipital nerves at the base of the skull. Continuous or intermittent stimulation may be used.

---

**MEDICAL POLICY CRITERIA**

Occipital nerve stimulation is considered **investigational** for all indications, including but not limited to headaches.

**NOTE:** A summary of the supporting rationale for the policy criteria is at the end of the policy.

---

**CROSS REFERENCES**

1. [Interferential Current Stimulation](#), Durable Medical Equipment, Policy No. 83.07  
2. [Spinal Cord Stimulation](#), Surgery, Policy No. 45  
3. [Peripheral Subcutaneous Field Stimulation](#), Surgery, Policy No. 188

---

**BACKGROUND**

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage.  
Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
Implanted peripheral nerve stimulators have been used for treatment of refractory pain for many years but only recently proposed for management of craniofacial pain. Occipital, supraorbital, and infraorbital stimulation have been reported in the literature.

There are four types of headache: vascular, muscle contraction (tension), traction, and inflammatory. Primary (not the result of another condition) chronic headache is defined as headache occurring more than 15 days of the month for at least three months. An estimated 45 million Americans experience chronic headaches. For at least half of these people, the problem is severe and sometimes disabling.

Migraine is the most common type of vascular headache. Migraine headaches are usually characterized by severe pain on one or both sides of the head, an upset stomach, and, at times, disturbed vision. One-year prevalence of migraine ranges from 6% to 15% in adult men and from 14% to 35% in adult women. Migraine headaches may last a day or more and can strike as often as several times a week or as rarely as once every few years. Drug therapy for migraine is often combined with biofeedback and relaxation training. Sumatriptan is commonly used for relief of symptoms. Drugs used to prevent migraine include methysergide maleate, propranolol hydrochloride, ergotamine tartrate; amitriptyline, valproic acid, and verapamil.

Hemicrania continua, also a vascular headache, causes moderate pain with occasional severe pain on only one side of the head. At least one of the following symptoms must also occur; conjunctival injection and/or lacrimation, nasal congestion and/or rhinorrhea, or ptosis and/or miosis. Headache occurs daily and is continuous with no pain-free periods. Hemicrania continua occurs mainly in women, and its true prevalence is not known. Indomethacin usually provides rapid relief of symptoms. Other NSAIDs, including ibuprofen, celecoxib, and naproxen, can provide some relief from symptoms. Amitriptyline and other tricyclic antidepressants are effective in some patients.

Cluster headache is a vascular headache that occurs in cyclical patterns or clusters of severe or very severe unilateral orbital or supraorbital and/or temporal pain. The headache is accompanied by at least one of the following autonomic symptoms: ptosis (drooping eyelid), conjunctival injection, lacrimation, rhinorrhea, and, less commonly, facial blushing, swelling, or sweating. Bouts of one headache every other day to 8 attacks per day may last from weeks to months, usually followed by remission periods when the headache attacks stop completely. The pattern varies from one person to another, but most people have one or two cluster periods a year. During remission, no headaches occur for months, and sometimes even years. The intense pain is caused by the dilation of blood vessels, which creates pressure on the trigeminal nerve. While this process is the immediate cause of the pain, the etiology is not fully understood. It is more common in men than in woman. One-year prevalence is estimated to be 0.5 to 1.0/1,000. Management of cluster headache consists of abortive and preventive treatment. Abortive treatments include subcutaneous injection of sumatriptan, topical anesthetics sprayed into the nasal cavity, and strong coffee. Some patients respond to rapidly inhaled pure oxygen. A variety of other pharmacologic and behavioral methods of aborting and preventing attacks have been reported with wide variation in patient response.

REGULATORY STATUS

The U.S. Food and Drug Administration (FDA) has not yet cleared any occipital nerve stimulation device for treatment of headache.
The Synergy™ IPG (implantable pulse generator) device from Medtronic received marketing clearance in 1999 for management of chronic, intractable pain of the trunk or limbs, and off-label use for headache is described in the literature.

The Genesis™ neuromodulation system (St. Jude Medical) is approved by the FDA for spinal cord stimulation and has received CE mark approval in Europe for the treatment of chronic migraines.

EVIDENCE SUMMARY

The principal outcomes associated with treatment of headache are relief of pain, return to work, and improved functional level. Relief of pain can be a subjective outcome associated with a placebo effect. Therefore, data from adequately powered, blinded, randomized controlled trials (RCT) are required to control for the placebo effect and determine whether any treatment effect provides a significant advantage.

The technology must also be evaluated in general groups of patients against existing treatments. In patients with mild to moderate symptoms, occipital nerve stimulation may be compared to other forms of conservative therapy such as topical anesthetics, rest, or non-steroidal anti-inflammatory or migraine medications.

Therefore, the focus of the evidence summary is on RCTs comparing ONS-treated patients with those in a sham treatment or standard of care group.

SYSTEMATIC REVIEW

Two SRs of the literature on occipital nerve stimulation (ONS) were published in 2015. Both included RCTs and observational studies. The study by Chen et al identified five RCTs and seven case series with at least 10 patients.[1] Three of the RCTs were industry-sponsored, multicenter, parallel-group trials and two were single-center crossover trials. All five included a sham control group and one trial also included a medication management group. Risk of bias was judged to be high or unclear for all trials. Meta-analyses were performed on two outcomes. A pooled analysis of 2 studies did not find a significant difference in response rate between active and sham stimulation (risk ratio [RR], 2.07; 95% confidence interval [CI], 0.50 to 8.55; p=0.31) and a pooled analysis of three studies showed a significantly greater reduction in the number of days with prolonged moderate-to-severe headache (mean difference, 2.59; 95% CI, 0.91 to 4.27; p=0.003.

In their SR, Yang et al identified the same five RCTs as Chen.[1] The Yang review only included studies conducted with patients with migraine of at least six months in duration who did not respond to oral medications. In addition to the RCTs, five case series met the inclusion criteria. Yang et al did not pool study findings. The definition of response rate varied across studies and could include frequency and/or severity of headaches. Response rates in three case series with self-reported efficacy were 100% each, and response rates in the other two series were 50% and 89%, respectively. Complication rates in the series ranged from 40% to 100%. The authors noted that the case series were subject to biases (e.g., inability to control for the placebo effect), that RCT evidence was limited, and that complication rates were high.

A 2015 SR by Sweet et al identified nine small case series (<15 patients each) assessing the efficacy of ONS for treating medically refractory occipital neuralgia.[2] The authors did not pool...
study findings. No conclusions can be drawn about the impact of ONS on occipital neuralgia due to the lack of RCTs or other controlled studies.

The National Institute for Health and Care Excellence (NICE, 2013) evaluated two RCTs and one case series to determine if ONS was effective in decreasing headache frequency, duration and severity.\[3\] Both RCTs compared ONS with sham stimulation at three months. Although the smaller RCT with 67 patients determined that the ONS group responded better than the sham group, the larger RCT with 157 patients showed no difference in responder rate. NICE concluded that ONS for intractable chronic migraines is efficacious in the short-term, but there is little evidence to indicate long-term outcome effects. NICE stated ONS should only be used for clinical governance, consent, and audit or research.

RANDOMIZED CONTROLLED TRIALS

In 2012, Serra and Marchioretto conducted a crossover RCT in which 30 patients with chronic migraine (100% of patients) and medication overuse headache (85% of patients) were implanted with an ONS and randomized to “Stimulation On” or “Stimulation Off” arms.\[4\] After one month, or if headaches worsened during the off period, patients were crossed over to the other arm. The mean number of days when patients randomized to the off condition turned on the generators was 4.65 days (range, 1-12 days). Follow-up examinations were conducted at one, three, six, and 12 months after nerve stimulator implantation, during which time the stimulation parameters were adjusted in order to optimize the perception of paresthesia. In addition, the patients were provided with remote controls to modify the stimulation amplitude. At baseline, the average frequency of migraines was 5.8 days per week and the median headache severity was eight on an 11-point numerical rating scale. Headache intensity and/or frequency were significantly lower in the on arm compared to the off arm and decreased from baseline to each follow-up visit in all patients with Stimulation On. For example, the number of headaches decreased from a median of 6.3 days per week in the off phase to 2.1 days per week in the on phase. The median Migraine Disability Assessment (MIDAS) score decreased from 79 at baseline to 10 at 12-month follow-up. Quality of life measured by the SF-36 significantly improved from baseline throughout the follow-up period. Use of triptans decreased from a median of 20 to three doses/month and use of nonsteroidal anti-inflammatory drug (NSAIDs) use decreased from a median of 25.5 to two doses/month. There were two infections (6.7%) and three lead migrations (10%) during the study. This study is limited by the lack of a control group during follow-up and lack of blinding, although blinding of patients may be difficult due to paresthesia with this treatment.

Also in 2012, Silberstein et. al, published an RCT of patients diagnosed with chronic migraine (CM), implanted with a neurostimulation device and randomized 2:1 to active (n=105) or sham (n=52) stimulation.\[5\] Authors defined the primary endpoint as the difference in the percentage of responders (defined as patients that achieved a ≥50% reduction in mean daily visual analog scale scores) in each group at 12 weeks. A significant difference was reported at a secondary endpoint of 30% reduction; however, no difference was reported between groups at the primary endpoint of 50% reduction. At a 30% reduction, significant difference in reduction of number of headaches, migraine-related disability, and direct reports of pain relief were reported compared to the sham group, but it is unknown if these results are clinically meaningful considering researchers did not meet their established primary endpoint of at least a 50% reduction in mean daily analog scores. In addition, the overall treatment effect was low, with only 17.1% of the active group and 13.5% of the control group classified as responders.
Results from the 52-week open-label extension of this study were published in 2014. Results were reported for the intent-to-treat (ITT) population and for the 125 patients who met criteria for intractable chronic migraine. Twenty-four patients were excluded from analysis due to explantation of the system (n=18) or other loss to follow-up. Mean headache days at baseline were 21.6 for the ITT population and 24.2 for the intractable chronic migraine group. In the ITT population, headache days were reduced by 6.7 days, and a 50% or greater reduction in headache days and/or pain intensity was observed in 47.8% of patients. Sixty-eight percent of patients were satisfied with the headache relief provided by the device. Seventy percent experienced at least one of 183 device-related adverse events, of which 8.6% required hospitalization and 40.7% required surgical intervention. Eighteen percent of patients had persistent pain and/or numbness with the device.

A small industry-sponsored feasibility RCT reported preliminary safety and efficacy data on occipital nerve stimulation (ONS) for treatment of medically intractable chronic migraine (CM). However, the findings from this small (n=110) and very short (follow-up=three months) study must be interpreted with caution due to the exploratory nature of the design:

- The sample size was chosen to gain experience with ONS and the study was not prospectively powered for efficacy evaluation.
- No primary end points were specified at the outset; at three months, a range of efficacy measures were evaluated in comparison to baseline.

Although the findings from this study may provide direction for future research, they do not provide reliable evidence on the clinical utility of ONS. Per the authors, “reliable conclusions regarding efficacy cannot be established on the basis of this study alone.”

NONRANDOMIZED STUDIES

Evidence from nonrandomized studies of occipital nerve stimulation (ONS) for treatment of headaches is considered insufficient due to methodological limitation such as nonrandom allocation of treatment, lack of adequate comparison groups, and short-term follow-up, all of which limit conclusions regarding the safety and effectiveness of ONS treatment. Of note, several of these nonrandomized studies reported high rates of ONS revision (20-60%) and/or complications (20-40%).

PRACTICE GUIDELINE SUMMARY

Congress of Neurological Surgeons

A 2015 evidence-based guideline from the Congress of Neurological Surgeons states: “the use of occipital nerve stimulation is a treatment option for patients with medically refractory occipital neuralgia.” The statement had a level III recommendation based on a SR of the literature that only included case series with methodological limitations.

National Institute for Health and Care Excellence

A 2013 National Institute for Health and Care Excellence (NICE) guideline noted that the evidence on ONS for intractable chronic migraine shows some efficacy for short-term outcomes but very little evidence about long-term outcomes. With regard to safety, NICE indicated that there are risks of complications that may need further surgery. Therefore, this procedure should only be used with special arrangements for clinical governance, consent, and audit or research. NICE has recommended that clinicians wanting to undertake ONS for
intractable chronic migraine should ensure that patients understand the uncertainty about the procedure's safety and efficacy, and provide them with clear written information.

**SUMMARY**

There is not enough research to show that occipital nerve stimulation (ONS) improves health outcomes for patients with any condition. Clinical guidelines based on research list ONS as a treatment option, but highlight the uncertainty around safety and health outcomes. Therefore, ONS is considered investigational for all indications, including but not limited to as a treatment of headache.

**REFERENCES**


These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.


<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>0466T</td>
<td>Insertion of chest wall respiratory sensor electrode or electrode array, including connection to pulse generator (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>61885</td>
<td></td>
<td>Insertion or replacement of cranial neurostimulator pulse generator or receiver, direct or inductive coupling; with connection to a single electrode array</td>
</tr>
<tr>
<td>61886</td>
<td></td>
<td>Insertion or replacement of cranial neurostimulator pulse generator or receiver, direct or inductive coupling; with connection to 2 or more electrode arrays</td>
</tr>
<tr>
<td>64553</td>
<td></td>
<td>Percutaneous implantation of neurostimulator electrode array; cranial nerve</td>
</tr>
<tr>
<td>64555</td>
<td></td>
<td>Percutaneous implantation of neurostimulator electrode array; peripheral nerve (excludes sacral nerve)</td>
</tr>
<tr>
<td>64568</td>
<td></td>
<td>Incision for implantation of cranial nerve (e.g., vagus nerve) neurostimulator electrode array and pulse generator</td>
</tr>
<tr>
<td>64569</td>
<td></td>
<td>Revision or replacement of cranial nerve (e.g., vagus nerve) neurostimulator electrode array, including connection to existing pulse generator</td>
</tr>
<tr>
<td>64570</td>
<td></td>
<td>Removal of cranial nerve (e.g., vagus nerve) neurostimulator electrode array and pulse generator</td>
</tr>
<tr>
<td>64575</td>
<td></td>
<td>Incision for implantation of neurostimulator electrode array; peripheral nerve (excludes sacral nerve)</td>
</tr>
<tr>
<td>64585</td>
<td></td>
<td>Revision or removal of peripheral neurostimulator electrode array</td>
</tr>
<tr>
<td>64590</td>
<td></td>
<td>Insertion or replacement of peripheral or gastric neurostimulator pulse generator or receiver, direct or inductive coupling</td>
</tr>
<tr>
<td>64999</td>
<td></td>
<td>Unlisted procedure, nervous system</td>
</tr>
<tr>
<td>95970</td>
<td></td>
<td>Electronic analysis of implanted neurostimulator pulse generator system (e.g., rate, pulse amplitude, pulse duration, configuration of wave form, battery status, electrode selectability, output modulation, cycling, impedance and patient compliance measurements); simple or complex brain, spinal cord, or peripheral (i.e., cranial nerve, peripheral nerve, sacral nerve, neuromuscular) neurostimulator pulse generator/transmitter, without reprogramming</td>
</tr>
<tr>
<td>95971</td>
<td></td>
<td>simple spinal cord, or peripheral (i.e., peripheral nerve, sacral nerve, neuromuscular) neurostimulator pulse generator/transmitter, with intraoperative or subsequent programming</td>
</tr>
<tr>
<td>95972</td>
<td></td>
<td>complex spinal cord, or peripheral (i.e., peripheral nerve, sacral nerve, neuromuscular) (except cranial nerve) neurostimulator pulse generator/transmitter, with intraoperative or subsequent programming</td>
</tr>
<tr>
<td>Codes</td>
<td>Number</td>
<td>Description</td>
</tr>
<tr>
<td>---------</td>
<td>--------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>HCPCS</td>
<td>C1820</td>
<td>Generator, neurostimulator (implantable), with rechargeable battery and charging system</td>
</tr>
<tr>
<td></td>
<td>L8679</td>
<td>Implantable neurostimulator, pulse generator, any type</td>
</tr>
<tr>
<td></td>
<td>L8680</td>
<td>Implantable neurostimulator electrode, each</td>
</tr>
<tr>
<td></td>
<td>L8681</td>
<td>Patient programmer (external) for use with implantable programmable neurostimulator pulse generator</td>
</tr>
<tr>
<td></td>
<td>L8682</td>
<td>Implantable neurostimulator radiofrequency receiver</td>
</tr>
<tr>
<td></td>
<td>L8683</td>
<td>Radiofrequency transmitter (external) for use with implantable neurostimulator radiofrequency receiver</td>
</tr>
<tr>
<td></td>
<td>L8685</td>
<td>Implantable neurostimulator pulse generator, single array, rechargeable, includes extension</td>
</tr>
<tr>
<td></td>
<td>L8686</td>
<td>Implantable neurostimulator pulse generator, single array, non-rechargeable, includes extension</td>
</tr>
<tr>
<td></td>
<td>L8687</td>
<td>Implantable neurostimulator pulse generator, dual array, rechargeable, includes extension</td>
</tr>
<tr>
<td></td>
<td>L8688</td>
<td>Implantable neurostimulator pulse generator, dual array, non-rechargeable, includes extension</td>
</tr>
<tr>
<td></td>
<td>L8689</td>
<td>External recharging system for battery (internal) for use with implantable neurostimulator</td>
</tr>
</tbody>
</table>

*Date of Origin: June 2010*
Regence

Medical Policy Manual

Topic: Orthognathic Surgery

Section: Surgery

Policy No: 137

Date of Origin: October 5, 2004

Last Reviewed Date: December 2016

Effective Date: January 1, 2017

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Orthognathic surgery involves the surgical manipulation of the facial skeleton, particularly the maxilla and mandible, to restore the proper anatomic and functional relationship in patients with dentofacial skeletal anomalies.[1]

Note: This policy does not address the surgical management of sleep apnea, which is addressed in a separate medical policy (see Cross References). Also, this policy does not address temporomandibular joint (TMJ) surgical interventions, which may require pre-authorization.

NOTE: Member contracts for covered services vary. Member contracts may have specific language defining congenital and developmental anomalies. Member contract language takes precedence over medical policy. A congenital anomaly is defined as an anomaly that is present at birth (e.g., cleft palate). Developmental anomalies are conditions that develop some time after birth.

MEDICAL POLICY CRITERIA

I. Orthognathic surgery for the treatment of obstructive sleep apnea in adults may be considered medically necessary when the criteria in Surgery, Policy No. 166 are met.
II. Orthognathic surgery to treat conditions other than obstructive sleep apnea may be considered medically necessary to correct jaw and craniofacial deformities when all of the following criteria (A-D) are met:

A. Significant functional impairment that is documented to be directly attributable to jaw and craniofacial deformities and to include one or more of the following:
   1. Chewing-induced trauma secondary to malocclusion
   2. Significantly impaired swallowing and/or choking due to inadequate mastication secondary to malocclusion
   3. Significant speech abnormalities (e.g., sibilant distortions or velopharyngeal distortion) which have not responded to speech therapy and are secondary to malocclusion
   4. Loss of masticatory or incisive function due to malocclusion or skeletal abnormality
   5. Airway restriction

B. Significant over- or underjet as documented by one of the following:
   1. In mandibular excess or maxillary deficiency, a reverse overjet of 3mm or greater
   2. In mandibular deficiency, an overjet of 5mm or greater
   3. Open bite of 4mm or greater
   4. Deep bite of 7mm or greater
   5. Less than six posterior teeth in functional opposition to other teeth secondary to a developmental or congenital growth abnormality (as opposed to a consequence of the loss of teeth)

C. The functional impairment and over- or underjet are not correctable with non-surgical treatment modalities.

D. The following documentation is required to determine medical necessity for orthognathic surgery:
   1. Intra-oral and extra-oral photographs
   2. Cephalometric and panoramic radiographs; when available, a written report should be submitted in addition to the radiographs
   3. Current history and physical and results of diagnostic evaluation

III. Reduction of the masseter muscle and bone may be considered medically necessary as a component of orthognathic surgery only when there is clinical documentation of the presence of masseteric hypertrophy.

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage.
Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
Orthognathic surgery in the absence of significant physical functional impairment is considered **cosmetic**, including but not limited to when used for altering or improving bite or for improvement of appearance.

**REFERENCES**


**CROSS REFERENCES**

- [Administrative Guidelines to Determine Dental vs Medical Services](#), Allied Health, Policy No. 35
- [Prefabricated Oral Appliances for Obstructive Sleep Apnea](#), Allied Health, Policy No. 36
- [Cosmetic and Reconstructive Surgery](#), Surgery, Policy No. 12
- [Surgeries for Snoring, Obstructive Sleep Apnea Syndrome and Upper Airway Resistance Syndrome in Adults](#), Surgery, Policy No. 166

<table>
<thead>
<tr>
<th>CODES</th>
<th>NUMBER</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>21085</td>
<td>Impression and custom preparation; oral surgical splint</td>
</tr>
<tr>
<td></td>
<td>21110</td>
<td>Application of interdental fixation device for conditions other than fracture or dislocation, includes removal</td>
</tr>
<tr>
<td></td>
<td>21120</td>
<td>Genioplasty; augmentation (autograft, allograft, prosthetic material)</td>
</tr>
<tr>
<td></td>
<td>21121</td>
<td>Genioplasty; sliding osteotomy, single piece</td>
</tr>
<tr>
<td></td>
<td>21122</td>
<td>Genioplasty; sliding osteotomies, two or more osteotomies (e.g., wedge excision or bone wedge reversal for asymmetrical chin)</td>
</tr>
<tr>
<td></td>
<td>21123</td>
<td>Genioplasty; sliding, augmentation with interpositional bone grafts (includes obtaining autografts)</td>
</tr>
<tr>
<td></td>
<td>21125</td>
<td>Augmentation, mandibular body or angle; prosthetic material</td>
</tr>
<tr>
<td></td>
<td>21127</td>
<td>Augmentation, mandibular body or angle; with bone graft, onlay or interpositional (includes obtaining autograft)</td>
</tr>
<tr>
<td></td>
<td>21141</td>
<td>Reconstruction midface, LeFort I; single piece, segment movement in any direction (e.g., for Long Face Syndrome), without bone graft</td>
</tr>
</tbody>
</table>

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
<table>
<thead>
<tr>
<th>CODES</th>
<th>NUMBER</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>21142</td>
<td>21142</td>
<td>Reconstruction midface, LeFort I; two pieces, segment movement in any direction, without bone graft</td>
</tr>
<tr>
<td>21143</td>
<td>21143</td>
<td>Reconstruction midface, LeFort I; three or more pieces, segment movement in any direction, without bone graft</td>
</tr>
<tr>
<td>21145</td>
<td>21145</td>
<td>Reconstruction midface, LeFort I; single piece, segment movement in any direction, requiring bone grafts (includes obtaining autografts)</td>
</tr>
<tr>
<td>21146</td>
<td>21146</td>
<td>Reconstruction midface, LeFort I; two pieces, segment movement in any direction, requiring bone grafts (includes obtaining autografts) (e.g., ungrafted unilateral alveolar cleft)</td>
</tr>
<tr>
<td>21147</td>
<td>21147</td>
<td>Reconstruction midface, LeFort I; three or more pieces, segment movement in any direction, requiring bone grafts (includes obtaining autografts) (e.g., ungrafted bilateral alveolar cleft or multiple osteotomies)</td>
</tr>
<tr>
<td>21150</td>
<td>21150</td>
<td>Reconstruction midface, LeFort II; anterior intrusion (e.g., Treacher-Collins Syndrome)</td>
</tr>
<tr>
<td>21151</td>
<td>21151</td>
<td>Reconstruction midface, LeFort II; any direction, requiring bone grafts (includes obtaining autografts)</td>
</tr>
<tr>
<td>21154</td>
<td>21154</td>
<td>Reconstruction midface, LeFort III (extracranial), any type, requiring bone grafts (includes obtaining autografts); without LeFort I</td>
</tr>
<tr>
<td>21155</td>
<td>21155</td>
<td>Reconstruction midface, LeFort III (extracranial), any type, requiring bone grafts (includes obtaining autografts); with LeFort I</td>
</tr>
<tr>
<td>21159</td>
<td>21159</td>
<td>Reconstruction midface, LeFort III (extra and intracranial) with forehead advancement (e.g., mono bloc), requiring bone grafts (includes obtaining autografts); without LeFort I</td>
</tr>
<tr>
<td>21160</td>
<td>21160</td>
<td>Reconstruction midface, LeFort III (extra and intracranial) with forehead advancement (e.g., mono bloc), requiring bone grafts (includes obtaining autografts); with LeFort I</td>
</tr>
<tr>
<td>21188</td>
<td>21188</td>
<td>Reconstruction midface, osteotomies (other than LeFort type) and bone grafts (includes obtaining autografts)</td>
</tr>
<tr>
<td>21193</td>
<td>21193</td>
<td>Reconstruction of mandibular rami, horizontal, vertical C, or L osteotomy; without bone graft</td>
</tr>
<tr>
<td>21194</td>
<td>21194</td>
<td>Reconstruction of mandibular rami, horizontal, vertical C, or L osteotomy; with bone graft</td>
</tr>
<tr>
<td>21195</td>
<td>21195</td>
<td>Reconstruction of mandibular rami and/or body, sagittal split; without internal rigid fixation</td>
</tr>
</tbody>
</table>

October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage.
Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
<table>
<thead>
<tr>
<th>CODES</th>
<th>NUMBER</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>21196</td>
<td>Reconstruction of mandibular rami and/or body, sagittal split; with internal rigid fixation</td>
</tr>
<tr>
<td></td>
<td>21198</td>
<td>Osteotomy, mandible, segmental;</td>
</tr>
<tr>
<td></td>
<td>21206</td>
<td>Osteotomy, maxilla, segmental (e.g., Wassmund or Schuchard)</td>
</tr>
<tr>
<td></td>
<td>21208</td>
<td>Osteoplasty, facial bones; augmentation (autograft, allograft, or prosthetic implant)</td>
</tr>
<tr>
<td></td>
<td>21209</td>
<td>Osteoplasty, facial bones; reduction</td>
</tr>
<tr>
<td></td>
<td>21210</td>
<td>Graft, bone; nasal, maxillary or malar areas (includes obtaining graft)</td>
</tr>
<tr>
<td></td>
<td>21215</td>
<td>Graft, bone; mandible (includes obtaining graft)</td>
</tr>
<tr>
<td></td>
<td>21230</td>
<td>Graft; rib cartilage, autogenous, to face, chin, nose or ear (includes obtaining graft)</td>
</tr>
<tr>
<td></td>
<td>21295</td>
<td>Reduction of masseter muscle and bone (eg, for treatment of benign masseteric hypertrophy); extraoral approach</td>
</tr>
<tr>
<td></td>
<td>21296</td>
<td>Reduction of masseter muscle and bone (eg, for treatment of benign masseteric hypertrophy); intraoral approach</td>
</tr>
<tr>
<td>CDT</td>
<td>D7940</td>
<td>Osteoplasty – for orthognathic deformities</td>
</tr>
<tr>
<td></td>
<td>D7941</td>
<td>Osteotomy; mandibular rami</td>
</tr>
<tr>
<td></td>
<td>D7943</td>
<td>Osteotomy; mandibular rami with bone graft; includes obtaining the graft</td>
</tr>
<tr>
<td></td>
<td>D7944</td>
<td>Osteotomy; segmented of subapical – per sextant or quadrant</td>
</tr>
<tr>
<td></td>
<td>D7945</td>
<td>Osteotomy; body of mandible</td>
</tr>
<tr>
<td></td>
<td>D7946</td>
<td>LeFort I (maxilla – total)</td>
</tr>
<tr>
<td></td>
<td>D7947</td>
<td>LeFort I (maxilla – segmented)</td>
</tr>
<tr>
<td></td>
<td>D7948</td>
<td>LeFort II or LeFort III (osteoplasty of facial bones for midface hypoplasia or retrusion); without bone graft</td>
</tr>
<tr>
<td></td>
<td>D7949</td>
<td>LeFort II or LeFort III; with bone graft</td>
</tr>
<tr>
<td></td>
<td>D7950</td>
<td>Osseous, osteoperiosteal, or cartilage graft of the mandible or facial bones – autogenous or nonautogenous, by report</td>
</tr>
<tr>
<td></td>
<td>D7995</td>
<td>Synthetic graft – mandible or facial bones, by report</td>
</tr>
</tbody>
</table>

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
<table>
<thead>
<tr>
<th>CODES</th>
<th>NUMBER</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>D7996</td>
<td>Implant – mandible for augmentation purposes (excluding alveolar ridge), by report</td>
</tr>
</tbody>
</table>

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Embolization involves occlusion of blood flow through the ovarian, internal iliac, and gonadal veins with coils, foam, or a chemical sclerosant as a treatment of pelvic congestion syndrome or varicoceles.

MEDICAL POLICY CRITERIA

NOTE: This policy does not address surgical ligation of the spermatic vein(s) or uterine artery embolization.

I  Embolization, ablation, and sclerotherapy of ovarian veins, internal iliac veins, or gonadal veins is considered investigational for the treatment of the following conditions:
   A  Pelvic congestion syndrome
   B  Varicoceles.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.
Enlarged ovarian and internal iliac veins can lead to pelvic congestion syndrome in women, and enlarged gonadal and internal iliac veins can lead to a varicoceles in men. Each are discussed separately below.

PELVIC CONGESTION SYNDROME

Pelvic congestion syndrome (PCS), also called pelvic venous incompetence, is a rare condition characterized by chronic pelvic pain. Although this condition is primarily found in women it can also be found in men. PCS is often aggravated by standing for long periods of time, and often manifests during or after pregnancy. The syndrome is thought to be associated with dilated and refluxing incompetent pelvic veins, similar to what happens in varicose veins of the legs. However, the cause of PCS is unclear. Furthermore, there are no definitive diagnostic criteria for PCS. Instead the diagnosis is generally based on a combination of symptoms, tenderness on physical exam, and documentation of pelvic vein dilation or incompetence after excluding all other causes for the nonspecific findings. Although imaging may show vein dilation or incompetence, these findings are common nonspecific findings and therefore no diagnostic.

There is no standard treatment approach for PCS, and the optimum treatment is unknown. Instead, therapy is individualized and based on symptoms. Medical therapy is generally the first line of treatment, as it is low risk and non-invasive. Other methods, such as embolization has been proposed as an alternative to surgical treatment for patients who fail medical therapy with analgesics. Embolization therapy involves the occlusion of blood flow through the ovarian and internal iliac veins with coils, glue, or chemical sclerosants. The internal iliac veins may be treated at the same time or a later date to prevent recurrence.

VARICOCELES

A varicocele is the dilation of the pampiniform plexus of the gonadal veins. Varicocele’s are present in 15 to 20% of post-pubertal males, and generally get larger over time. Most varicoceles occur in the left hemiscrotum because the left gonadal vein is one of the longest veins in the body and it enters the left renal vein at a perpendicular angle increasing pressure which can dilate the veins and cause incompetence of the valves, similar to what happens in varicose veins of the legs. Although varicoceles on the left are more common, bilateral varicoceles can occur; however, this could be caused by a possible underlying pathology warranting more investigation. Symptoms of a varicocele include dull, aching, left scrotal pain, which is often aggravated by standing for long periods of time, testicular atrophy, and decreased fertility. Although there are no clear guidelines regarding the established treatment for varicoceles, surgical ligation is the preferred first-line treatment.

EVIDENCE SUMMARY

The primary beneficial outcomes of interest for treatments of pelvic pain in both men and woman are symptom reduction and improvement in the ability to function. These are subjective outcomes that are typically associated with a placebo effect. Therefore, data from adequately...
powered, randomized controlled trials (RCTs) with sufficient long-term follow-up are required to control for the placebo effect, determine its magnitude, and to determine whether any treatment effect from provides a significant advantage over placebo or other treatment options.

**TREATMENT FOR PELVIC CONGESTION SYNDROME**

**Health Technology Assessments**

In 2016, Champaneria et al. published a health technology assessment from the National Institute for Health Research that examined the diagnosis and treatment of pelvic vein incompetence and chronic pelvic pain in women.[1] Forty studies were included in the review; six association studies, ten studies involving ultrasound, two studies involving magnetic resonance venography, 21 case series, and one poor-quality randomized trial of embolization. The authors found that there were no consistent diagnostic criteria for pelvic congestion syndrome (PCS). Although the studies have showed associations between chronic pelvic pain (CPP) and pelvic vein incompetence (PVI), the prevalence of PVI ranged widely. The authors identified that transvaginal ultrasound with doppler and magnetic resonance venography are both useful screening methods; however, there is limited data on the accuracy of these methods for PCS. Finally, although the research showed embolization provides symptomatic relief in the majority of women, these studies were small case series. The authors concluded that more research is needed to determine what the diagnostic criteria for PCS are, and the efficacy of embolization as a treatment for PCS.

**Systematic Reviews**

A 2016 systematic review by Mahmoud et al. identified 20 case series (total N=1081 patients) who underwent vein embolization for pelvic congestion syndrome.[2] The authors did not require any particular diagnostic criteria for pelvic congestion syndrome. The length of follow-up in the studies ranged from one month to six years. Seventeen studies (n=648 patients) reported the proportion of patients who reported symptom relief. Overall, 571 (88.1%) patients reported short-term symptom relief and 77 (11.9%) reported little or no relief. Seventeen studies (n=721 patients) reported symptom relief at 12 months. A total of 88.6% had symptom improvement and 13.4% reported little or no relief. Only one study used a comparison group, but patients in it received conservative treatment because they were ineligible for vein embolization therapy, so outcomes after the two interventions cannot be compared.

A systematic review by Daniels et al. (2016) assessed the effectiveness of sclerotherapy or embolization for the treatment of chronic pelvic pain.[3] The review included 21 case series and one poor-quality randomized trial. Due to the overall low quality and heterogeneity of the studies, a meta-analysis was not performed. However, the authors reported that approximately 75% of women who underwent embolization experienced early pain relief. Adverse events noted included, transient pain following foam embolization and a small (<2%) risk of coil migration.

In 2015 Hansrani et al. published a systematic review that evaluated the effectiveness of transvenous occlusion as a treatment of chronic pelvic pain.[4] Thirteen studies were included comprising 866 women. The authors noted that all 13 studies were of poor methodological quality, and most studies did not use objective outcome measures or have consistent follow-up of outcomes. Studies on embolization for treatment of PCS were rated as poor due to lack of randomization and control groups, unclear patient selection criteria, and heterogeneous outcome measures that did not permit between-study comparison or estimates of overall.
treatment effects. There was one RCT included in the review, in which embolization resulted in significantly better pain reduction than hysterectomy, but the study also had significant limitations, including but not limited to, the randomization protocol was not described, and the hysterectomy patients (bilateral compared to unilateral salpingo-oophorectomy) were not blinded to their treatment allocation, small sample size limits the ability to rule out the role of chance as an explanation of study findings, and a discrepancy between reported outcomes in text and data tables. The authors recommended that more high quality studies are needed that compare embolization, with other treatments, including surgical treatments, hormonal therapy, and other noninvasive treatments.

**Randomized Controlled Trials**

No randomized controlled trials have been published comparing embolization therapy for pelvic congestion syndrome to an alternative or sham/placebo treatment. Randomized controlled trials are especially needed in situations such as this where the primary symptom is pain, a subjective outcome for which a placebo response to treatment is likely.

**Nonrandomized Studies**

The remainder of the published literature regarding the clinical outcomes of embolization therapy consists of case series and retrospective reviews.[5-26] Collectively, conclusions concerning safety and effectiveness cannot be reached from these studies due to significant limitations in the data, including but not limited to:

- Lack of established diagnostic criteria for pelvic congestion syndrome. Without consistent criteria for patient selection it is unknown which patients are most likely to benefit, or not benefit, from treatment. Furthermore, it is unknown how results from the various case series can be applied to the overall population of patients with this condition.
- Lack of randomization and comparison groups. Failure to randomize patients to different treatment groups may introduce bias on the part of both the study participant and researchers in favor of the new technology. As noted above, for pain treatments, a comparator (preferably sham treatment) is necessary, in order to guard against this bias and to distinguish treatment from placebo effects.
- Retrospective design and failure to control for other treatments. Retrospective study designs do not allow for control of co-treatments or confounding factors that may influence results. This design may also introduce bias to interpretation of results. Control for additional factors, such as other medical therapies, is necessary to isolate treatment response to embolization therapy.
- Failure to define relevant study endpoints. Bias may also be introduced by failure to define study endpoints and treatment success prior to commencement of the study.

**Adverse Effects**

The following adverse effects associated with embolization of the uterine and internal iliac veins, though uncommon, have been reported in the literature.[5,13]

- Embolization of coils to the pulmonary circulation
- Embolization of coils to the renal circulation
- Accidental embolization of glue fragments
- Perforations of the ovarian vein with extravasation of contrast
- Transient cardiac arrhythmia
Treatment of Varicoceles

Systematic Reviews

In 2012 Kroese et al. published results from a systematic review and meta-analysis that examined the effect of treatment, surgery or embolization, for varicoceles in subfertile men.[27] Ten studies were included in the review, which comprised 894 men. The authors concluded that there is evidence to suggest treatment improves a couple’s chance of pregnancy; however, findings are inconclusive. Furthermore, the available evidence is of low quality and limited to men from couples with subfertility problems. Therefore further research is needed to determine the efficacy of treatment, surgery or embolization, for the treatment of varicoceles.

Randomized-Controlled Trials

No randomized controlled trials have been published comparing embolization therapy for the treatment of varicoceles to an alternative or sham/placebo treatment. Randomized controlled trials are especially needed in situations such as this where the primary symptom is pain, a subjective outcome for which a placebo response to treatment is likely.

Nonrandomized studies

The remainder of the published literature regarding the clinical outcomes of embolization therapy consists of case series and retrospective reviews.[28-45] Collectively, conclusions concerning safety and effectiveness cannot be reached from these studies due to significant limitations in the data.

PRACTICE GUIDELINE SUMMARY

PELVIC CONGESTION SYNDROME

American Congress of Obstetricians and Gynecologists

No relevant policy positions on embolization for treating pelvic congestion syndrome were identified on the American Congress of Obstetricians and Gynecologists (ACOG) website.[46]

Society for Vascular Surgery (SVS) and the American Venous Forum

The 2011 Society for Vascular Surgery (SVS) and the American Venous Forum (AVF) guidelines for the care of patients with varicose veins and associated chronic venous diseases provided a Grade 2B recommendation in favor of coil embolization, plugs, or transcatheter sclerotherapy for treatment of PCS. A Grade 2B recommendation is defined as a weak recommendation based on medium quality evidence.[47]

SUMMARY

There is not enough research to show that embolization, ablation, or sclerotherapy improves long term health outcomes for people with pelvic congestion syndrome or varicoceles, compared to other forms of therapy. Therefore, embolization, ablation, or sclerotherapy of ovarian veins, internal iliac veins, or gonadal veins are considered investigational for the treatment of pelvic congestion syndrome or varicoceles.


### CODES

There are no specific codes for ovarian and internal iliac vein embolization; however, the following codes may be used:

<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>36012</td>
<td>Selective catheter placement, venous system: second order or more selective, branch (eg, left adrenal vein, petrosal sinus)</td>
</tr>
<tr>
<td></td>
<td>37241</td>
<td>Vascular embolization or occlusion, inclusive of all radiological supervision and interpretation, intraprocedural roadmapping, and imaging guidance necessary to complete the intervention; venous, other than hemorrhage (eg, congenital or acquired venous malformations, venous and capillary hemangiomias, varices, varicoceles)</td>
</tr>
<tr>
<td></td>
<td>75894</td>
<td>Transcatheter therapy, embolization, any method, radiological supervision and interpretation</td>
</tr>
</tbody>
</table>

**HCPCS** None

*Date of Origin:* October 2005
Medical Policy Manual

Topic: Percutaneous Angioplasty and Stenting of Veins  
Date of Origin: January 1996

Section: Surgery  
Last Reviewed Date: December 2016

Policy No: 109  
Effective Date: January 1, 2017

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Dilation and/or stent placement in veins is intended to restore blood flow in a narrowed or collapsed vein.

Background

Percutaneous Transluminal Angioplasty of the Veins

Percutaneous transluminal angioplasty (PTA) of the veins is a procedure that has been used as an alternative to open vascular surgery in order to restore blood flow through narrowed veins. Techniques may include balloon angioplasty, laser angioplasty, and stent placement.

Intravascular Stents

Intravascular stents are used as an adjunct to angioplasty to prevent vessel wall collapse. They can be placed via transluminal catheters or placed with catheters during open vascular procedures. Drug-eluting stents are intended to prevent restenosis by reducing the growth of neointimal tissue. A number of different drugs are being evaluated for this use, including paclitaxel and sirolimus. These stents are coated with a mixture of synthetic polymers blended with the drug. A second coat of drug-free polymers

October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
is then added to serve as a diffusion barrier, thus allowing the gradual release of drug to the precise site of interest while avoiding systemic side effects.

Iliac Vein Compression Syndrome

Iliac vein compression syndrome (IVCS) is deep vein thrombosis (DVT) that occurs as a result of compression of the left common iliac vein between the overlying right common iliac artery and the body of the fifth lumbar vertebra. This syndrome is relatively uncommon. If DVT occurs, it is treated with anticoagulation therapy. However, the underlying mechanical compression must be treated with surgery or stent placement. Left untreated it may result in recurrent DVT or postthrombotic syndrome (PTS) characterized by chronic swelling and pain in the affected extremity. Some patients also develop varicosities and stasis ulcers. This condition may also be referred to by other terms including but not limited to May-Thurner syndrome, nonthrombotic iliac vein lesions (NIVL), and Cockett syndrome.

Proximal Upper Extremity Venous Thrombosis

Proximal upper extremity venous thrombosis occurs as a result of mechanical compression of the subclavian vein at the thoracic outlet. The natural history of the disorder is typically one of chronic venous obstruction with development of a painful, swollen extremity.[1,2] Thrombosis may affect the brachiocephalic, subclavian, and/or axillary veins. Typical management of this condition involves thrombolysis and surgical decompression after a variable interval of oral anticoagulation. Venous stent placement may be helpful in maintaining patency of the vein following thoracic outlet decompression surgery that includes first rib resection. This condition may also be referred to by other terms including but not limited to axillary-subclavian venous thrombosis, effort thrombosis, Paget-Schroetter syndrome, or venous thoracic outlet syndrome.

Idiopathic Intracranial Hypertension

Idiopathic intracranial hypertension (IIH) is characterized by elevated intracranial pressure (ICP). The most common symptoms are headache and papilledema. Other symptoms include transient visual obscurations, pulsatile tinnitus, diplopia, and sustained visual loss. Initial evaluation of patients presenting with headache and papilledema consists of CT or MRI scan for possible hydrocephalus or tumor. Occlusion of the venous sinus, particularly the transverse sinus, is considered an uncommon cause of increased ICP. There has been some debate as to whether this occlusion is the cause or the effect of ICP. The hypothesis is that obstruction of venous return decreases venous outflow from the brain which also decreases cerebrospinal fluid (CSF) outflow with subsequent increase in intracranial CSF pressure. Medical treatment includes medications that lower CSF production and/or therapeutic lumbar puncture. Since most patients with IIH are obese, weight loss is commonly recommended. If medical treatment fails to control IIH, surgical treatments include ventriculoperitoneal shunting, optic nerve sheath fenestration (optic nerve decompression), and subtemporal decompression. Angioplasty with stenting has been proposed for maintaining venous sinus patency. IIH may also be referred to as pseudotumor cerebri or benign intracranial hypertension, though these terms are considered inadequate and IIH is the preferred term.

Chronic Cerebrospinal Venous Insufficiency in Multiple Sclerosis

Multiple sclerosis (MS) is generally considered a chronic inflammatory demyelinating disease of the central nervous system (brain, spinal cord, and optic nerve) believed to be triggered by an autoimmune response to myelin. However, in part due to the periventricular predilection of the lesions of MS,
vascular etiologies (CCSVI) have also been considered. The core foundation of this vascular theory is that venous drainage from the brain is abnormal due to outflow obstruction in the draining jugular vein and/or azygos veins. This abnormal venous drainage, which is characterized by special ultrasound criteria, is said to cause intracerebral flow disturbance or outflow problems that lead to periventricular deposits. In the CCSVI theory, these deposits have a similarity to the iron deposits seen around the veins in the legs of patients with chronic deep vein thrombosis. Balloon dilatation, with or without stenting, has been proposed as a means to treat the outflow problems, thereby alleviating CCSVI and MS complaints.

**Regulatory Status**

While there are several types of stents that are approved by the U.S. Food and Drug Administration (FDA) for improvement of outflow for arteriovenous (A-V) access grafts in hemodialysis patients, and for the creation of intrahepatic shunt connections between the portal venous system and hepatic vein [i.e., transjugular intrahepatic portosystemic shunt (TIPS)], there are currently no stents with FDA approval for use in veins for any other indications.

In May 2012, the FDA issued an alert concerning the potential for adverse events following endovascular interventions to treat chronic cerebrospinal venous insufficiency (CCSVI).

Reports of adverse events obtained by the FDA included death, stroke, detachment and/or migration of stents, vein damage, thrombosis, cranial nerve damage, and abdominal bleeding. This alert included the caveat that clinical trials of this procedure require FDA approval and an investigational device exemption due to potential for harms.

*Note:* This policy addresses percutaneous angioplasty and stenting of **veins** only. This policy does **not** address percutaneous angioplasty and stenting of peripheral arteries, including repair of aneurysms, which are considered medically necessary. Carotid and intracranial vessels are addressed in separate policies (see Cross References below).

---

**MEDICAL POLICY CRITERIA**

1. Percutaneous transluminal angioplasty, with or without stenting, may be considered **medically necessary** for the treatment of venous vascular stenoses in the following instances:

   A. Stenotic lesions of arteriovenous dialysis fistulas and grafts, and ipsilateral venous stenosis in the outflow of a functioning dialysis fistula and graft

   B. Superior vena cava syndrome with significant symptoms, from either extrinsic compression or intrinsic stenosis/occlusion [when standard treatments (radiation and/or chemotherapy) have failed]

   C. Left iliac vein compression syndrome (May-Thurner Syndrome)

   D. As an adjunct to prior or concurrent ipsilateral first rib resection for proximal upper extremity venous thrombosis due to persistent extrinsic compression (Paget-Schroetter syndrome) documented by pre-procedure imaging (i.e., ultrasound, venography, CT, or MRI)
II. The use of angioplasty and/or endoprostheses for creation of intrahepatic shunt connections between the portal venous system and hepatic vein may be considered medically necessary.

III. Percutaneous transluminal angioplasty, with or without stenting, is considered investigational for all other venous indications, including but not limited to:

A. Deep vein thrombosis that is not related to upper extremity venous compression or iliac vein compression syndrome (I.C.-D.) (eg, inferior vena cava, iliac, lower extremity)

B. Chronic cerebrospinal venous insufficiency in multiple sclerosis or other conditions

C. Venous sinus obstruction or occlusion in idiopathic intracranial hypertension

SCIENTIFIC EVIDENCE

The following discussion focuses on the investigational indications noted in III.A-C above.

Deep Vein Thrombosis (DVT)

There are several objectives for treatment of venous thromboembolism including:

- Prevention of pulmonary embolism;
- Restoration of unobstructed blood flow through the thrombosed vein;
- Preservation of venous valve function; and
- Prevention of recurrent thrombosis.

The current standard of treatment for achieving these goals is anticoagulant therapy (i.e., intravenous unfractionated heparin) to achieve a therapeutic partial thromboplastin time (PTT). After completion of an initial course of anticoagulation therapy, patients with venous thromboembolism (VTE) require continuing therapy to prevent recurrence. Thus, anticoagulation therapy is the standard against which percutaneous transluminal angioplasty (PTA) with or without stenting must be compared in order to evaluate the safety, efficacy, and final health outcomes. In addition, long-term follow-up is needed to determine the rates of restenosis, device failure, reoperation, and VTE recurrence.

The following literature appraisal is focused on the published evidence for DVT that is not related to left iliac vein compression syndrome or proximal upper extremity venous thrombosis.

Systematic Reviews

No systematic reviews were identified.

Randomized Controlled Trials (RCTs)

There are no randomized controlled clinical trials in which PTA with or without stenting was compared to standard medical management of DVT.

Nonrandomized Studies

October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
• The bulk of the current literature investigating thrombolysis followed by angioplasty and stenting is limited to small (n<50), non-randomized, non-comparative retrospective reviews and case series of short- to medium-term duration.[5-9]
• The majority of studies are for DVT related to extrinsic compression (e.g., May-Thurner syndrome), or have heterogeneous patient populations that include both compression-related and noncompression-related DVT.

**Idiopathic Intracranial Hypertension (IIH)**

Studies for the diagnosis and treatment of IIH must answer the following questions:

1. Is venous sinus occlusion the cause or the effect of increased intracranial pressure (ICP)?
2. Is venous PTA with or without stenting safe and effective in reducing ICP compared with conventional treatment?

To assess the effectiveness and safety of intracranial venous stenting as a treatment of IIH, health outcomes must be compared with current standard treatments. The ideal clinical trial design is random allocation of similar patients to active or sham venous angioplasty, and/or conventional medical or surgical treatments.

**Systematic Reviews**

A 2015 updated Cochrane review was conducted to assess interventions for IIH that included RCTs in which any intervention used to treat IIH had been compared to placebo or another form of treatment.[10] Stenting of the transverse intracerebral venous sinus was assessed as a treatment, however the reviewers found no studies that met their inclusion criteria due to the lack of a control group for comparison. The review excluded five small case series, one retrospective review and two small clinical trials.

A 2014 systematic review of various treatments for IIH found only case series, of which 30 had extractable data.[11] Of the 332 total patients, 88 had venous sinus stenting. However, the studies only reported secondary outcomes related to symptoms of headache, papilledema, and visual acuity. The primary outcome of increased intracranial pressure was not reported. The authors concluded that the evidence was insufficient to recommend for or against any treatment modalities for IIH.

**Randomized Controlled Trials**

There are no randomized controlled clinical trials in which PTA with or without stenting was compared to standard medical or surgical management of IIH.

**Nonrandomized Studies**

Current evidence is limited to small retrospective reviews and case series. All but one of these studies included 18 or fewer subjects.[12-15] The largest study was a retrospective review of 52 patients at a single center who underwent stenting due to IIH unresponsive to maximum acceptable medical treatment.[16] The follow-up period ranged from 2 months to 9 years. All 52 patients were reported to have immediate elimination of the transverse sinus stenosis gradient and rapid improvement in IIH symptoms including resolution of papilledema. Six patients had relapse of symptoms (headache) and increased venous pressure with recurrent stenosis adjacent to the previous stent. In these patients, an additional stent was placed, with response similar to that following the first stent placement.
Chronic Cerebrospinal Venous Insufficiency (CCSVI) in Multiple Sclerosis (MS)

Systematic Reviews

A Cochrane review\cite{17} and five systematic reviews\cite{18-22} with critical analyses of the current literature concluded that there is insufficient evidence to verify a relationship between CCSVI and MS. The authors noted the high degree of heterogeneity between study outcomes, sensitivity, and specificity, and marked variability of odds ratios.

Two meta-analyses\cite{23,24} reported outcomes after exclusion of outlier studies (e.g., studies with disproportionately high ORs and/or potential bias). Tsivgoulis et al. (2014) reported on the association between CCSVI and MS and included 19 studies with a total of 1250 MS patients and 899 healthy controls.\cite{23} When data from all 19 studies were pooled, CCSVI was associated with MS with an odds ratio (OR) of 8.35 (95% confidence interval [CI], 3.44 to 20.31; p<0.001). However, in additional sensitivity analyses, the OR associating CCSVI and MS decreased. In the most conservative sensitivity analysis, which excluded 8 outlier studies, MS was not associated with CCSVI with an OR of 1.35 (95% CI, 0.62 to 2.93; p=0.453). The Zwischenberger et al. meta-analysis of 13 studies with a total of 1141 MS patients and 738 healthy controls reported CCSVI and MS was associated with MS (OR 2.57; p<0.001).\cite{24} In a subsequent analysis of 9 studies with 4 outliers (studies with disproportionately high ORs) removed, the OR decreased, but still associated CCSVI with MS.

A systematic review of the association between CCSVI and MS was published in 2011 by Laupacis et al.\cite{21} This review included 8 studies that used ultrasound to diagnose CCSVI by the Zamboni criteria and compared the rate of CCSVI in patients with MS to those without MS. These studies were mostly small, with the median number of patients with MS of 50. A large degree of heterogeneity existed across studies in the rate of CCSVI among MS patients. Two smaller studies reported a rate of 0% for CCSVI in a total of 20 and 56 patients with MS. In contrast, the original study by Zamboni et al. reported a 100% rate of CCSVI in 109 patients with MS. A small study of 25 patients also reported a very high rate of CCSVI at 84% (21/25). There was no obvious reason identified for this large discrepancy in CCSVI rates; the authors hypothesized that the most likely reason was variability in ultrasound technique and interpretation. The analysis suggested a significant association of CCSVI with MS in combined analysis, with an OR of 13.5 (95% CI, 2.6 to 71.4). A substantial degree of heterogeneity existed in this measure as well, with a reported I2 of 89%. Several sensitivity analyses showed marked variability of the OR from a low of 3.7 to more than 58,000. However, in all cases the association of CCSVI with MS remained significant.

Another systematic review published in 2011 included a smaller number of studies (N=4) but reached conclusions similar to the other analyses.\cite{22} The rate of CCSVI in MS patients ranged from 7% to 100%, and the rate in non-MS patients ranged from 2% to 36%. A significant association was detected between MS and CCSVI but with a high degree of heterogeneity (I2=96%) and an OR for association that varied widely, from approximately 2 to more than 26,000.

Randomized Controlled Trials (RCT)

In 2014, Siddiqui et al. published results from a prospective, double-blind, sham-controlled randomized clinical trial (RCT) of venous angioplasty in MS patients with CCSVI.\cite{25} This trial enrolled 9 patients in intervention group and 10 in the sham-controlled group. All patients met the criteria for diagnosis of CCSVI.\cite{26} The primary end points of the trial included safety at 24 hours and 30 days postangioplasty;
greater than 75% restoration of venous outflow at 30 days; the presence of new MS lesions; and relapse rate over 6 months. Secondary end points included changes in disability scores, brain volume, cognitive test scores, and quality-of-life measures. All patients tolerated the procedures well; no operative or postoperative complications were identified. One patient in the angioplasty group experienced an episode of symptomatic bradycardia. No significant differences were observed in venous outflow characteristics between the treated and control groups, nor were any significant improvements observed in clinical disease scores among treated patients compared with controls. The results of this RCT are limited by the small number of patients. However, the failure to show a beneficial effect of venous angioplasty on MS activity supports a lack of efficacy for this treatment.

**Nonrandomized Studies**

The studies that focused on the potential relationship between CCSVI and MS reported varying and contradictory outcomes. For example, while Zamboni et al. and other authors\[27-30\] reported a strong association between CCSVI and MS, numerous studies have reported insignificant or no difference in the prevalence of CCSVI in MS patients compared to healthy controls, or no association between CCSVI and MS occurrence or symptoms[26,29,31-37].

The studies that focused on outcomes of PTA with or without stent placement reported few adverse events, but mixed efficacy outcomes.[38-43] For example, while Zamboni et al.[39] reported significant improvement in all measures for patients with relapsing-remitting MS, Kostecki and colleagues reported a significant improvement only in heat intolerance and fatigue severity 6 months post endovascular treatment.[38] No trials were found that compared PTA with concurrent control groups. All authors noted the need for well-designed randomized clinical trials. Many authors asserted that PTA with or without stenting in these patients should not be performed outside the clinical trial setting.

**Adverse Events**

Burton et al. described five patients who had undergone venoplasty and presented with complications of the procedure.[44] The complications were internal jugular vein stent thrombosis, cerebral sinovenous thrombosis, stent migration, cranial nerve injury, and injury associated with venous catheterization. There was not a denominator in these studies to determine the rate of these events.

Petrov et al. reported on the safety profile of 495 venoplasty procedures performed in 461 patients with MS, including 98 stent implantations.[40] There were no deaths, major bleeding events, or acute exacerbations of MS. The most common procedure-related complication was vein dissection, which occurred in 3.0% of cases. Other complications included cardiac arrhythmias (1.2%), groin hematoma (1.0%), vein rupture (0.4%), and acute stent thrombosis (1.6%).

Mandato et al. reported adverse events within 30 days of endovascular intervention for 240 patients with MS over an 8-month period.[45] Neck pain occurred in 15.6% of patients, most commonly following stent implantation. Headache occurred in 8.2% of patients and was persistent past 30 days in 1 patient (0.4%). Intraprocedural arrhythmias occurred in 1.3%, and 1 patient was diagnosed with a stress-induced cardiomyopathy following the procedure.

An FDA alert issued in May 2012 reported the potential for adverse events following endovascular interventions for MS. Reports of adverse events obtained by FDA included death, stroke, detachment and/or migration of stents, vein damage, thrombosis, cranial nerve damage, and abdominal bleeding.
This alert included the caveat that clinical trials of this procedure require FDA approval and an investigational device exemption because of the potential for harms.

**Clinical Practice Guidelines**

**Deep Vein Thrombosis**

Two consensus-based clinical practice guidelines from the Society of Interventional Radiology and the American Heart Association, respectively, provided evidence appraisals and noted a benefit in venous stenting for DVT.\[^{47,48}\] However, the majority of the references listed were related to May-Thurner syndrome which is caused by extrinsic compression for which stenting is considered medically necessary. Both guidelines graded the available evidence as very limited.

**Society of Vascular Surgery / American Venous Forum**

In the 2014 joint guidelines published by Society of Vascular Surgery and American Venous Forum on the management of proximal chronic total venous occlusion/severe stenosis.\[^{49}\] The guideline states the following:

\[
\text{In a patient with inferior vena cava or iliac vein chronic total occlusion or severe stenosis, with or without lower extremity deep venous reflux disease, that is associated with skin changes at risk for venous leg ulcer (C4b), healed venous leg ulcer (C5), or active venous leg ulcer (C6), we recommend venous angioplasty and stent recanalization in addition to standard compression therapy to aid in venous ulcer healing and to prevent recurrence.}
\]

This was a grade 1 recommendation (strong) but the evidence was considered low/very low quality which was primarily focused on May-Thurner syndrome.

**American College of Radiology (ACR)**

The 2012 ACR Appropriateness Criteria® for radiologic management of lower extremity venous insufficiency recommendation did not address angioplasty or stenting for these indications.\[^{50}\] However, they suggest that patients with venous insufficiency and associated venous occlusion or stenosis of the common iliac vein may require venous recanalization with angioplasty and stenting as an adjunctive treatment, based on three case reports and one small retrospective analysis.

**Chronic Cerebrospinal Venous Insufficiency (CCSVI) in Multiple Sclerosis (MS)**

**Society of Interventional Radiology (SIR)**

In 2010 the SIR published a position statement on the association of CCSVI with MS and the efficacy of endovascular treatments.\[^{51}\] Their recommendations included the following statements:

- At present, SIR considers the published literature to be inconclusive on whether CCSVI is a clinically important factor in the development and/or progression of MS, and on whether balloon angioplasty and/or stent placement are clinically effective in patients with MS.
- SIR strongly supports the urgent performance of high-quality clinical research to determine the safety and efficacy of interventional MS therapies, and is actively working to promote and expedite the completion.
Summary

There is not enough research to show that percutaneous venous angioplasty with or without stenting improves health outcomes for patients with deep vein thrombosis that is not related to upper extremity venous compression or iliac vein compression syndrome, chronic cerebrospinal venous insufficiency, or venous sinus obstruction or occlusion in idiopathic intracranial hypertension. Many studies have limitations including small sample sizes, lack of an appropriate comparator group, lack of long-term data, and different patient populations. In addition, there are no evidence-based clinical practice guidelines that strongly recommend venous angioplasty with or without stenting for these indications. Therefore, this procedure is considered investigational for all conditions that do not meet the policy medical necessary criteria.

REFERENCES


**CROSS REFERENCES**

*Extracranial Carotid Angioplasty/Stenting*, Surgery, Policy No. 93

*Endovascular Angioplasty and/or Stenting for Intracranial Arterial Disease (Atherosclerotic and Aneurysms)*, Medical Policy, Surgery, Policy No. 141

<table>
<thead>
<tr>
<th>CODES</th>
<th>NUMBER</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>35476</td>
<td>Transluminal balloon angioplasty, percutaneous; venous (Deleted 1/1/2017)</td>
</tr>
<tr>
<td></td>
<td>36481</td>
<td>Percutaneous portal vein catheterization by any method</td>
</tr>
<tr>
<td></td>
<td>36901</td>
<td>Introduction of needle(s) and/or catheter(s), dialysis circuit, with diagnostic angiography of the dialysis circuit, including all direct puncture(s) and catheter placement(s), injection(s) of contrast, all necessary imaging from the arterial anastomosis and adjacent artery through entire venous outflow including the inferior or superior vena cava, fluoroscopic guidance, radiological supervision and interpretation and image documentation and report</td>
</tr>
</tbody>
</table>

October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
<table>
<thead>
<tr>
<th>CODES</th>
<th>NUMBER</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>36902</td>
<td>36903</td>
<td>;with transluminal balloon angioplasty, peripheral dialysis segment, including all imaging and radiological supervision and interpretation necessary to perform the angioplasty and transcatheter placement of intravascular stent(s), peripheral dialysis segment, including all imaging and radiological supervision and interpretation necessary to perform the stenting, and all angioplasty within the peripheral dialysis segment</td>
</tr>
<tr>
<td>36904</td>
<td>Percutaneous transluminal mechanical thrombectomy and/or infusion for thrombolysis, dialysis circuit, any method, including all imaging and radiological supervision and interpretation, diagnostic angiography, fluoroscopic guidance, catheter placement(s), and intraprocedural pharmacological thrombolytic injection(s)</td>
<td></td>
</tr>
<tr>
<td>36905</td>
<td>;with transluminal balloon angioplasty, peripheral dialysis segment, including all imaging and radiological supervision and interpretation necessary to perform the angioplasty</td>
<td></td>
</tr>
<tr>
<td>36906</td>
<td>;with transcatheter placement of intravascular stent(s), peripheral dialysis segment, including all imaging and radiological supervision and interpretation necessary to perform the stenting, and all angioplasty within the peripheral dialysis circuit</td>
<td></td>
</tr>
<tr>
<td>36907</td>
<td>Transluminal balloon angioplasty, central dialysis segment, performed through dialysis circuit, including all imaging and radiological supervision and interpretation required to perform the angioplasty (List separately in addition to code for primary procedure)</td>
<td></td>
</tr>
<tr>
<td>36908</td>
<td>Transcatheter placement of intravascular stent(s), central dialysis segment, performed through dialysis circuit, including all imaging radiological supervision and interpretation required to perform the stenting, and all angioplasty in the central dialysis segment (List separately in addition to code for primary procedure)</td>
<td></td>
</tr>
<tr>
<td>36909</td>
<td>Dialysis circuit permanent vascular embolization or occlusion (including main circuit or any accessory veins), endovascular, including all imaging and radiological supervision and interpretation necessary to complete the intervention (List separately in addition to code for primary procedure)</td>
<td></td>
</tr>
<tr>
<td>37238</td>
<td>Transcatheter placement of an intravascular stent(s), open or percutaneous, including radiological supervision and interpretation and including angioplasty within the same vessel, when performed; initial vein</td>
<td></td>
</tr>
<tr>
<td>37239</td>
<td>; each additional vein (List separately in addition to code for primary procedure)</td>
<td></td>
</tr>
</tbody>
</table>

October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
<table>
<thead>
<tr>
<th>CODES</th>
<th>NUMBER</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>37248</td>
<td>Transluminal balloon angioplasty (except dialysis circuit), open or percutaneous, including all imaging and radiological supervision and interpretation necessary to perform the angioplasty within the same vein; initial vein</td>
</tr>
<tr>
<td></td>
<td>37249</td>
<td>Each additional vein (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td></td>
<td>75978</td>
<td>Transluminal balloon angioplasty, venous (eg, subclavian stenosis), radiological supervision and interpretation (Deleted 1/1/2017)</td>
</tr>
<tr>
<td>HCPCS</td>
<td>C2623</td>
<td>Catheter, transluminal angioplasty, drug-coated, non-laser</td>
</tr>
</tbody>
</table>
Percutaneous Tibial Nerve Stimulation

Effective: June 1, 2017

Next Review: May 2018
Last Review: May 2017

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Percutaneous tibial nerve stimulation (PTNS) is a technique of electrical neuromodulation for the treatment of voiding dysfunction and fecal incontinence in patients who have failed behavioral and/or pharmacologic therapies.

MEDICAL POLICY CRITERIA

Note:

- Stimulation of the sacral nerve as a treatment of incontinence is discussed in a separate Medical Policy (see Cross References).
- Pelvic floor stimulation as a treatment of urinary incontinence refers to electrical stimulation of the pudendal nerve and is addressed in a separate Medical Policy (see Cross References).

Percutaneous tibial nerve stimulation is considered investigational for all indications, including but not limited to the following:

A. Urinary dysfunction, including but not limited to overactive bladder syndrome, neurogenic bladder, urinary frequency, urgency, incontinence and retention

B. Fecal incontinence
NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

CROSS REFERENCES

1. Pelvic Floor Stimulation as a Treatment of Urinary Incontinence, Allied Health, Policy No. 4
2. Biofeedback, Allied Health, Policy No. 32
3. Sacral Nerve Modulation/Stimulation for Pelvic Floor Dysfunction, Surgery, Policy No. 134

BACKGROUND

Percutaneous tibial nerve stimulation (PTNS, also known as posterior tibial nerve stimulation) is a technique of electrical neuromodulation primarily for the treatment of voiding dysfunction in patients who have failed behavioral and/or pharmacologic therapies. The posterior tibial nerve is derived from the lumbar-sacral nerves (L4-S3) which control the bladder detrusor and perineal floor. The goal of PTNS is to alter the function of the posterior tibial nerve to improve voiding function and control. Voiding dysfunction includes urinary frequency, urgency, incontinence, and nonobstructive retention. Urgency symptoms and/or urge incontinence may also be referred to as overactive bladder (OAB). Common causes of voiding dysfunction are pelvic floor dysfunction (from pregnancy, childbirth, surgery, etc.), inflammation, interstitial cystitis, medication (e.g., diuretics and anticholinergics), obesity, psychogenic factors and disease (e.g., multiple sclerosis, spinal cord injury, detrusor hyperreflexia, diabetes with peripheral nerve involvement).

PTNS was developed as a less-invasive treatment alternative to traditional sacral root neuromodulation which has been successfully used in the treatment of urinary dysfunction, but requires implantation of a permanent device. The procedure for PTNS consists of the insertion of a needle above the medial malleolus into the posterior tibial nerve followed by the application of low voltage (10mA, 1-10 Hz frequency) electrical stimulation which produces sensory and motor responses (i.e., a tickling sensation and plantar flexion or fanning of all toes). Noninvasive PTNS has also been delivered with surface electrodes. PTNS studies have been designed as 30-minute sessions given weekly for 10-12 weeks. Consideration has been given to increasing the frequency of treatments to three times per week to speed achievement of desired outcomes. A shorter initial weekly treatment period might be as effective as the 12 week regimen which being studied. However, an optimal treatment protocol has not been established.

PTNS must be distinguished from acupuncture with electrical stimulation. In electrical acupuncture, needles are also inserted just below the skin, but the placement of needles is based on specific theories regarding energy flow throughout the human body. Thus, in PTNS, the location of stimulation is directly in the posterior tibial nerve rather than using the theories of energy flow that guide placement of stimulation for acupuncture.

REGULATORY STATUS

The Urgent® PC Neuromodulation System (Uroplasty, Inc.) – Formerly called the Stoller Afferent Nerve Stimulator (PerQ SANS System), received U.S. Food and Drug Administration (FDA) 510(k) approval for the treatment of overactive bladder (OAB) and associated symptoms of urinary urgency, urinary frequency, and urge incontinence.
In order to isolate the specific therapeutic effects of posterior tibial nerve stimulation (PTNS) and adequately control for placebo effects and individual patient differences (clinical and demographic, known and unknown), well-designed randomized clinical trials (RCTs) that compare PTNS with the current standard of care and sham treatment are needed. The RCT is the most rigorous and reliable study design for demonstrating a causal relationship between the therapy under investigation and the health outcomes of interest. The RCT study design is important to understand whether an intervention such as PTNS can positively impact the health outcomes of patients with voiding dysfunction.

**NON-NEUROGENIC URINARY INCONTINENCE INCLUDING OVERACTIVE BLADDER**

**Systematic Reviews and Technology Assessments**

In 2014, BCBSA published an updated TEC assessment which concluded that PTNS met the TEC criteria for treatment of voiding dysfunction. The Assessment included six RCTs which are described in more detail in the RCT section of this policy. The 2014 assessment concluded that the RCT evidence supports the short-term efficacy of PTNS compared with a placebo when applied during a standard 12-week regimen.

This conclusion was based upon two short-term sham controlled trials and four RCTs which compared PTNS to active intervention, which included antimuscarinics, ES, or Kegel exercises. Only one of these trials was noted as being of “high” quality, while four were noted of being of “poor” quality due to various limitations which including lack of blinding, significant dropout rates, no sham control group, suboptimal administration of comparison medication, and small sample sizes in six RCTs.

Evidence is still lacking regarding the efficacy of PTNS past a 12-week regimen; however, 12- to 36-month evidence appears consistent in direction with 12-week data outcomes. This conclusion is based upon data provided by two extension studies regarding PTNS maintenance effects. Responders were followed for 12 months in one study and 36 months in another; however, patients in the control groups were not followed past 12 weeks, limiting comparison between groups. In addition, there was a high drop-out rate in both extension studies which limited the ability to control for placebo affects or draw conclusions about the long-term efficacy of PTNS treatment.

In 2013, the National Institute for Clinical Excellence (NICE) published a technology assessment for management of urinary incontinence in women. The authors concluded that although PTNS was offered as a conservative treatment for OAB, there is limited evidence it is effective. Additional studies must establish cost-effectiveness and/or study groups of patients who are not eligible or who did not have good outcomes from botulinum toxin A, percutaneous sacral nerve stimulation or OAB drug treatment.

In 2012, the Agency for Healthcare Research and Quality (AHRQ) Effective Health Care Program published a comparative effectiveness review on the broader topic of nonsurgical treatments for urinary incontinence in adult women. The review identified four reports of RCTs comparing PTNS with no active treatment in patients with OAB. Two of the four articles reported 12 week results of the sham-controlled SUmiT trial; one of these included a subgroup of SUmiT participants and was only published as an abstract. The other two studies consisted of the Finazzo-Agro et al. RCT which reported outcomes at four weeks and the Schriner and
colleagues et al. RCT[5] which reported outcomes at 12 weeks. The AHRQ report included a pooled analysis of data from three studies that found statistically significantly greater improvement in urinary incontinence in the PTNS compared to control group (RR: 1.9, 95% CI: 1.1 to 3.2). This pooled analysis included a total of 405 patients; 220 in the SUltit trial, 150 in the SUltit trial sub-analysis and 35 in the Finazzo-Agro trial. A limitation of the analysis was that the 150 patients in the SUltit sub-analysis were included twice. The authors did not discuss evidence on the efficacy of PTNS beyond 12 weeks.

In addition, several systematic reviews (SRs) and meta-analysis have been published regarding the use of PTNS as a treatment for OAB, reporting a positive success rate of 37-82%[12], 54-93%[13], 37-100%[14] and 36.7-80%[15], when compared to placebo or medication. Some of the trials included in these reviews are RCTs addressed separately within this policy or were non-randomized, observational studies. All studies used in each of the reviews were limited by short-term follow-up of 12 weeks and relatively small sample size[12,16,17] between 16 and 32 patients. Although the authors reported promising results for use of PTNS in patients with OAB, many stated that larger, long-term, RCTs are needed.[13-17]

Randomized Controlled Trials

Boudaoud (2015) reported on 20 children with OAB who were randomized to 12 weeks of treatment with PTNS (n=11) or a sham intervention (n=9).[18] At the end of the treatment period, there were no statistically significant differences between groups on outcomes, including the proportion of patients with “good” versus “poor” urinary scores (p=0.65). (A 13-point scale was used; a “poor score” was defined as a decrease of 3 or fewer points post-treatment and a “good” score was a decrease of four to six points.)

Preyer (2015) published a non-blinded study comparing 12 weeks of PTNS versus torderodine in 36 women with OAB.[19] Post-treatment, there were no significant differences between groups on the reduction of incontinence episodes in 24 hours (p=0.89) or quality of life (p=0.07).

The following is a summary of the six RCTs analyzed in the 2014 BCBSA TEC assessment cited above.

Peters (2009) published an industry-sponsored non-blinded comparison of PTNS and extended-release torderodine (Detrol LA) for treatment of overactive bladder syndrome (the OrBIT trial).[20] The study included 100 patients, over 90% women, with at least eight voids per 24 hours (mean 12.3). The primary outcome was the non-inferiority of PTNS in the mean reduction in the number of voids per 24 hours after 12 weeks of treatment. Non-inferiority was defined as no more than a 20% difference in the mean void reduction.

A total of 87 of the 100 (87%) patients completed the study and voiding diary data were available for only 84 patients, 41 of 50 (82%) in the PTNS group and 43 of 50 (86%) in the torderodine group. Study findings showed non-inferiority of PTNS, with a decrease in voids per day of 2.4 in the PTNS group and 2.5 in the torderodine group. The study reported mixed findings for a number of secondary outcomes, some of which were based on patient reports. There were no statistically significant differences in the PTNS and torderodine groups for other symptoms recorded in the voiding diary. This finding includes episodes of nocturia (-0.7 and -0.6, respectively) and episodes of moderate to severe urgency per day (-2.2 and -2.9, respectively), and episodes of urge incontinence per day (-1.0 and -1.7, respectively). There
was a statistically significant difference in the proportion of patients reporting improvement or cure in symptoms in favor of the PTNS group (79.5 vs. 54.8%).

Limitations of this study include the following:

- Lack of blinding of patient and providers;
- Lack of comparative data beyond the end of the initial 12-week treatment period;
- Lack of a sham/placebo group both to mitigate the potential bias due to subjective outcomes and to evaluate whether either treatment is better than placebo;
- Data were not reported for compliance with medication therapy;
- The authors did not clearly define criteria for “improvement” or “cure”; and
- Different methods of data collection in the 2 groups for adverse event outcomes and possibly also for other self-report outcomes; specifically, The PTNS group was assessed in person while the medication group was assess by telephone.

MacDiarmid (2010) reported one-year follow-up data for patients from the OrBIT trial who had been assigned to the PTNS group and had responded to the initial course of treatment, defined as reporting symptom improvement at 12 weeks. Thirty-three of the 35 responders were included. They received a mean of 12.1 (SD=4.9) treatments between the 12-week and 12-month visits, and there was a median of 17 days between treatments. Data were available for 32 of the 33 (97%) participants at six months and 25 of the 33 (76%) participants at 12 months. The mean reduction in number of voids per day from baseline (the original primary outcome of the study) was 3.2 (SD=3.7) at six months and 2.8 (SD=3.7) at 12 months. Other voiding diary outcomes at 12 months, based on 25 responses, were mean changes in nocturia episodes of -0.8, in episodes of moderate to severe urgency per day of -3.7, and in episodes of urge incontinence per day of -1.6. As noted above, this analysis was limited in that no data from the tolterodine group were available to compare long-term outcomes. Additionally, not all patients in the PTNS group were included in the follow-up analysis; only PTNS responders were eligible. Therefore, a potential bias is that the initial subjective outcome measure may be subject to the placebo effect. Patients in the PTNS group who responded to initial treatment may be particularly susceptible to a placebo response and/or may represent those with the best treatment response. Thus, these individuals may also be susceptible to a placebo response during maintenance treatments, especially treatments offered on an as-needed basis. It is important that long-term response data from RCTs reflect the patient population at the beginning of the study. In addition, since subjects were not counseled on fluid management, it is unknown if subject fluid management habits influenced results. The authors note that, “with an average overactive bladder (OAB) symptom duration of more than 10 years, subjects may have already learned fluid management as a means to mediate OAB symptoms.” Due to these significant study design flaws, the data in this study are unreliable and do not permit conclusion about long-term efficacy.

The SUmiT trial was a randomized, sham-controlled trial that included 220 OAB patients with a score of at least 4 on the overactive bladder questionnaire (OAB-q) short form for urgency, self-report bladder symptoms lasting at least three months, and having failed conservative care. Patients were randomized at a 1:1 ratio to either active or sham PTNS. Both groups received 12 weekly 30-minute intervention sessions. In the sham group, a blunt (placebo) instrument was used to simulate the location and sensation of needle electrode insertion in active treatment. An inactive PTNS surface electrode was used and also two active TENS surface electrodes. The TENS unit was used to deliver low-level sensation to simulate the
PTNS intervention. The 12-week course of treatment was completed by 103 of 110 (94%) in the PTNS group and 105 of 110 (95%) in the sham group.

The primary study outcome was response to treatment based on a single-item global response assessment (GRA) variable at 13 weeks. Possible responses were that symptoms were markedly worse, moderately worse, mildly worse, the same, slightly improved, moderately improved, or markedly improved. The proportion of patients who responded to treatment based on the GRA (i.e., answered that symptoms were moderately or markedly improved) was 60 of 110 (54.5%) in the PTNS group and 23 of 110 (20.9%) in the sham group (p<0.001). Intention-to-treat analysis was used for the primary endpoint only. Several secondary outcomes also favored the PTNS group. The mean reduction in a symptom severity score (a lower score indicates less severity) was 36.7 (SD=21.5) in the PTNS group and 29.2 (SD=20.0) in the sham group (p=0.01). Similarly, the mean reduction in a quality of life scale, the SF-36 (a higher score indicates higher quality of life), was 34.2 (SD=21.3) in the PTNS group and 20.6 (SD=20.6) in the sham group (p=0.006).

For the four voiding diary variables used, there was a statistically significant difference between groups favoring PTNS. The mean change from baseline in the number of voids per day was -2.4 (SD=2.5) in the PTNS group and -1.5 (SD=2.4) in the sham group (difference between groups 0.9 voids per day, p=0.01). The mean change in nocturia episodes was -0.7 (SD=1.2) in the PTNS group and -0.3 (SD=1.4) in the sham group (difference between groups 0.4 nighttime voids, p=0.04). The mean change in moderate to severe urgency per day was -3.7 in the PTNS group and -2.0 in the sham group (difference between groups 1.7 episodes, p less than 0.001). Finally, the mean change in urge incontinence episodes was -1.3 in the PTNS group and -0.3 in the sham group (difference between groups one episode per day, p less than 0.002). (Standard deviations were not reported for the latter two outcomes.)

Advantages of the SUmiT trial were that it included a sham comparison and the primary endpoint analysis was intention to treat. A limitation was that the primary outcome, the GRA, was a single-item subjective measure. For the more objective measures, the voiding diary variables, there was statistically significantly greater benefit with PTNS compared to sham treatment; however, the clinical significance of the difference between the PTNS and sham groups was unclear e.g., on average, there was one fewer episode of urge incontinence a day in the PTNS group. In addition, as in the OrBIT trial, the SUmiT trial only reported comparative data immediately following the initial course of treatment; the study did not evaluate the long-term effectiveness of PTNS. Unlike medication which can be taken on an ongoing basis, PTNS involves an initial 12-week course of treatment followed by maintenance therapy, which to date has not been well-defined. Therefore, the assumption cannot be made that short-term treatment effects will be maintained.

Results from a long-term extension of the SUmiT study were published in 2012.[9] Fifty patients were included and were prescribed a fixed schedule 14 week tapering protocol followed by a personal treatment plan. Only 29 patients (58%) completed the study and of those who did, 77% showed a moderate or marked improvement in OAB symptoms. Like the OrBIT trial extension, the STEP (Sustained Therapeutic Effects of Percutaneous Tibial Nerve Stimulation) study only included patients assigned to the PTNS group who responded to treatment and did not include additional follow-up of initial non-responders or comparative data from patients assigned to the sham-control group. Given this design, it is unlikely that the study results adequately resolve outstanding issues. It is critically important that long-term response rates reflect the patient population at the beginning of the study, not just those considered
successes at 12 weeks. Other methodological limitations include the addition of an external intervention in the form of a personalized treatment plan which may have biased outcomes. In addition, the high loss-to-follow-up rate severely limited the reliability of any conclusion regarding the long-term utility of PTNS treatment for patients with OAB.

Finazzi-Agro and colleagues studied the effect of more frequent treatment sessions for a reduced initial period.[3] Patients, who had urge incontinence and detrusor overactivity on urodynamic testing, were randomized to 30-minute PTNS (n=18) or sham treatment (n=17) sessions three times a week for four weeks. One patient dropped out of the PTNS group and 2 dropped out of the sham group. The primary outcome, percent responders at four weeks (defined as at least 50% reduction in incontinent episodes), was attained by 12/17 (71%) in the PTNS group and 0/15 (0%) in the sham group. The study did not conduct intention-to-treat analysis, was not double-blind, and did not report follow-up data beyond four weeks.

Schreiner and colleagues randomized 51 women above 60 years old who complained of urge urinary incontinence to 12 weeks of conservative treatment (Kegel exercises and bladder training) alone (n=26) or conservative treatment plus 12 weekly sessions of PTNS (n=25).[5] The response rate at 12 weeks, defined as a reduction of at least 50% in the number of incontinence episodes reported by the patient in a bladder diary, was 76% in the PTNS group and 27% in the conservative treatment only group; p=0.001. Blinding was not discussed and this study was also limited by small sample size.

Gungor Ugurlucan (2013) published findings of an RCT comparing transvaginal electrical stimulation (ES) (n=38) and PTNS (n=21) in women with OAB.[6] The ES protocol consisted of 20-minute treatments three times a week for 6-8 weeks. PTNS was performed with an Urgent PC device used for 12 30-minute weekly sessions. A total of 52 of 59 (88%) patients completed the study. The authors assessed numerous outcome variables and did not specify primary outcomes or adjust p-values for multiple comparisons. Four bladder diary variables were reported. From baseline to the end of the treatment period, the groups did not differ significantly at the p<0.05 level in mean change in urgency episodes, nocturia or incontinence episodes. For example, the mean number of urgency episodes was 2.9 (SD: 4.1) at baseline and 1.6 (SD: 0.5) after treatment in the ES group and 2.0 (SD: 3.1) at baseline and 1.3 (SD: 0.5) after treatment in the PTNS group, p=0.54. There was a statistically significant difference in daytime frequency. The mean daytime frequency was 7.8 (SD: 2.7) at baseline and 5.8 (SD: 1.9) after treatment in the ES group and 7.6 (SD: 2.6) at baseline and 7.4 (SD: 2.9) in the PTNS group (p=0.03). The authors reported that a significantly higher proportion of patients in the ES group described themselves as cured, but they did not provide proportions or p-values.

Vecchioli-Scaldazza and colleagues studied 40 women with OAB in a randomized controlled crossover study to evaluate the effectiveness of solifenacin succinate (SS) versus PTNS.[7] Group A received SS and then PTNS and group B received PTNS and then SS. The primary efficacy outcome was reduction in the number of voids in a 24-hour period and outcomes were measured through voiding diaries, quality of life surveys and perception of urgency ratings both before and after each treatment. In addition, a global impression score was completed at the end of the study. Only 30 of the 40 subjects (75%) completed the study. Improved outcomes were observed in both groups, however greater improvement in voided volume and greater effectiveness overall was found in PTNS compared to SS. However, much of the reported improvements were based upon subjective data, which limit conclusions regarding the superiority of PTNS over SS. In addition, authors did not compare the efficacy of PTNS to
medication. Other study limitations include a lack of blinding and uncertainty regarding the clinical significance of these findings.

Other Randomized Controlled Trials

Several other RCTs have been published which were not included in the 2010 and 2014 TEC assessments; however, both are limited by short-term follow-up as none reported on the efficacy of PTNS beyond 12 weeks.

Raheem and colleagues reported on 28 patients with refractory monosymptomatic nocturnal enuresis in a randomized control study comparing PTNS treatment to placebo.[21] The treatment group received a weekly session of PTNS for 12 weeks and a follow-up assessment was made at three months post-treatment. Consistent with the 2010 TEC assessment conclusions, short-term treatment effects were observed in patients who received PTNS compared to the placebo group, however response rates decreased from 78.6% to 42.9% at the three-month follow-up. The decrease in response rates also support the TEC assessment conclusion that efficacy of long-term treatment effect of PTNS has not been established.

Sancaktar and colleagues evaluated 40 women with severe overactive bladder without any prior treatment who were randomized into medication alone and combination treatment groups.[22] All subjects received 4 mgs of tolterodine daily and 20 subjects also received Stoller afferent neuro-stimulation (SANS), a form of PTNS, for 12 weeks. Subjects completed a IIQ-7 questionnaire and a seven-day voiding diary at baseline and after treatment and results were compared. Of the 38 women completing the study, severity of symptoms were reduced in both groups, although a more significant decrease was observed in the combination group. This study is limited by small sample size and relatively short term follow-up.

NEUROGENIC BLADDER

Systematic Reviews

Schneider (2015) published a systematic review of literature on tibial nerve stimulation (transcutaneous and percutaneous) for treating neurogenic lower urinary tract dysfunction.[23] Sixteen studies were identified; four RCTs, nine prospective cohort studies, two retrospective case series and one case report. Sample sizes of the included studies were generally small; most included fewer than 50 patients and none had a sample size larger than 100 patients. Three of the four RCTs used transcutaneous tibial nerve stimulation and the fourth study, which was conducted in Iran, stated that PTNS was used but did not specify the device. The four RCTs included different study populations; women with neurogenic bladder (n=1), men with neurogenic overactive bladder (n=1), men with multiple sclerosis patients (n=1) and Parkinson disease patients (n=1). Comparison interventions were tolterodine, pelvic floor muscle training, lower limb stretching and sham (1 study each). Pooled analyses were not conducted and the systematic review mainly discussed intermediate outcomes e.g., maximum cystometric capacity and maximum detrusor pressure. In the articles reporting on RCT results, none reported statistically significant between-group differences in clinical outcome variables e.g., number of episodes of urgency, frequency or nocturia.

Randomized Controlled Trials

Monteiro (2014) published an RCT evaluating PTNS for neurogenic OAB in in 24 adult men with no prior symptoms who were between six months and three years post-stroke.[24] Patients were randomized to six weeks of PTNS twice a week or a control group that received general...
advice and stretching exercises. Sessions in both groups lasted 30 minutes. The proportion of patients experiencing urinary urgency, urge incontinence, and nocturnal enuresis did not differ significantly between groups immediately after treatment or at the 12-month follow-up. For example, after treatment, eight patients (67%) in the PTNS group and nine patients (75%) in the control group reported urge incontinence (p=0.65). Rates of nocturia did not differ between groups after treatment, but there was a significant difference at 12 months, favoring PTNS. Advantages of this study were a placebo treatment and longer-term follow-up. However, the study was limited by small-sample size. Additional studies with larger sample sizes are needed before conclusions can be drawn about the efficacy of PTNS for treatment of neurogenic bladder.

LOWER URINARY TRACT SYMPTOMS

A SR by Zecca (2016) evaluated PTNS for the treatment of lower urinary symptoms in patients with multiple sclerosis.[25] The review included randomized controlled studies, case-control studies and prospective cohort studies. A total of seven studies were included with a total of 313 multiple sclerosis patients. The review concluded that the current data is limited but PTNS seems effective and safe.

FECAL INCONTINENCE

The Urgent PC Neuromodulation System is not FDA-cleared for the treatment of fecal incontinence. The company’s website states that the treatment can be used for this condition and that the recommended initial course of treatment includes 12 weekly sessions.

Systematic Reviews and technology Assessments

In 2015, NICE published a technology assessment for guidance on percutaneous tibial nerve stimulation for faecal incontinence.[26] This included one nonrandomized comparative study and six case series. The guidance’s limited evidence showed PTNS effective for a limited number of patients short-term. The authors stated PTNS should only be used under certain circumstance.

Two SRs of the literature on tibial nerve stimulation for fecal incontinence have been published; neither conducted pooled analyses of PTNS outcomes compared to a sham or alternative intervention.[27,28] Most recently, in 2015, Edenfeld et al identified 17 studies, 13 case series and 4 RCTs.24 Three of the RCTs evaluated TENS stimulation and 1 used PTNS.[27] Edenfeld stated multiple low-quality studies show improvement in fecal incontinence after PTNS, but more high-quality studies are needed to establish the utility of PTNS.

Horrocks (2014) published a SR of literature on tibial nerve stimulation (percutaneous and transcutaneous) to treat fecal incontinence.[28] The authors included all study designs and identified a total of 12 articles, two RCTs and 10 case series. Six studies evaluated PTNS, five evaluated transcutaneous tibial nerve stimulation (TTNS), and 1 of the RCTs compared the 2 treatments. The other RCT compared TTNS with a sham treatment. Three of the five case series on PTNS and one RCT reported the outcome, 50% or greater reduction in the number of fecal incontinence episodes per week immediately after treatment. In these studies, a median of 71% of patients (range, 63%-82%) reported at least a 50% reduction in episodes. However, this analysis is limited due to the absence of a control group and did not include data from all published studies.

Randomized Controlled Trials
A larger sham-controlled RCT, known as the CONFIDeNT trial, was published in 2015 by Knowles et al in the U.K.\[29\] The study was double-blind and multicenter. A total of 227 patients with fecal incontinence sufficiently severe to warrant intervention (per the principal investigator at each site) were randomized to receive PTNS (n=115) or sham stimulation (n=112). Both groups received 12 weekly intervention sessions lasting 30 minutes each. The primary outcome was at least a 50% reduction in the mean number of episodes of fecal incontinence per week compared with baseline. The mean number of episodes was calculated from 2-week bowel diaries. Twelve patients withdrew from the study. After treatment, 39 of 103 (38%) in the PTNS group and 32 of 102 (31%) in the sham group had at least a 50% reduction in the number of fecal incontinence episodes. The difference between groups was not statistically significant (adjusted OR, 1.28; 95% CI, 0.72 to 2.28; p=0.396). There were also no significant differences between the PTNS and sham groups in the proportion of patients achieving more than 25%, more than 75%, or 100% reduction in mean weekly episodes. There was, however, a significantly greater reduction in the absolute mean number of weekly fecal incontinence episodes in the active PTNS group. The mean number of weekly fecal incontinence episodes in the PTNS group was 6.0 at baseline and 3.5 after treatment. This compares to means of 6.9 and 4.8, respectively, in the sham group. The difference between groups was -2.26 (95% CI, -4.18 to -0.35; p=0.021).

Thin (2015) published an RCT assessing the efficacy of PTNS compared to sacral nerve stimulation (SNS) as a treatment of fecal incontinence in 40 patients (39 women).\[30\] Within-group effect sizes demonstrated a slightly greater benefit with SNS compared to PTNS over a six month follow-up period. Fecal incontinence (FI) episodes (mean, standard deviation) at baseline, three months and six months were 11.4(12.0), 4.0(4.0) and 4.9(6.9) respectively for SNS compared with 10.6(11.2), 5.8(6.9) and 6.3(6.9) for PTNS. Mean Cleveland Clinic Incontinence Score values at baseline, and three and six months were: 16.2(3.0), 11.1(5.2) and 10.4(5.6) for SNS versus 15.1(2.7), 11.7(4.4) and 12.1(5.2) for PTNS. Authors reported a minimum 50% improvement if FI episodes at six months in 11/18 SNS patients and 7/15 PTNS patients; however, it is unclear if these results are statistically or clinically significant. Limitations of this study include the small number of patients included and the lack of sham comparator group.

George (2013) published an RCT evaluating PTNS for fecal incontinence.\[31\] Thirty patients (28 women) who had failed conservative therapy for fecal incontinence were randomized to PTNS (n=11), TTNS (n=11) or sham transcutaneous stimulation (n=9). Patients in all groups received a total of 12 treatments given twice-weekly sessions for six weeks. (This differs from the PTNS manufacturer’s recommended course of 12 weekly treatments). The primary study end point was at least a 50% reduction in the mean number of incontinence episodes per week at the end of the six week treatment period. Only one patient did not complete the study, and data were analyzed on an ITT basis. Nine of 11 patients in the PTNS group, 5 of 11 in the TTNS group, and one of eight in the sham group attained the primary end point; however, the difference among groups was not statistically significant, p=0.035. All of the responders reported no weekly episodes of fecal incontinence after treatment. Study limitations include a small sample size and short-term follow-up.

**Nonrandomized Studies**

Kelly and colleagues evaluated women (n=60) with fecal incontinence who underwent PTNS after a failure to respond to biofeedback.\[32\] The authors concluded that PTNS may have an
effect on bowel related function in two thirds of patients. In addition, PTNS had more of an effect on bowel related function than pelvic function.

A small, comparative cohort study comparing the use of sacral nerve stimulation (n=10) to PTNS (n=9) for the treatment of fecal incontinence in men was published in 2016.[33] Anal continence was evaluated using the Wexner continence grading system and quality of life was measured. Both of the treatments improved incontinence and quality of life but there was no significant difference between groups for both measures.

**PRACTICE GUIDELINE SUMMARY**

**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE (NICE)**

**Urinary Incontinence in Women**

NICE published a 2013 updated guideline for management of women with urinary incontinence.[10] The guideline stated there is insufficient evidence to recommend the use of percutaneous posterior tibial nerve stimulation routinely for OAB. The authors stated PTNS may be offered only after a multidisciplinary team (MDT) review, failed drug treatment and urodynamic testing.

**Fecal Incontinence in Adults**

Nice published a 2007 guideline for the management of faecal Incontinence in adults stating “People with faecal incontinence should be offered sacral nerve stimulation on the basis of their response to percutaneous nerve evaluation during specialist assessment, which is predictive of therapy success.”[34]

**Fecal Incontinence**

Nice published a 2011 guidance on percutaneous tibial nerve stimulation for faecal incontinence. The limited evidence showed PTNS as a safe treatment for faecal incontinence.[26] PTNS was only effective for a limited number of patients short-term. The authors stated PTNS should only be used under certain circumstance.

**Over Active Bladder**

Nice published a 2010 guidance on percutaneous posterior tibial nerve stimulation for overactive bladder syndrome stating current evidence on PTNS for OAB is effective in the short and medium term.[35] There were no major concerns and the recommendation was PTNS may be used if appropriate processes are in place.

**AMERICAN UROLOGICAL ASSOCIATION**[36]

In 2014, the American Urological Association (AUA) and the Society of Urodynamics published a guideline on the diagnosis and treatment of overactive bladder in adults. The following recommendation was made as a third-line treatment option:

“Clinicians may offer peripheral tibial nerve stimulation (PTNS) (also known as posterior tibial nerve stimulation) as third-line treatment in a carefully selected patient population.”

This statement was based on a grade C, which states the following: the balance of benefits and risks/burdens are uncertain.
SUMMARY

There is not enough research to show that percutaneous tibial nerve stimulation (PTNS) improves health outcomes for any indication, including but not limited to urinary dysfunction and fecal incontinence. No clinical guidelines based on research recommend PTNS. Therefore, PTNS is considered investigational for all indications, including but not limited to urinary dysfunction and fecal incontinence.

REFERENCES

5. Schreiner, L, dos Santos, TG, Knorst, MR, da Silva Filho, IG. Randomized trial of transcutaneous tibial nerve stimulation to treat urge urinary incontinence in older women. *International urogynecology journal.* 2010 Sep;21(9):1065-70. PMID: 20458465
10. NICE. Urinary incontinence in women: management National Institue of Health and Care Excellence (NICE); 2013.
11. Shamiyin, T, Wyman, J, Kane, RL. Nonsurgical Treatments for Urinary Incontinence in Adult Women: Diagnosis and Comparative Effectiveness [Internet]. *AHRQ Comparative Effectiveness Reviews.* 2012 Apr Comparative Effectiveness;11(12):EHC074-EF. PMID: 22624162

October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.


### CODES

CPT codes for percutaneous implantation of neurostimulator electrodes (i.e., 64553, 64555, 64561, 64565, 64590) are not appropriate since PTNS uses percutaneously temporarily inserted needles and wires rather than percutaneously implanted electrodes that are left in place.

<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>64999</td>
<td>Unlisted procedure, nervous system</td>
</tr>
<tr>
<td></td>
<td>64566</td>
<td>Posterior tibial neurostimulation, percutaneous needle electrode, single treatment, includes programming</td>
</tr>
<tr>
<td>HCPCS</td>
<td>L8680</td>
<td>Implantable neurostimulator electrode, each</td>
</tr>
</tbody>
</table>

*Date of Origin: August 2006*
Medical Policy Manual

Radiofrequency Ablation of Tumors (RFA)

Effective: July 1, 2017

Next Review: November 2017
Last Review: June 2017

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

RFA kills cells using the heat produced by radiofrequency energy delivered into the tumor via a probe.

MEDICAL POLICY CRITERIA

Note: This policy does not address liver tumors (primary or metastatic). See Cross References.

1. Radiofrequency ablation may be considered medically necessary to treat tumors when one or more of the following criteria are met (A.-F.):
   
   A. Localized renal cell carcinoma that is no more than 4 cm in size when one or both of the following criteria are met:
      1. Preservation of kidney function is necessary (i.e., the patient has one kidney or renal insufficiency defined by a glomerular filtration rate (GFR) of less than 60 mL/min per m2) and standard surgical approach (i.e., resection of renal tissue) is likely to substantially worsen kidney function; or
      2. Patient is not considered a surgical candidate

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
B. Osteoid osteomas that are unresponsive to initial medical treatment
C. To palliate pain in patients with osteolytic bone metastases who have failed or are poor candidates for standard treatments such as radiation or opioids
D. Isolated peripheral non-small cell lung cancer (NSCLC) lesion that is no more than 3 cm in size when the following criteria are met:
   1. Surgical resection or radiation treatment with curative intent is considered appropriate based on stage of disease, however, medical co-morbidity renders the individual unfit for those interventions; AND
   2. Tumor is located at least 1 cm from the trachea, main bronchi, esophagus, aorta, aortic arch branches, pulmonary artery and the heart.
E. Malignant non-pulmonary tumor(s) metastatic to the lung that are no more than 3 cm in size when the following criteria are met:
   1. In order to preserve lung function when surgical resection or radiation treatment is likely to substantially worsen pulmonary status OR the patient is not considered a surgical candidate; AND
   2. There is no evidence of extrapulmonary metastases; AND
   3. The tumor is located at least 1 cm from the trachea, main bronchi, esophagus, aorta, aortic arch branches, pulmonary artery and the heart.
F. Renal angiomyolipomas when at least one of the following criteria are met:
   1. Symptomatic lesion (e.g., hemorrhage)
   2. Asymptomatic lesion larger than 4 cm
II. Radiofrequency ablation is considered **investigational** as a technique for ablating all other benign or malignant tumors, including but not limited to:
   A. Adrenal cancer
   B. Breast cancer
   C. Breast fibroadenomas
   D. Chondroblastomas
   E. Chordomas
   F. Hamartomas
   G. Head and neck cancers
   H. Initial treatment of osteoid osteomas
   I. Initial treatment of painful bony metastases
   J. Primary or metastatic lung (pulmonary) tumors that do not meet the above medical necessity criteria
   K. Lymphoma
   L. Ovarian cancer
   M. Pancreatic cancer

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
Policy Guidelines

Note: A summary of the supporting rationale for the policy criteria is at the end of the policy.

**Policy Guidelines**

**Required Documentation**

It is critical that the list of information below is submitted for review to determine if the policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome.

1. Specific description of the tumor(s) targeted for treatment including the following:
   - Tumor type (primary vs. metastatic; primary tumor type)
   - The location of tumor(s)
   - The number and size(s) of lesion(s) being treated
2. Rationale for the determination that the patient is not a surgical candidate or the tumor is unresectable
3. Whether the goal of treatment is curative or palliative
4. Comorbidities and any contraindicated treatments (e.g., surgery; radiation therapy)
5. Prior treatments, if any, and tumor response
6. Documentation of whether this treatment is to preserve organ function

**Neuroendocrine Tumors**

Neuroendocrine tumors are rare, slow-growing, hormone-secreting tumors that may occur in numerous locations in the body.\(^1\) Neuroendocrine tumors include the following:

- Carcinoid Tumors
- Islet Cell Tumors (also known as Pancreatic Endocrine Tumors)
- Neuroendocrine Unknown Primary
- Adrenal Gland Tumors
- Pheochromocytoma/paraganglioma
- Poorly Differentiated (High Grade or Anaplastic)/Small Cell
- Multiple Endocrine Neoplasia, Type 1 (also known as MEN-1 syndrome or Wermer’s syndrome)
- Multiple Endocrine Neoplasia, Type 2 a or b (also known as pheochromocytoma and amyloid producing medullary thyroid carcinoma, PTC syndrome, or Sipple syndrome)

Neuroendocrine tumors may also be referred to by their location (e.g., pulmonary neuroendocrine tumors; gastroenteropancreatic neuroendocrine tumors).

Some appendiceal carcinoids, also called adenocarcinoids, goblet cell carcinoids, or crypt cell carcinoids, have mixed histology, including elements of adenocarcinoma. While these biphasic tumors have both neuroendocrine and adenocarcinoma components, the National
Comprehensive Cancer Network (NCCN) recommends they be managed according to colon cancer guidelines.

**CROSS REFERENCES**

1. Radioembolization for Primary and Metastatic Tumors of the Liver, Medicine, Policy No. 140
2. Cryosurgical Ablation of Miscellaneous Solid Tumors, Surgery, Policy No. 132
3. Magnetic Resonance (MR) Guided Focused Ultrasound (MRgFUS) and High Intensity Focused Ultrasound (HIFU) Ablation, Surgery, Policy No. 139
4. Microwave Tumor Ablation, Surgery, Policy No. 189
5. Ablation of Primary and Metastatic Liver Tumors, Surgery, Policy No. 204

**BACKGROUND**

Radiofrequency ablation (RFA) is one of a number of locoregional thermal ablation therapies to treat various benign or malignant tumors. RFA kills cells (cancerous and normal) by applying a heat-generating rapidly alternating radiofrequency current through probes inserted into the tumor. The cells killed by RFA are not removed but are gradually replaced by fibrosis and scar tissue. If there is local recurrence, it occurs at the edge of this scar tissue and, in some cases, may be retreated. RFA can be performed as an open surgical procedure, laparoscopically, or percutaneously with ultrasound or computed tomography (CT) guidance. The goals of RFA may include 1) controlling local tumor growth and preventing recurrence; 2) palliating symptoms; and 3) extending survival duration for patients with certain cancerous tumors.

Reports have been published on use of RFA to treat renal cell carcinomas, breast cancer, pulmonary (including primary and metastatic lung tumors), bone, and other tumors including those that are non-cancerous (benign). Well-established local or systemic treatment alternatives are available for each of these tumor types.

**REGULATORY ISSUES**

The U.S. Food and Drug Administration (FDA) issued the following statement September 24, 2008 concerning the regulatory status of radiofrequency ablation. The FDA has cleared RF ablation devices for the general indication of soft tissue cutting, coagulation, and ablation by thermal coagulation necrosis. Some RF ablation devices have been cleared for additional specific treatment indications, including partial or complete ablation of nonresectable liver lesions and palliation of pain associated with metastatic lesions involving bone. The FDA has not cleared any RF ablation devices for the specific treatment indication of partial or complete ablation of lung tumors, citing lack of sufficient clinical data to establish safety and effectiveness for this purpose. The FDA has received reports of death and serious injuries associated with the use of RF ablation devices in the treatment of lung tumors."

**EVIDENCE SUMMARY**

**RENNAL CELL CARCINOMA (RCC)**

**BACKGROUND**

Radical nephrectomy, partial nephrectomy, or nephron-sparing surgery remains the principal treatments of RCC.
RFA may be considered a treatment option when surgical excision is not an option such as the following:

- When preservation of renal function is necessary (e.g., in patients with marginal renal function, a solitary kidney, bilateral tumors)
- In patients with comorbidities that would render them unfit for surgery.
- In patients at high risk of developing additional renal cancers (as in von Hippel-Lindau disease).

**SYSTEMATIC REVIEWS**

An AHRQ Evidence Report, most recently amended in 2016, included thermal ablation (RFA or cryoablation; surgical or image-guided) as an available management strategies for stage I or II RCC. The report noted that better oncologic outcomes were believed to be achieved with partial or radical nephrectomy; however, these procedures were associated with significantly higher complication rates than thermal ablation or active surveillance.

In 2014 Wang et al. published a meta-analysis of 145 studies published through July 2013 comparing effectiveness and complications of radiofrequency ablation and partial nephrectomy (PN) for treatment of stage T1 renal tumors. The rate of local progression was greater with RFA than laparoscopic/robotic or open partial nephrectomy (4.6%, 1.2%, 1.9%, respectively; p<0.001.) RFA had more frequent minor complications than laparoscopic/robotic or open partial nephrectomy (13.8%, 7.5%, 9.5%, respectively; p<0.001). However, the rate of major complications was greater with open partial nephrectomy than laparoscopic/robotic partial nephrectomy or RFA (7.9%, 7.9%, 3.1%, respectively, p<0.001). Several limitations to this meta-analysis were discussed in the article. These included the limited follow-up duration of the included studies and the unavailability of the original study data. Despite the limitations, the data was sufficient for the authors to conclude that both RFA and PN were viable in terms of short-term outcomes and low complication rates. RFA showed a higher risk of local tumor progression but lower complication rates.

In 2014 Katsanos et al. reviewed one RCT and five cohort studies (N=587) on thermal ablation (five studies with RFA and 1 study with microwave) or nephrectomy for small renal tumors with a mean size of 2.5 cm. The local recurrence rate was 3.6% in both groups (risk ratio [RR], 0.92; 95% confidence interval [CI], 0.4 to 2.14; p=0.79). Disease-free survival was also similar in both groups up to 5 years (hazard ratio, 1.04; 95% CI, 0.48 to 2.24; p=0.92). However, the overall rate of complications was significantly lower in the ablation patients than nephrectomy (7.4 vs 11.1 %; pooled RR=0.55; 95 % CI, 0.31 to 0.97; p=0.04). RCT data was insufficient to determine any clear advantage of any one ablation method over the others. The systematic review is subject to the limitations in the included trials, such as the small group sizes, lack of randomized controlled trials, and inconsistent reporting of overall survival data.

**NONRANDOMIZED STUDIES**

Published studies have consistently reported fairly high success rates at up to six years follow-up; two to five re-ablation sessions were often necessary to achieve 95% tumor necrosis. Numerous case series, while unreliable, consistently suggest that the benefits of RFA outweigh the risks in patients for whom nephrectomy is not possible. Current studies suggest that physician specialty (i.e., interventional radiology, urology) and experience, and procedure...
approach (i.e., percutaneous, open, laparoscopic) may impact tumor recurrence and patient survival outcomes, and authors have recommended further study on these variables.

**ADVERSE EVENTS**

Reported complication rates have been low.[7,12-33,35] Complications reported in the literature to date have included the following:

- Perinephric hematomas
- Hemorrhage
- Ureteral strictures
- Percutaneous urinary fistula
- Appendiceal perforation

**BREAST TUMORS**

**BACKGROUND**

The standard treatment for breast cancer is surgical excision by lumpectomy or mastectomy. Adjuvant radiation therapy, chemotherapy, and/or hormone therapy may also be used. If treated, fibroadenomas, benign tumors of the breast, are typically surgically excised.

**SYSTEMATIC REVIEWS**

In 2016, Chen et al. reported results from a meta-analysis of clinical trials assessing the effect of radiofrequency ablation for breast cancer.[36] The authors pooled data from fifteen nonrandomized studies that were published between 2001 and 2012. Of the 15 studies, eight studies reported that the tumor size was <2 cm, five studies reported <3 cm, and the remaining two studies reported <5 cm; eleven studies reported complete ablation rate, from which pooled estimates were 89% (95% CI: 85-93%) of patients receiving RFA achieved a complete ablation. Five studies reported recurrence rate, from which pooled data suggest no local recurrence at a maximum follow-up of 76 months. A statistical test of publication bias showed no potential publication bias (Z=0.78, P=0.436). The analyses were limited by small sample size of the included studies, and heterogeneity in patient selection; the authors conclude large, well-designed studies are necessary.

In 2010, Zhao et al. conducted a systematic review of 38 studies on ablation techniques for breast cancer treatment published from 1994 to 2009.[37] Nine of the studies reviewed focused on RFA for small breast tumors ranging in size from 0.5 – 7 cm. Tumor resection was performed immediately after ablation or up to 4 weeks after RFA. Complete coagulation necrosis rates of 76% to 100% were reported. These studies were limited to feasibility or pilot studies that were difficult to compare due to heterogeneous patient and tumor characteristics and energy sources. In addition, the studies were conducted in the research setting rather than in clinical practice. The authors concluded that RFA for breast cancer tumors was feasible but further studies with longer follow-up on survival, tumor recurrence and cosmetic outcomes are needed.

Similarly, another 2010 review of 17 studies by Soukup and colleagues reported that RFA for the treatment of breast tumors was feasible and promising.[38] However, while minimal adverse effects and complications occurred with breast RFA, the authors noted that incomplete tumor...
ablation remained a concern. Additional studies of health outcomes and refinement of the procedure were recommended.

**NONRANDOMIZED STUDIES**

Current published evidence is limited to preliminary nonrandomized pilot and feasibility studies with small numbers of patients.[39-53] These studies preclude conclusions due to methodologic limitations such as non-random allocation of treatment and a lack of appropriate comparison groups.

The bulk of the published studies measured secondary outcomes such as tissue analysis for viable cancer cells less than one month following RFA. No long-term follow-up data has been reported on local control and survival rates for RFA of breast cancer compared with conventional breast-conserving treatment. Small study populations limit the ability to rule out the role of chance as an explanation of study findings. The heterogeneity of the patient selection criteria between studies limits meaningful comparison of outcomes. The role of various patient characteristics (e.g., tumor size and location; number of tumors) cannot be ruled out as an explanation for study findings.

**LUNG (PULMONARY) TUMORS**

**BACKGROUND**

Surgery is the preferred treatment for primary non-small cell lung carcinoma (NSCLC). Patients with early stage NSCLC who are not surgical candidates may be candidates for radiation treatment with curative intent. RFA is being investigated as a treatment of small primary lung cancers or lung metastases in patients who are not surgical candidates.

**SYSTEMATIC REVIEWS**

In a 2013 Agency for Healthcare Research and Quality (AHRQ) Comparative Effectiveness Review on local nonsurgical therapies for stage I non–small-cell lung cancer (NSCLC), no comparative RFA studies were identified.[54] The AHRQ report found available evidence is insufficient to draw conclusions on the comparative effectiveness of local nonsurgical therapies for NSCLC including RFA.

In a 2013 systematic review of RFA, surgical excision and stereotactic radiotherapy (SBRT) for colorectal cancer lung metastases, no randomized trials were identified and evidence was also insufficient to draw conclusions on the comparative effectiveness of these therapies.[55]

A 2011 systematic review also reported low quality evidence consisting of nonrandomized observational case series with no control group. The review included 46 studies with a total of 2,905 ablations in 1,584 patients.[56] The mean tumor size of 2.8 ± 1.0 cm. Local recurrence occurred in 282 cases (12.2%) and ranged from 0% to 64% as reported in 24 studies. Overall survival rates ranged from 25% to 100% with a mean of 59.4% as reported in 21 studies with a mean of 17.7 ± 12.4 months follow-up. The mean cancer-specific survival rate was 82.6% as reported in 24 studies with a range of 55% to 100% with a mean of 17.4 ± 14.1 months follow-up. Mean overall morbidity was 24.6% and most commonly included pneumothorax, pleural effusion and pain. Mortality related to the RFA procedure was 0.21% overall. The authors concluded RFA for the treatment of lung tumors demonstrated promise but that higher quality studies comparing RFA to other local treatment options “are urgently needed.”
In a 2012 review of evidence from 16 studies, Bilal and colleagues compared RFA to stereotactic ablative radiotherapy (SABR) in patients with inoperable early stage non-small cell lung cancer (NSCLC).\[57\] The authors found overall survival rates for RFA and SABR were similar in patients at 1 year (68.2–95% vs. 81–85.7%) and 3 years (36–87.5% vs. 42.7–56%). However, survival rates at 5 years were lower with RFA (20.1–27%) than with SABR (47%). Caution must be used in interpreting these findings drawn from comparisons of results from uncontrolled, case series and retrospective reviews.

NONRANDOMIZED STUDIES

Current studies consist of small case series, retrospective reviews, or uncontrolled cohort studies which focused primarily on technical feasibility and initial tumor response.\[58-90\]

One larger nonrandomized case series was published in 2011. Huang and colleagues prospectively followed 329 consecutive patients treated with RFA for lung tumors.\[91\] Complications were experienced by 34.3% (113) patients and was most commonly pneumothorax (19.1%). Overall survival at 2 and 5 years was 35.3% and 20.1%, respectively. The risk of local progression was not significantly different in tumors < 4 cm but became significant in tumors > 4 cm.

In 2015 de Baere et al. review of a database from two cancer centers that included all consecutive patients (N=566) with lung metastases treated with RFA.\[92\] Median follow-up was 35.5 months (range 20-53 months) with 235 patients followed for more than 2 years. During follow-up, 176 patients died, of which 112 had progression of their lung tumor disease. Disease progression was also found in 227 of the 390 patients who were alive at last follow-up. Four-year local efficacy was 89% and lung disease control was 44.1%. Median overall survival was 62 months. Limitations of this study included the lack of a control group, and the lack of consideration of the impact of adjuvant chemotherapy.

Study quality concerns include lack of long-term follow-up; significant interstudy heterogeneity in terms of study design, patient populations and RFA methods used; and, non-uniformity of reporting and efficacy scoring criteria. These differences limit meaningful comparison between studies because they may significantly impact study findings.

ADVERSE EVENTS

Acute, delayed or recurrent pneumothorax is the most commonly reported complication of lung RFA for primary or metastatic tumors (30-56% of treatment sessions).\[83,91,93-96\] Most cases resolved without chest tube placement.

Other complications reported in the literature to date are considered uncommon and include the following:\[95-100\]

1. Pleural effusion
2. Intrathoracic hemorrhage with or without hemothorax
3. Hemoptysis
4. Pneumonia
5. Fever
6. Post procedure chest pain
7. Exacerbation of interstitial pneumonia
8. Bronchopleural fistula
9. Seeding of the needle tract with cancer cells
10. Lung inflammation; aseptic pleuritis
11. Infection or abscess
12. Cough
13. Subcutaneous emphysema
14. Pain duration ablation procedure
15. Pleuritic chest pain
16. Pneumonitis
17. Stellate ganglion injury
18. Brachial plexus injury
19. Death

OSTEOID OSTEOMAS

BACKGROUND

Osteomas usually heal spontaneously in three to four years and standard initial treatment includes medical management with NSAIDs. Invasive procedures including open surgery, laser photocoagulation, radiofrequency ablation, or core drill excision may be necessary if symptoms cannot be managed with NSAIDs.

NONRANDOMIZED STUDIES

Numerous nonrandomized uncontrolled case series have consistently suggested that the benefits of RFA outweigh the risks in patients who require treatment due to failed response to nonsurgical treatments.\[101-107]\]

SECTION SUMMARY

Despite the weaknesses in the published clinical evidence, RFA of osteomas has become a standard of care for osteomas that have failed standard treatments. This was based on the lower morbidity and quicker recovery time associated with the procedure compared with open surgery. The risk of osteoma recurrence with RFA is 5–10%; recurrent tumors can be retreated with RFA. There are minimal clinical trial data on the risks and benefits of RFA as initial treatment of osteoid tumors. Since most of these tumors heal spontaneously with medical treatment, the necessity of surgical intervention as initial treatment is unclear.

PALLIATION OF PAIN FROM BONE METASTASES

BACKGROUND

External beam irradiation is often the initial palliative therapy for osteolytic bone metastases. However, pain from bone metastases is refractory to radiation therapy in 20% to 30% of patients, while recurrent pain at previously irradiated sites may be ineligible for additional radiation due to risks of normal tissue damage. Other alternatives include hormonal therapy, radiopharmaceuticals such as strontium-89, and bisphosphonates. Less often, surgery or chemotherapy may be used for palliation and intractable pain may require opioid medications. RFA may be considered another alternative for palliating pain from bone metastases.

NONRANDOMIZED STUDIES

October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
Current evidence is limited to data from small, poorly designed case series. However, though small and uncontrolled, available studies consistently reported significant improvement in pain following RFA in patients who failed or were poor candidates for standard treatments. Clinical trial data is lacking for use of RFA as an alternative to conventional techniques for initial treatment of painful bony metastases.

ANGIOMYOLIPOMA

BACKGROUND

Angiomyolipomas (AMLs) or angiomyolipomata are rare benign tumors that contain blood vessels, smooth muscle, and fat. They are usually associated with the kidneys but may also be in the liver or other locations. They are more frequently seen in patients with tuberous sclerosis complex (TSC). These lesions are usually asymptomatic but may hemorrhage, particularly if large (4 cm or larger). Treatment consists of surveillance as long as the lesion remains small and asymptomatic. Treatment or prevention of hemorrhage may include surgical resection, arterial embolization, or laparoscopic or percutaneous ablation.

PUBLISHED STUDIES

Due to the rare nature of these tumors, there is limited published evidence on the tumor management. The current studies have significant methodological limitations including retrospective records review, small size (n=4-32), heterogeneity of patients and treatment modalities, and short-term follow-up. However, the available studies consistently reported low rates of complications and high rates of successful ablation, generally without recurrence at mean follow-up ranging between 9 and 45 months. Some larger tumors (>3.5 cm) required two RFA sessions. Minor complications included transient perinephric hematoma, intercostal nerve transection. A patient in one early study developed a small skin metastasis at the electrode insertion site which was resected and did not recur.

SECTION SUMMARY

Because this is a rare tumor that is often identified incidentally and may not require treatment, it is unlikely that large randomized controlled trials or comparative studies will become available. Due to the risk of potentially life-threating hemorrhage in large (>4 cm) AMLs and the low rate of adverse effects, treatment of symptomatic or large lesions may be warranted.

HEAD AND NECK TUMORS

BACKGROUND

Tumors of the head and neck arise in the lip, oral cavity, pharynx, larynx, paranasal sinuses and salivary glands. Treatment depends on the location and extent of the disease. Standard treatment for patients with early-stage disease (stage I or II) is single-modality with surgery or radiation therapy. The two modalities result in similar survival. Combined modality therapy is required for locally advanced disease. In patients with recurrent head and neck cancer, surgical salvage attempts are poor in terms of local control, survival and quality of life, and these recurrent tumors are often untreatable with standard salvage therapies. Palliative chemotherapy or comfort measures may be offered.

RANDOMIZED CONTROLLED TRIALS
There are no randomized trials on the safety and effectiveness of RFA for treatment of head and neck tumors.

NONRANDOMIZED STUDIES

Current published evidence is limited to poorly designed case series, feasibility, and retrospective studies that are considered unreliable due to lack of a control group for comparison and lack of randomization to control for bias.[120-124]

In addition to these methodological limitations, prospective case series included small numbers of patients. Small study populations limit the ability to rule out the role of chance as an explanation of study findings.

ADVERSE EVENTS

Complications and adverse events are reported to be uncommon, but are often severe. They are generally related to burning of local soft tissue (e.g., fistula formation).[120-123]

THYROID TUMORS

BACKGROUND[125]

Thyroid carcinoma is uncommon, with a lifetime risk of being diagnosed with thyroid carcinoma less than 1%. Thyroid carcinoma occurs 2 to 3 times more often in women than men. The main histological types of thyroid carcinoma include: 1) differentiated (including papillary, follicular, and Hürthle); 2) medullary; 3) anaplastic (aggressive undifferentiated tumor). All anaplastic thyroid carcinomas are considered stage IV and are almost uniformly lethal, however most deaths are from papillary, follicular, and Hürthle cell carcinomas, which account for nearly 95% of thyroid carcinoma cases. The treatment of choice for differentiated thyroid carcinoma is surgery followed by radiiodine in selected patients and thyroxine therapy in most patients. There is no effective therapy for anaplastic thyroid carcinoma; most are unresectable, but EBRT may improve local control and provide palliation.

SYSTEMATIC REVIEW

Benign Tumors: In 2014 Fuller et al. reported on a systematic review and meta-analysis of studies on RFA for benign thyroid tumors.[126] Included in the review were nine studies (five observational studies[127-131], four randomized studies[132-135]) totaling 306 treatments. After RFA, statistically significant improvements were reported in nodule size reduction (29.77 mL; 95% CI, -13.83 to -5.72), combined symptom improvement and cosmetic scores on the 0 to 6 scale (mean, -2.96; 95% CI, -2.66 to -3.25) and withdrawal from methimazole (odds ratio, 40.34; 95% CI, 7.78 to 209.09). Twelve adverse events were reported, two of which were considered significant but did not require hospitalization.

Malignant Tumors: No systematic reviews of studies for malignant thyroid tumors were identified.

RANDOMIZED CONTROLLED TRIALS

No new RCTs were published since those included in the 2014 systematic review summarized above.
NONRANDOMIZED STUDIES

Since the systematic review summarized above, no comparative nonrandomized studies have been published. The few new studies for RFA of benign or malignant thyroid lesions were case series and small feasibility studies.

CHOLANGIOCARCINOMAS

BACKGROUND

Cholangiocarcinomas are tumors that originate in the bile duct epithelium; 90% are adenocarcinomas. Intrahepatic cholangiocarcinomas (ICC) are located within the hepatic parenchyma and are reviewed under Ablation of Primary and Metastatic Liver Tumors, Surgery, Policy No. 204 (see Cross References for a link to the policy). They may also be referred to as peripheral cholangiocarcinomas. Extrahepatic cholangiocarcinomas (ECC) are more common than intrahepatic cholangiocarcinoma and are located within the extrahepatic bile duct. Complete resection with negative margin is potential curative, though recurrence is common and most cases are unresectable due to advanced disease when diagnosed. For unresectable or metastatic cholangiocarcinomas at any location, the primary treatment may include chemotherapy, treatment within a clinical trial, or best supportive care. RFA and other locoregional therapies may be an option. Biliary drainage with biliary stenting may be warranted for unresectable or metastatic extrahepatic disease. Liver transplantation is potentially curative in carefully selected patients with lymph node negative, nondisseminated locally advanced hilar cholangiocarcinomas and otherwise normal biliary and hepatic function or underlying liver disease precluding surgery.

NONRANDOMIZED STUDIES

The evidence for ECC consists of a single short-term case series.[136] This study included 11 patients with hilar ECC. At 1-month follow-up after RFA, the reduction in tumor size was 30% in 6 tumors, 20% in 2 tumors, and size was unchanged in 3 tumors. At 6 months following RFA, the overall size reduction was 35%, with the largest reduction 60%. Overall survival ranged from 10-30 months.

UTERINE FIBROIDS (LEIOMYOMAS OR MYOMAS)

BACKGROUND[137]

Uterine fibroids, also known as leiomyomas or myomas, are benign smooth muscle tumors of the uterus occurring in women during their reproductive years. They frequently occur in multiples, and the tumor location within the uterus is often used to describe the fibroids (intramural, submucosial, subserosal, or cervical myomas). Surgery, including hysterectomy and various myomectomy procedures, is considered the criterion standard treatment for symptom resolution. There has been long-standing research interest in developing minimally invasive alternatives for treating uterine fibroids, including procedures that retain the uterus and allow for future childbearing. Various techniques to induce myolysis have also been studied including Nd:YAG lasers, bipolar electrodes, cryomyolysis, and radiofrequency ablation. With these techniques, an energy source is used to create areas of necrosis within uterine fibroids, reducing their volume and thus relieving symptoms.

RANDOMIZED CONTROLLED TRIALS

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
In 2014, Brucker et al in Germany published a single-center manufacturer-sponsored randomized controlled trial (RCT) comparing radiofrequency volumetric thermal ablation (RFVTA) with the Acessa system to laparoscopic myomectomy. The trial included 51 premenopausal women at least 18 years old with symptomatic uterine fibroids less than 10 cm in any diameter and a uterine size of less than 17 weeks of gestation. Pregnancy and lactation were exclusion criteria. Prior to randomization, all women underwent laparoscopic ultrasound mapping. Data on 50 of the 51 women were analyzed. The primary study outcome, mean (SD) time to hospital discharge, was 10.0 (5.5) hours in the RFVTA group and 29.9 (14.2) hours in the myomectomy group. The criterion for noninferiority (no more than 10% longer hospital stay with RFVTA than laparoscopic myomectomy) was met at a significance level of p<0.001. All patients in the myomectomy group were hospitalized overnight; although not explicitly stated, this appeared to be the standard procedure at the study hospital. In the Acessa group, there was 1 unplanned hospitalization due to unexplained vertigo and 4 hospitalizations as standard procedure because the patients also underwent adhesiolysis.

Secondary outcomes of the RCT were reported in a 2015 publication by Hahn et al (12-month outcomes) and a 2016 publication by Kramer et al (24-month outcomes). Analysis was per protocol and 43 (84%) of 51 randomized participants were available for both the 12- and 24-month analyses. Each publication reported on 12 symptoms: heavy menstrual bleeding, increased abdominal gait, dyspareunia, pelvic discomfort/pain, dysmenorrhea, urinary frequency, urinary retention, sleep disturbance, backache, localized pain, and “other symptoms” (not specified). At 12 months, no participants reported 4 of the symptoms (dyspareunia, urinary retention, sleep disturbance, uterine pain) and there were no statistically significant between-group differences in the frequency of any of the remaining 8 symptoms (at the p<0.05 level). The most commonly reported symptom at 12 months (heavy menstrual bleeding) occurred in 7 (33%) of women in the RFVTA group and 2 (9%) of women in the laparoscopic myomectomy group (p=0.069) after controlling for baseline bleeding. At 24 months, no participants reported urinary retention or “other” symptoms, and there were no statistically significant between-group differences in any of the 10 reported symptoms. The most commonly reported symptom at 24 months (dysmenorrhea) occurred in 8 (38%) in the RFVTA group and in 7 (32%) in the laparoscopic myomectomy group (p=0.67). Patients were also assessed using several validated questionnaires (eg, the Uterine Fibroid Symptom and Quality of Life). There were no statistically significant between-group differences at 12 or 24 months on these validated questionnaires. In addition, the authors described pregnancy outcomes. Three patients in the RFVTA group conceived and all delivered a healthy neonate; the number of women who desired to become pregnant was not reported. Limitations of the 12- and 24-month analyses included lack of intention-to-treat analysis and failure to describe secondary study hypotheses and statistical analyses clearly. The RCT was relatively small in size and thus may have been underpowered to detect clinically meaningful differences in secondary outcomes, so these results do not rule out potential differences between treatments.

NONRANDOMIZED STUDIES

A large retrospective case series was published by Yin et al in 2015. The study was conducted in China and used Chinese gynecologic radiofrequency ablation devices. It included 1216 consecutive patients treated at a single hospital over a 10-year period. All fibroids were less than 6 cm in size and mean diameter was 4.5 cm (range, 3.1-6.0 cm). Mean follow-up time was 36.5 months. Among the 476 premenopausal women, the mean reduction in myoma
diameter was 2.7 cm at 6 months, 2.4 cm at 12 months, and 2.2 cm at 24 months. Among the 740 peri- or postmenopausal women, mean reduction was 3.3 cm at 6 months, 2.3 cm at 12 months, and 2.3 cm at 24 months. Myoma diameter was significantly lower at each of these time points posttreatment compared with pretreatment. In the premenopausal subgroup, the proportion of women with dysmenorrhea decreased from 43.7% at baseline to 7.6% at 12 months and to 6.7% at 24 months; rates were significantly lower after treatment.

In 2013, Chudnoff et al published a prospective industry-funded multicenter study.\[142\] It included 135 premenopausal women at least 25 years old with symptomatic uterine fibroids, a uterine size of 14 weeks of gestation or less, and 6 or fewer treatable fibroids, with no single fibroid larger than 7 cm. In addition, women desired to preserve their uteri but not to have children in the future. RFVTA was conducted using the Acessa system. According to the study protocol, most fibroids less than 1 cm in diameter were not treated. The primary efficacy outcomes were change in the volume of menstrual bleeding and the surgical reintervention rate after 12 months. A total of 127 (94%) of 135 women completed the study. From baseline to 12 months, 53 (42%) of 127 women (95% confidence interval, 32% to 49%) experienced at least a 50% reduction in the volume of menstrual bleeding. Most women (104/127 [82%]) experienced a decrease in menstrual bleeding at 12 months. Only 1 woman underwent a surgical reintervention through 12 months (this woman had been lost to follow-up and was not included in the other efficacy analyses). Three-year outcomes were reported by Berman et al in 2014.\[143\] A total of 104 (77%) of the 135 women who participated in the study were evaluable at 3 years. Fourteen underwent reintervention over the 3 years to treat uterine fibroid symptoms. Eleven women had hysterectomies, 2 had myomectomies, and 1 had uterine artery embolization. Bleeding outcomes were not reported at 3 years, but the authors stated that quality-of-life variables improved from baseline to 36 months and that most of the improvement in quality of life occurred within 3 months of the procedure.

MISCELLANEOUS TUMORS

BACKGROUND

The standard treatment of miscellaneous tumors depends on the type, location, and extent of the cancer. A large number of phase II or III clinical trials involving the use of RFA in the treatment of primary or metastatic cancers are underway.\[144\]

PUBLISHED STUDIES

The current published evidence on RFA for other tumors is either absent or is limited to unreliable data from small case series and retrospective reviews. Evidence from these studies is considered unreliable due to methodological limitations such as non-random allocation of treatment and a lack of appropriate comparison groups.\[120,127,128,145-158\]

PRACTICE GUIDELINE SUMMARY

NATIONAL COMPREHENSIVE CANCER NETWORK (NCCN)

The NCCN guidelines for thyroid carcinoma (v.2.2017) state that for papillary carcinoma with locoregional recurrence surgery is preferred if resectable, and/or local therapies when available, including RFA.\[125\] In symptomatic disease or progression of medullary carcinoma, consider palliative resection ablation (e.g., radiofrequency ablation, embolization, other regional therapy), or other regional treatment. (category 2A)
NCCN guidelines for colon cancer (v.2.2017) indicate that “ablative techniques can be considered [in patients whose primary colon tumor was resected for cure when metastatic lung tumors are] unresectable and amenable to complete ablation” (category 2A).[159] The guidelines also state that “ablative techniques may be considered alone or in conjunction with resection. All original sites of disease need to be amenable to ablation or resection.”

NCCN guidelines for kidney cancer (v.2.2017) indicate RFA is an ablative option for the treatment of kidney cancer in select patients with clinical stage T1 lesions who are not candidates for surgery, though ablative techniques have shown higher local recurrence rates than surgery.[160] RFA is also an option in select patients (eg, elderly patients, others) with competing health risks.

AMERICAN COLLEGE OF RADIOLOGY (ACR)

The 2014 ACR Appropriateness Criteria® considers RFA to be an alternative to partial nephrectomy for small (<4 cm) RCC tumors.[161]

The 2014 ACR Appropriateness Criteria on early-stage NSCLC that current evidence from a number of retrospective series involving varied patient populations reported a wide range of responses to RFA, ranging from 38% to 93%.[162] Primary tumor relapse rate after RFA ranged from 8% to 43% and 2-year cancer-specific survival after RFA ranged from 57% to 93%, with 3-year OS of 15% to 46%. Predictors of complete response included smaller tumor size metastases, and ablation zone four times the tumor diameter. The document quoted the 2012 ACCP/STS guidelines[163] summarized above.

AMERICAN COLLEGE OF CHEST PHYSICIANS (ACCP)

The American College of Chest Physicians (ACCP) guidelines on the treatment of stage I and II NSCLC indicate RFA has been used effectively in clinical stage 1 NSCLC. Therefore, in medically inoperable patients, peripheral NSCLC tumors less than 3 cm may be treated with RFA.[164]

The ACCP also joined with the Society of Thoracic Surgeons (STS) to develop consensus guidelines on the treatment of high-risk patients with stage I NSCLC.[163] These consensus guidelines indicate RFA is an alternative treatment option in patients who are not surgical candidates due to severe medical comorbidity.

AMERICAN THYROID ASSOCIATION (ATA)

The 2012 ATA guidelines consider the evidence to be insufficient to allow conclusions as to the role of RFA, cryoablation, and embolization for the management of anaplastic thyroid cancer (ATC).[165] Therefore, a definitive recommendation could not be made for these treatments. (Strength of Recommendation: Weak; Quality of Evidence: Insufficient)

SUMMARY

RENEAL CELL CARCINOMA

Although there are currently no high-quality studies of radiofrequency ablation (RFA) of renal cell carcinoma (RCC), the overall body of published evidence suggests RFA may be beneficial in the short- to mid-term for small (4 cm or smaller), localized RCCs in patients.
who are not considered candidates for partial or complete surgical removal of the kidney. Therefore, RFA may be medically necessary for small RCCs in patients who are not surgical candidates or when preservation of kidney function is necessary, such as in patients with only one kidney.

Surgical excision is the preferred treatment for renal cell carcinoma (RCC) in patients who are considered to be healthy enough for surgery. There is insufficient evidence to determine whether radiofrequency ablation (RFA) is effective as surgical excision for treatment of RCC tumors. Therefore, RFA is considered investigational for treatment of RCC tumors for which surgical resection is an option.

**BREAST TUMORS**

There is insufficient evidence to determine the effectiveness of radiofrequency ablation for treatment of benign or malignant breast masses. Therefore, this treatment is considered investigational for the treatment of these tumors.

**LUNG TUMORS**

Surgical resection is the treatment of choice for primary non-small cell lung cancer (NSCLC) or metastatic tumors in the lung. For those patients who are unable to tolerate surgery, radiofrequency ablation (RFA) may be a treatment option in certain cases. While available studies are limited by study design, accumulating evidence suggests that RFA may be similar to surgery in survival rates and rates of procedure-related complications and mortality. Therefore, in patients with NSCLC or metastatic tumors in the lung who are ineligible for surgical treatment, RFA may be medically necessary when the policy criteria are met. RFA is considered investigational when the policy criteria are not met.

**OSTEOID OSTEOMAS**

Although the published evidence is limited to studies of lower methodological quality, radiofrequency ablation (RFA) of osteomas has become a standard of care based on expert opinion that the potential benefits of RFA outweigh risks in patients with osteoid tumors who have failed nonsurgical treatments. Therefore, RFA may be medically necessary for selected patients.

The current preferred treatment of osteoid osteomas is non-surgical medical treatment. There is insufficient evidence to determine the effectiveness of radiofrequency ablation (RFA) for initial (first-line) treatment of osteoid tumors. RFA is, therefore, considered investigational as initial treatment of these tumors in patients who have not undergone standard medical management.

**ANGIOMYOLIPOMAS**

The current published evidence on radiofrequency ablation (RFA) of angiomyolipomas (AMLs) is limited to studies of lower methodological quality. However, because these tumors are rare, it is unlikely that evidence from large comparative studies will become available. Given the potential for life-threatening hemorrhage from large AMLs (4 cm or larger), and the consistent reports that the potential benefits of treatment outweigh any risks, RFA may be...
medical necessary to treat symptomatic or large asymptomatic AMLs. Treatment of asymptomatic AMLs smaller than 4 cm is considered investigational.

PALLIATION OF PAIN FOR BONE METASTASES

The current evidence for radiofrequency ablation (RFA) for treatment of painful metastatic tumors in the bone is limited to studies of lower methodological quality; however, these studies have consistently reported significant improvement in pain following RFA in patients who have failed or are poor candidates for standard treatments. In light of this evidence, the unlikelihood of randomized controlled trials in these patients, and the lack of treatment options, the potential benefits of RFA appear to outweigh risks. Therefore, RFA may be medically necessary in patients with painful metastatic bone lesions who have failed or are poor candidates for standard treatments.

Because of the lack of data on the effectiveness of radiofrequency ablation (RFA) for initial (first-line) treatment of painful bony metastases, this indication is considered investigational.

HEAD AND NECK CANCERS

There is insufficient evidence to determine whether radiofrequency ablation (RFA) is effective for treatment of tumors of the head and neck. Therefore, RFA is considered investigational for the treatment of head and neck cancers.

THYROID TUMORS

While radiofrequency ablation (RFA) has been shown to reduce the size of thyroid tumors and improve clinical symptoms, complications can be common. The available evidence is insufficient to determine whether any beneficial effects of RFA outweigh the risks. Therefore, RFA for the treatment of benign or malignant thyroid tumors is considered investigational.

UTERINE FIBROIDS

There is not enough research to show that radiofrequency ablation (RFA) improves health outcomes for people with uterine fibroids. Additionally, no clinical guidelines based on evidence recommend this treatment option. Therefore, RFA is considered investigational for treating uterine fibroids.

MISCELLANEOUS TUMORS

There is insufficient evidence to determine whether radiofrequency ablation (RFA) is effective for treatment of other tumors. Therefore, RFA is considered investigational for all other tumors.

REFERENCES

2. FDA Public Health Notification: Radiofrequency Ablation of Lung Tumors - Clarification of Regulatory Status. 2008. [cited 07/06/2015]; Available from:


October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.


137. BlueCross BlueShield Association Medical Policy Reference Manual "Laparoscopic and Percutaneous Techniques for the Myolysis of Uterine Fibroids." Policy No. 4.01.19


144. ClinicalTrials.gov website; Radiofrequency Ablation. [cited 07/20/2016]; Available from: http://www.clinicaltrials.gov/ct2/results?term=%22radiofrequency+ablation%22


166. BlueCross BlueShield Association Medical Policy Reference Manual "Radiofrequency Ablation of Miscellaneous Solid Tumors Excluding Liver Tumors." Policy No. 7.01.95

<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>20982</td>
<td>Ablation therapy for reduction or eradication of 1 or more bone tumors (eg, metastasis) including adjacent soft tissue when involved by tumor extension, percutaneous, including imaging guidance when performed; radiofrequency</td>
</tr>
<tr>
<td></td>
<td>31641</td>
<td>Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with destruction of tumor or relief of stenosis by any method other than excision (eg, laser therapy, cryotherapy)</td>
</tr>
<tr>
<td></td>
<td>32998</td>
<td>Ablation therapy for reduction or eradication of one or more pulmonary tumor(s) including pleura or chest wall when involved by tumor extension, percutaneous, radiofrequency, unilateral</td>
</tr>
<tr>
<td></td>
<td>50542</td>
<td>Laparoscopy, surgical; ablation of renal mass lesion(s), including intraoperative ultrasound guidance and monitoring, when performed</td>
</tr>
<tr>
<td></td>
<td>50592</td>
<td>Ablation, one or more renal tumor(s), percutaneous, unilateral, radiofrequency</td>
</tr>
<tr>
<td></td>
<td>58674</td>
<td>Laparoscopy, surgical, ablation of uterine fibroid(s) including intraoperative ultrasound guidance and monitoring, radiofrequency</td>
</tr>
<tr>
<td></td>
<td>0404T</td>
<td>Transcervical uterine fibroid(s) ablation with ultrasound guidance, radiofrequency</td>
</tr>
<tr>
<td>HCPCS</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

Date of Origin: December 1998
Reconstructive Breast Surgery/Mastopexy, and Management of Breast Implants

Effective: October 1, 2017

Next Review: August 2018
Last Review: September 2017

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Policy provides breast reconstruction and implant management criteria based on Public Law 105-277, the Women’s Health and Cancer Rights Act of 1998.

MEDICAL POLICY CRITERIA

Notes:

- Contractual limitations and exclusions may apply to both reconstructive and cosmetic procedures, to illnesses and conditions initially occurring prior to coverage, and to complications of non-covered procedures.
- For the purposes of this policy, mastectomy is defined as complete or partial, including lumpectomy.
- Some codes listed may have specific criteria to be met in other medical policies (e.g., reduction mammoplasty), or may not be considered medically necessary for any indication. See Cross References to confirm the correct policy is applied.

I. Reconstructive breast surgery of a diseased or injured breast may be considered medically necessary when either of the following criteria is met and the treating physician recommends it:
A. After prophylactic or therapeutic mastectomy
B. After accidental injury or trauma to the breast

II. Reconstructive breast surgery of an unaffected breast to achieve symmetry with the contralateral breast which has been reconstructed following mastectomy for disease, injury, or trauma may be considered medically necessary when it is recommended by the treating physician.

III. Explantation of a breast implant(s) is considered medically necessary, when the implant(s) was/were placed after mastectomy, accidental injury, or trauma. Explantation of implants requires documentation of the original indication for implantation.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

CROSS REFERENCES
1. Transgender Services, Medicine, Policy No. 153
2. Endometrial Ablation, Surgery, Policy No. 01
3. Cosmetic and Reconstructive Surgery, Surgery, Policy No. 12
4. Reduction Mammoplasty, Surgery, Policy No. 60
5. Autologous Fat Grafting to the Breast and Adipose-derived Stem Cells, Surgery, Policy No. 182

BACKGROUND

Reconstructive breast surgery is defined as those surgical procedures which are intended to restore the normal appearance of the breast after surgery, accidental injury, or trauma. The most common indication for reconstructive breast surgery is mastectomy. In contrast, cosmetic breast surgery is defined as surgery intended to alter or enhance the appearance of a breast which does not have a significantly altered appearance due to surgery, accidental injury, or trauma. Reduction mammoplasty and surgery to alter the appearance of a congenital breast abnormality are examples of breast surgeries which may be cosmetic. (See Surgery Policy No. 60, Reduction Mammoplasty and Surgery Policy No. 12, Cosmetic and Reconstructive Surgery). The most common type of reconstructive breast surgery is insertion of a silicone gel-filled or saline-filled breast implant, either inserted immediately at the time of mastectomy -or sometime afterward in conjunction with the previous use of a tissue expander. Significant local complications of breast implants, such as contracture, may require removal of the implant. Other types of reconstruction include nipple/areola reconstruction, nipple tattooing, and/or the use of autologous tissue, such as a transverse rectus abdominis myocutaneous flap (TRAM procedure) or a latissimus dorsi flap. In addition, mastopexy, reduction mammoplasty, or implant on the contralateral breast may be performed in order to achieve symmetry with the reconstructed breast.

POSITION STATEMENT

This policy is written to assist in interpreting Public Law 105-277, the Women's Health and Cancer Rights Act of 1998[1] which requires all health insurance carriers that cover mastectomies to also cover the following in a manner determined in consultation with the attending physician and patient:

- All stages of reconstruction of the breast on which the mastectomy was performed
- Surgery and reconstruction of the contralateral breast to produce a symmetrical appearance
- Prostheses
- Treatment of physical complications of mastectomy, including lymphedema

REFERENCES


CODES

<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>11920</td>
<td>Tattooing, intradermal introduction of insoluble opaque pigments to correct color defects of skin, including micropigmentation; 6.0 sq. cm or less</td>
</tr>
<tr>
<td></td>
<td>11921</td>
<td>Tattooing, intradermal introduction of insoluble opaque pigments to correct color defects of skin, including micropigmentation; 6.1 to 20.0 sq cm</td>
</tr>
<tr>
<td></td>
<td>11970</td>
<td>Replacement of tissue expander with permanent prosthesis</td>
</tr>
<tr>
<td></td>
<td>11971</td>
<td>Removal of tissue expander(s) without insertion of prosthesis</td>
</tr>
<tr>
<td></td>
<td>19316</td>
<td>Mastopexy</td>
</tr>
<tr>
<td></td>
<td>19318</td>
<td>Reduction mammoplasty</td>
</tr>
<tr>
<td></td>
<td>19324</td>
<td>Mammoplasty, augmentation; without prosthetic implant</td>
</tr>
<tr>
<td></td>
<td>19325</td>
<td>Mammoplasty, augmentation; with prosthetic implant</td>
</tr>
<tr>
<td></td>
<td>19328</td>
<td>Removal of intact mammary implant</td>
</tr>
<tr>
<td></td>
<td>19330</td>
<td>Removal of mammary implant material</td>
</tr>
<tr>
<td></td>
<td>19340</td>
<td>Immediate insertion of breast prosthesis following mastopexy, mastectomy, or in reconstruction</td>
</tr>
<tr>
<td></td>
<td>19342</td>
<td>Delayed insertion of breast prosthesis following mastopexy, mastectomy, or in reconstruction</td>
</tr>
<tr>
<td></td>
<td>19350</td>
<td>Nipple/areola reconstruction</td>
</tr>
<tr>
<td></td>
<td>19355</td>
<td>Correction of inverted nipples</td>
</tr>
<tr>
<td></td>
<td>19357</td>
<td>Breast reconstruction, immediate or delayed, with tissue expander, including subsequent expansion</td>
</tr>
<tr>
<td></td>
<td>19361</td>
<td>Breast reconstruction with latissimus dorsi flap, without prosthetic implant</td>
</tr>
<tr>
<td></td>
<td>19364</td>
<td>Breast reconstruction with free flap</td>
</tr>
<tr>
<td></td>
<td>19366</td>
<td>Breast reconstruction with other technique</td>
</tr>
<tr>
<td></td>
<td>19367</td>
<td>Breast reconstruction with transverse rectus abdominis myocutaneous flap (TRAM) single pedicle, including closure of donor site</td>
</tr>
<tr>
<td></td>
<td>19368</td>
<td>Breast reconstruction with transverse rectus abdominis myocutaneous flap (TRAM) double pedicle, including closure of donor site</td>
</tr>
<tr>
<td></td>
<td>19369</td>
<td>Breast reconstruction with transverse rectus abdominis myocutaneous flap (TRAM) double pedicle, including closure of donor site</td>
</tr>
<tr>
<td></td>
<td>19370</td>
<td>Open periprosthetic capsulotomy, breast</td>
</tr>
<tr>
<td></td>
<td>19371</td>
<td>Periprosthetic capsulotomy, breast</td>
</tr>
<tr>
<td></td>
<td>19380</td>
<td>Revision of reconstructed breast</td>
</tr>
<tr>
<td>HCPCS</td>
<td>L8039</td>
<td>Preparation of moulage for custom breast implant</td>
</tr>
<tr>
<td></td>
<td>L8600</td>
<td>Implantable breast prosthesis, silicone or equal</td>
</tr>
<tr>
<td>Codes</td>
<td>Number</td>
<td>Description</td>
</tr>
<tr>
<td>-------</td>
<td>--------</td>
<td>-------------</td>
</tr>
<tr>
<td>S2066</td>
<td>Breast reconstruction with gluteal artery perforator (GAP) flap, including harvesting of the flap, microvascular transfer, closure of donor site and shaping the flap into a breast, unilateral</td>
<td></td>
</tr>
<tr>
<td>S2067</td>
<td>Breast reconstruction of a single breast with &quot;stacked&quot; deep inferior epigastric perforator (DIEP) flap(s) and/or gluteal artery perforator (GAP) flap(s), including harvesting of the flap(s), microvascular transfer, closure of donor site(s) and shaping the flap into a breast, unilateral</td>
<td></td>
</tr>
<tr>
<td>S2068</td>
<td>Breast reconstruction with deep inferior epigastric perforator (DIEP) flap or superficial inferior epigastric artery (SIEA) flap, including harvesting of the flap, microvascular transfer, closure of donor site and shaping the flap into a breast, unilateral</td>
<td></td>
</tr>
</tbody>
</table>

*Date of Origin: January 1996*
Reduction Mammaplasty

Effective: September 1, 2017

Next Review: July 2018
Last Review: July 2017

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Reduction mammaplasty is the surgical excision of a substantial portion of the breast, including the skin and underlying glandular tissue, until a clinically normal size is obtained.

MEDICAL POLICY CRITERIA

Notes:

- This policy is not applicable when there has been a prior mastectomy for which the Women's Health & Cancer Rights Act applies. The Reconstructive Breast Surgery/Mastopexy, and Management of Breast Implants policy (Surgery, Policy No. 40 – see cross references) may be applicable. Please refer to the Surgery, Policy No. 40 for reconstruction after partial or complete mastectomy.

- This policy is not intended to address treatment of gender dysphoria which is addressed in the Transgender Services medical policy (Medicine, Policy No. 153 – see cross references), which may be applicable.

I. Reduction mammaplasty as a preparatory first stage procedure preceding a nipple-sparing mastectomy, may be considered medically necessary when the amount of breast tissue removed from each breast is at least the minimum in grams per breast for
the patient’s body surface area* according to the Schnur Sliding Scale (see Policy Guidelines below for body surface area/breast weight table).

II. Reduction mammaplasty may be considered **medically necessary** when **all three** of the following criteria (A - C) are met:

A. The patient is aged 18 years or older.

B. The amount of breast tissue removed from each breast, not including fat removed by liposuction, must be at least the minimum in grams per breast for the patient’s body surface area* according to the Schnur Sliding Scale (see Policy Guidelines), OR, in cases of asymmetry where one breast meets criterion but the other breast does not, the combined weight of the tissue removed from both breasts must total at least twice the Schnur Sliding Scale minimum for the patient’s body surface area. (The health plan may review medical records to confirm the amount of breast tissue removed during the procedure.)

C. Two or more of the following clinical indications have been present for at least 12 months and these have failed to respond to appropriate conservative therapy (identified below):

1. Pain in the upper back, neck, shoulders, and/or arms, which must be of long-standing duration and increasing intensity as documented in the medical records by the referring physician or provider. This documentation should specify the following:
   a. The pain has been evaluated to determine that it is not associated with another diagnosis such as arthritis, if applicable; AND
   b. The pain is not relieved by at least three months of conservative therapy such as an appropriate support bra with wide straps, exercises, heat/cold treatments and appropriate non-steroidal anti-inflammatory agents/muscle relaxants.

2. Dermatitis of the shoulder or shoulder grooving not responding to at least three months of conservative treatment including a support bra or appropriate dermatologic treatments, (e.g. taking steps to eliminate friction, heat, and maceration by keeping skin cool and dry and where appropriate, topical agents).

3. Intertrigo between the pendulous breasts and the chest wall persisting despite at least three months of conservative dermatologic treatments (e.g. taking steps to eliminate friction, heat, and maceration by keeping skin cool and dry and where appropriate, antimycotic agents).


5. Ulnar paresthesia not relieved by at least three months of conservative therapy such as an appropriate support bra with wide straps, range of motion exercises, physical therapy, and appropriate non-steroidal anti-inflammatory agents/muscle relaxants.

III. Reduction mammaplasty is considered **not medically necessary** when criteria I. or criteria II. (A - C) is not met.

IV. Reduction mammaplasty for gynecomastia is considered **not medically necessary**.
V. The use of liposuction as the sole procedure for breast reduction is considered **investigational**.

VI. The use of liposuction as an additional procedure with breast reduction surgery is considered **not medically necessary**.

*Body surface area in meters squared (m²) is calculated using the Mosteller formula (see Policy Guidelines).

**NOTE:** A summary of the supporting rationale for the policy criteria is at the end of the policy.

**POLICY GUIDELINES**

It is critical that the list of information below is submitted for review to determine if the policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome:

1. Total amount of breast tissue to be removed, include if L/R or bilateral
2. Height and weight
3. Any two of the following detailed in chart notes, history and physical, physical therapy notes, radiologic exams, dermatology treatments notes, and/or any other clinical notes:
   A. Medical records by the referring physician, which include pain in the upper back, neck, shoulders and/or arms with documentation of long standing pain, and detailed notes regarding treatment with at least three months of conservative therapy, and that the pain is not associated with another diagnosis such as arthritis;
   B. Documentation of shoulder grooving or dermatitis of the shoulder with description of at least three months of conservative treatment with dermatology notes and outcome;
   C. Intertrigo despite three months detailed documentation of conservative therapy;
   D. X-ray showing kyphosis;
   E. Ulnar paresthesia despite three months documentation of conservative therapy and outcome with chart notes detailing specific treatment.

Mosteller formula: body surface area (m²) = ( [height (cm) x weight (kg) ] / 3600 )¹⁄² [1]

[Click here for link to Body Surface Area Calculator](#)

**Schnur Sliding Scale**

<table>
<thead>
<tr>
<th>Body Surface Area (m²) and Minimum Requirement for Breast Tissue Removal</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Body Surface Area m²</strong></td>
</tr>
<tr>
<td>---------------------------</td>
</tr>
<tr>
<td>1.350-1.374</td>
</tr>
<tr>
<td>1.375-1.399</td>
</tr>
</tbody>
</table>

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
<table>
<thead>
<tr>
<th>Range</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.400-1.424</td>
<td>218</td>
</tr>
<tr>
<td>1.425-1.449</td>
<td>227</td>
</tr>
<tr>
<td>1.450-1.474</td>
<td>238</td>
</tr>
<tr>
<td>1.475-1.499</td>
<td>249</td>
</tr>
<tr>
<td>1.500-1.524</td>
<td>260</td>
</tr>
<tr>
<td>1.525-1.549</td>
<td>272</td>
</tr>
<tr>
<td>1.550-1.574</td>
<td>284</td>
</tr>
<tr>
<td>1.575-1.599</td>
<td>297</td>
</tr>
<tr>
<td>1.600-1.624</td>
<td>310</td>
</tr>
<tr>
<td>1.625-1.649</td>
<td>324</td>
</tr>
<tr>
<td>1.650-1.674</td>
<td>338</td>
</tr>
<tr>
<td>1.675-1.699</td>
<td>354</td>
</tr>
<tr>
<td>1.700-1.724</td>
<td>370</td>
</tr>
<tr>
<td>1.725-1.749</td>
<td>386</td>
</tr>
<tr>
<td>1.750-1.774</td>
<td>404</td>
</tr>
<tr>
<td>1.775-1.799</td>
<td>422</td>
</tr>
<tr>
<td>1.800-1.824</td>
<td>441</td>
</tr>
<tr>
<td>1.825-1.849</td>
<td>461</td>
</tr>
<tr>
<td>1.850-1.874</td>
<td>482</td>
</tr>
<tr>
<td>1.875-1.899</td>
<td>504</td>
</tr>
<tr>
<td>1.900-1.924</td>
<td>527</td>
</tr>
<tr>
<td>1.925-1.949</td>
<td>550</td>
</tr>
<tr>
<td>1.950-1.974</td>
<td>575</td>
</tr>
<tr>
<td>1.975-1.999</td>
<td>601</td>
</tr>
<tr>
<td>2.000-2.024</td>
<td>628</td>
</tr>
</tbody>
</table>

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage.
Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
| 2.025-2.049 | 657  |
| 2.050-2.074 | 687  |
| 2.075-2.099 | 717  |
| 2.100-2.124 | 750  |
| 2.125-2.149 | 784  |
| 2.150-2.174 | 819  |
| 2.175-2.199 | 856  |
| 2.200-2.224 | 895  |
| 2.225-2.249 | 935  |
| 2.250-2.274 | 978  |
| 2.275-2.299 | 1022 |
| 2.300-2.324 | 1068 |
| 2.325-2.349 | 1117 |
| 2.350-2.374 | 1167 |
| 2.375-2.399 | 1219 |
| 2.400-2.424 | 1275 |
| 2.425-2.449 | 1333 |
| 2.450-2.474 | 1393 |
| 2.475-2.499 | 1455 |
| 2.500-2.524 | 1522 |
| 2.525-2.549 | 1590 |
| 2.550 or greater | 1662 |

**CROSS REFERENCES**

1. Transgender Services, Medicine, Policy No. 153
2. Cosmetic and Reconstructive Surgery, Surgery, Policy No. 12
3. Reconstructive Breast Surgery/Mastopexy, and Management of Breast Implants, Surgery, Policy No. 40
4. Autologous Fat Grafting to the Breast and Adipose-derived Stem Cells, Surgery, Policy No. 182

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
BACKGROUND

Female breast hypertrophy, or macromastia, is the development of abnormally large breasts in the female. This condition can cause significant clinical manifestations when the excessive breast weight adversely affects the supporting structures of the shoulders, neck and trunk. Macromastia is distinguished from large, normal breasts by the presence of persistent symptoms such as shoulder, neck, or back pain, shoulder grooving, or intertrigo. This condition can be improved and the associated signs and symptoms can be alleviated by reduction mammoplasty surgery.

EVIDENCE SUMMARY

The following literature appraisal is focused on the investigational technique of reduction mammoplasty by liposuction alone. In order to understand the impact on health outcomes of reduction mammoplasty by liposuction alone, prospective clinical trials are needed, comparing liposuction with standard reduction mammoplasty. These comparisons are necessary in order to understand the safety and efficacy of liposuction and to determine whether liposuction offers advantages over conventional surgical procedures with respect to patient satisfaction, complications, durability, and cosmesis.

While there are some published articles concerning the use of liposuction as the sole procedure for breast reduction, none compare the outcomes of liposuction alone to standard excisional reduction mammoplasty.[2-9] Examples of these articles are detailed below:

Moskovitz (2007) conducted a study of liposuction alone for treatment of macromastia in twenty-four African-American women due to their high risk for complex scar formation following standard excision mammoplasty.[8] The mean aspirate was 1075 cc of fat per breast; however, the before and after liposuction pictures indicate that the participants continued to support large breasts. Outcome measures included the SF-36, EuroQol, Multidimensional Body-Self Relations Questionnaire, McGill Pain Questionnaire and Breast-Related Symptoms Questionnaire. Statistical analysis demonstrated a significant improvement in breast-related symptoms and pain. This was a relatively small, non-randomized trial and patients were not blinded to the intervention. Conclusions concerning the effect of liposuction alone on breast-related symptoms in patients with macromastia cannot be made.

Jakubietz (2011) reported the indications and limitations of this procedure compared to conventional surgical excision.[9] Advantages included selective removal of fat, ease of procedure, and the advantages of less invasive procedures such as faster recovery time and reduced scarring. One disadvantage of liposuction alone included the inability to correct shape and ptosis, making aesthetic results optimal only for young patients. In addition, there are concerns about the extent to which subsequent breast imaging may be impaired, and the possible spread of cancer cells. The authors recommended caution when considering use of this technique.

In summary, high quality evidence on the use of liposuction for reduction mammoplasty has not been identified; comparative trials of sufficient size and duration are needed before any conclusions can be made about the use of this technique for breast reduction.

PRACTICE GUIDELINE SUMMARY

AMERICAN SOCIETY OF PLASTIC SURGEONS
In 2011, the American Society of Plastic Surgeons (ASPS) released an evidence-based clinical practice guideline on the use of reduction mammaplasty. Several clinical questions were addressed, including whether women who did not meet standard health insurance criteria for volume of breast resection experience postoperative relief. On the basis of a single study which compared satisfaction outcomes of women who met standard insurance criteria with women who did not meet such criteria, the society concluded that, “resection volume is not correlated to the degree of postoperative symptom relief.” The society recommended extending the option of reduction mammaplasty to this category of patient. However, among women not meeting standard criteria for resection volume, no comparisons were made between surgical and standard conservative treatment, limiting interpretation of the above findings. Additionally, these recommendations did not specifically address the safety and effectiveness of reduction mammaplasty by liposuction.

**SUMMARY**

Female breast hypertrophy, or macromastia, is the development of abnormally large breasts in the female, which can cause medical problems. There is enough research to show that reduction mammaplasty can improve health outcomes for certain patients with this condition. Therefore, reduction mammaplasty may be considered medically necessary when policy criteria are met. Reduction mammaplasty as treatment for macromastia is considered not medically necessary when policy criteria are not met.

There is not enough research to show that liposuction mammaplasty can improve health outcomes more than traditional mammaplasty techniques. Therefore, reduction mammaplasty by liposuction alone is considered investigational.

Gynecomastia refers to the benign enlargement of the male breast, mainly due to excessive growth of glandular tissue. Reduction mammaplasty (partial removal) for the treatment of gynecomastia is considered not medically necessary as the current standard of care is for the removal of most or all glandular tissue.

**REFERENCES**


These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.

**CODES**

<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>15877</td>
<td>Suction assisted lipectomy; trunk</td>
</tr>
<tr>
<td></td>
<td>19318</td>
<td>Reduction mammoplasty</td>
</tr>
</tbody>
</table>

**Date of Origin:** January 1996
Regence

Medical Policy Manual

Topic: Sacral Nerve Modulation/Stimulation for Pelvic Floor Dysfunction

Date of Origin: February 1999

Section: Surgery

Last Reviewed Date: January 2017

Policy No: 134

Effective Date: February 1, 2017

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Sacral nerve neuromodulation involves the implantation of a permanent electrical stimulation device that modulates the neural pathways controlling bladder or rectal function.

Background

Sacral nerve neuromodulation (SNM), previously known as sacral nerve stimulation is defined as the implantation of a permanent device that modulates the neural pathways controlling bladder or rectal function. The SNM device consists of an implantable pulse generator that delivers controlled electrical impulses. This pulse generator is attached to wire leads that connect to the sacral nerves, most commonly the S3 nerve root. Two external components of the system help control the electrical stimulation. A control magnet is kept by the patient and can be used to turn the device on or off. A console programmer is kept by the physician and used to adjust the settings of the pulse generator.

Treatment using SNM is one of several alternative modalities for patients with fecal or urinary incontinence who have failed behavioral (e.g., prompted voiding) and/or pharmacologic therapies.

- Urge incontinence is defined as leakage of urine when there is a strong urge to void.
- Urgency-frequency is an uncontrollable urge to urinate, resulting in very frequent, small volumes and is a prominent symptom of interstitial cystitis (also called bladder pain syndrome).
Overactive bladder (OAB) is a type of urinary urgency, usually with urinary frequency and nocturia, with or without urgency urinary incontinence.[1]

- **Urinary retention** is the inability to completely empty the bladder of urine.
- **Fecal incontinence** can arise from a variety of mechanisms, including rectal wall compliance, efferent and afferent neural pathways, central and peripheral nervous systems, and voluntary and involuntary muscles. Fecal incontinence is more common in women, due mainly to muscular and neural damage that may occur during vaginal delivery.

Prior to implantation of the permanent device, patients undergo a peripheral nerve stimulation test to estimate potential response to SNM. This procedure is done under local anesthesia, using a test needle to identify the appropriate sacral nerve(s). Once identified, a temporary wire lead is inserted through the test needle and left in place for several days. This lead is connected to an external stimulator which is carried by patients in their pocket or on their belt. Patients then keep track of voiding symptoms while the temporary device is functioning. The results of this test phase are used to determine whether patients are appropriate candidates for the permanent device. If patients show a 50% or greater reduction in incontinence frequency, they are deemed eligible for the permanent device. According to data from the manufacturer, approximately 63% of patients have a successful peripheral nerve evaluation and are thus candidates for the permanent SNM.

The permanent device is implanted with the patient under general anesthesia. An incision is made over the lower back and the electrical leads are placed in contact with the sacral nerve root(s). The wire leads are extended through a second incision underneath the skin across the flank to the lower abdomen. Finally, a third incision is made in the lower abdomen where the pulse generator is inserted and connected to the wire leads. Following implantation, the physician programs the pulse generator to the optimal settings for that patient. The patient can switch the pulse generator between on and off by placing the control magnet over the area of the pulse generator for 1-2 seconds.

**Regulatory Status**

In 1997, the Medtronic Interstim® Sacral Nerve Stimulation™ system received U.S. Food and Drug Administration (FDA) approval for marketing for the indication of urinary urge incontinence in patients who have failed or could not tolerate more conservative treatments. In 1999 the device received FDA approval for the additional indications of urgency-frequency and urinary retention in patients without mechanical obstruction.

In 2006, the Medtronic Interstim® II System received FDA approval for treatment of intractable cases of overactive bladder and urinary retention. The new device is smaller and lighter than the original system and is reported to be suited for those with lower energy requirements or small stature. The device also includes updated software and programming options.

In 2011, the Medtronic InterStim System received FDA approval for the indication of chronic fecal incontinence in patients who have failed or could not tolerate more conservative treatments.

The Interstim device has not been specifically approved by FDA for treatment of chronic pelvic pain.

**Note:** Sacral nerve neuromodulation should be distinguished from pelvic floor stimulation. Pelvic floor stimulation refers to electrical stimulation of the pudendal nerve. This therapy is addressed in a separate medical policy (see Cross References).
MEDICAL POLICY CRITERIA

Note: This policy only addresses the initial placement of sacral nerve neuromodulation devices; it does not address device replacement.

I. Urinary Incontinence and Non-obstructive Retention

A. A trial period of sacral nerve neuromodulation (peripheral nerve stimulation test) with a temporarily implanted lead may be considered medically necessary in patients who meet all of the following criteria (I.A.1-3):

1. There is a diagnosis of at least one of the following:
   a. Urge incontinence
   b. Urgency-frequency syndrome
   c. Non-obstructive urinary retention
   d. Overactive bladder

2. There is documented failure or intolerance to at least two conventional conservative therapies (e.g., behavioral training such as bladder training, prompted voiding, or pelvic muscle exercise training, pharmacologic treatment for at least a sufficient duration to fully assess its efficacy, and/or surgical corrective therapy)

3. Incontinence is not related to a neurologic condition;

B. Permanent implantation of a sacral nerve neuromodulation device may be considered medically necessary in patients who meet all of the following criteria (I.B.1-2):

1. All of the criteria in I. A (1-3) above are met

2. A trial stimulation period demonstrates at least 50% improvement in symptoms over a period of at least 1 week.

II. Fecal Incontinence

A. A trial period of sacral nerve neuromodulation with either a percutaneous nerve stimulation or a temporarily implanted lead may be considered medically necessary in patients with fecal incontinence who meet all of the following criteria (II.A.1-5):

1. There is a diagnosis of chronic fecal incontinence of greater than 2 incontinent episodes on average per week with duration greater than 6 months or for more than 12 months after vaginal childbirth

2. There is documented failure or intolerance to conventional conservative therapy (e.g., dietary modification, the addition of bulking and pharmacologic treatment for at least a sufficient duration to fully assess its efficacy)

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
3. The condition is not related to an anorectal malformation (e.g., congenital anorectal malformation; defects of the external anal sphincter over 60 degrees; visible sequelae of pelvic radiation; active anal abscesses and fistulae) or chronic inflammatory bowel disease.

4. Incontinence is not related to another neurologic condition.

5. The patient has not had rectal surgery in the previous 12 months, or in the case of rectal cancer, the patient has not had rectal surgery in the past 24 months.

B. Permanent implantation of a sacral nerve neuromodulation device may be considered medically necessary in patients with fecal incontinence who meet all of the following criteria:

   1. All of the criteria in II. A (1-5) above are met
   2. A trial stimulation period demonstrates at least 50% improvement in symptoms over a period of at least 1 week.

III. Sacral nerve neuromodulation for the treatment of all other indications is considered investigational, including but not limited to the following:

   A. Chronic constipation
   B. Chronic pelvic pain
   C. Stress incontinence
   D. Urge incontinence due to a neurologic condition including but not limited to:
      1. Detrusor hyperreflexia
      2. Multiple sclerosis
      3. Spinal cord injury
      4. Diabetes with peripheral nerve involvement
   E. Other types of chronic voiding dysfunction

SCIENTIFIC EVIDENCE[2]

Literature Appraisal

Assessment of the safety and efficacy of sacral nerve modulation (SNM) as a treatment for urinary or fecal incontinence requires large, blinded, long-term randomized controlled trials to determine whether 1) the benefits of SNM outweigh any risks, and 2) whether SNM offers advantages over conventional conservative treatments. The appropriate control group(s) against which SNM should be compared is...
sham stimulation, on- versus off-phases in which patients act as their own controls, or conventional conservative therapies.

**Urinary Dysfunction**

**Urge Incontinence**

**Systematic Reviews**

Initially, the policy for SNM as a treatment of urge incontinence was based on a 1998 BlueCross BlueShield Association Technology Evaluation Center (TEC) assessment. Based on a multicenter RCT conducted as part of the FDA approval process, the TEC Assessment concluded that SNM reduced urge incontinence compared with control patients.

Brazzelli et al. performed a review of articles published between 1966 and 2003 which included four randomized controlled trials and 30 case series. The authors reported that about 80% of patients in the randomized trials achieved continence or greater than 50% improvement in their main incontinence symptoms after SNM compared with about 3% of controls receiving conservative treatments. The case series, which were larger but methodically less reliable, showed similar results. Benefits were reported to persist 3 to 5 years after implantation. The authors noted that technical changes over time were associated with decreased complication rates.

**Randomized Controlled Trials**

No new RCTs for urge incontinence were identified since the above systematic reviews were published.

**Nonrandomized Studies**

A 2011 series by Groen and colleagues reported the longest follow-up. A total of 60 patients had at least 5 years of follow-up after SNM for refractory idiopathic urge urinary incontinence. Success was defined as at least a 50% decrease in the number of incontinent episodes or pads used per day. The success rate was 52 of 60 (87%) at 1 month and gradually decreased to 37 (62%) at 5 years. The number of women who were completely continent was 15 (25%) at 1 month and 9 (15%) at 5 years. At the 5-year follow-up, SNM was still used by 48/60 (80%) women. A total of 57 adverse events were reported in 32 of 60 (53%) patients. The most frequent adverse events were hardware-related or pain or discomfort. There were a total of 23 reoperations in 15 patients. In most cases, pain problems were managed conservatively.

**Urinary Urgency/Frequency**

**Systematic Reviews**

No recent systematic reviews were identified.

**Randomized Controlled Trials**

In the multicenter randomized clinical study of 581 patients with a variety of urinary dysfunctions, 220 had significant urgency-frequency symptoms. After 6 months of SNM therapy, 83% of patients with urgency-frequency symptoms reported increased voiding volumes with the same or reduced degree of
frequency. At 12 months, 81% of patients had reached normal voiding frequency. Compared to a control group, patients with implants reported significant improvements in quality of life, as evaluated by the SF-36 health survey.

In 2016, Amundsen et al. reported on a RCT comparing intradetrusor injection of onabotulinumtoxinA (n=192) with SNM (n=189) in women with refractory urgency urinary incontinence, defined as at least one supervised behavioral or physical therapy intervention and the use of a minimum of two anticholinergics (or inability to tolerate or contraindications to the medication).[8] In intention-to-treat analysis, onabotulinumtoxinA-treated patients had greater reductions in urge incontinence per day than SNM-treated patients: 3.9 vs 3.3/ day (mean difference: 0.63; 95% CI 0.13 to 1.14, P=0.01). OnabotulinumtoxinA-treated patients had greater reductions in some overactive bladder-related quality of life questionnaire-related measures, although the clinical meaningfulness of the changes was uncertain. Patients in the onabotulinumtoxinA-treated group were more likely to have urinary tract infections (UTIs, 35% vs 11%; risk difference -23%, 95% CI -33% to -13%, P<0.001).

In 2014 Siegel et al. published an industry-sponsored FDA-mandated postapproval randomized study and is known as the Insite trial.[9] This study compared SNM using a 2-stage surgical procedure with standard medical therapy. Study inclusion criteria included a diagnosis of overactive bladder (OAB) (at least 8 voids per day and/or at least 2 involuntary leaking episodes in 72 hours) and a failed trial of at least 1 anticholinergic or antimuscarinic medication. In addition, there needed to be at least 1 such medication that had not yet been attempted. Patients with neurologic diseases and with primary stress incontinence were excluded. A total of 70 patients were allocated to SNM and 77 to standard medical therapy. Of the 70 patients in the SNM group, 11 elected not to receive test stimulation with the tined lead and 8 received the lead but did not receive a full system implant due to lack of response to a 14-day test stimulation period (response was defined as at least a 50% reduction in average leaks and/or voids). Patients in the medical treatment group tried the next recommended medication or restarted a discontinued medication. Therapeutic success was defined as at least a 50% improvement in average leaks/day or at least a 50% improvement in the number of voids per day or a return to fewer than 8 voids per day. In an intention-to-treat analysis, the therapeutic success rate at 6 months was 61% in the SNM group and 42% in the standard medical treatment group; the difference between groups was statistically significant (p=0.02). Quality of Life (QOL) at 6 months was a secondary outcome. Several validated QOL scales were used, and all favored the SNM group compared with the standard medical treatment group (p<0.002 for all comparisons).

In 2014, Noblett et al. published twelve-month follow-up results of the Insite trial. The analysis included patients included in the SNM group of initial RCT plus additional patients enrolled and implanted in the interim.[10] A total of 340 patients underwent test stimulation, 272 underwent implantation, and 255 completed 12 months of follow-up. In a modified completers’ analysis, the therapeutic success rate was 82%. This modified completers’ analysis included patients who were implanted and had either a baseline or 12-month evaluation, or withdrew from the trial due to a device-related adverse event or lack of efficacy. In an analysis limited to study completers, the therapeutic response rate was 85%. The Noblett analysis did not include data from the control group of patients receiving only standard medical therapy.

In 2014 Tang et al. published the results of an RCT in which 240 women with OAB were randomized to receive tolterodine with (n=120) or without (n=120) sacral neuromodulation.[11] Participants were also divided into subgroups based on the presence or absence of urinary incontinence. The treatment period was 3 months; results were measured by voiding diaries and urodynamic parameters, in addition to psychological depression and anxiety scores. The group receiving SNM reported significantly greater
improvements in the conditions of first desire to void, maximum cystometric capacity, daily average volumes, and daily single maximum voided volumes compared to the group receiving medication alone (p=.001). The SNM group also reported greater decreases in self-rated depression and anxiety scales (p<.001). The authors concluded that combined treatment with SNM and tolterodine could improve the quality of life in women with OAB by decreasing voiding dysfunction symptoms and related depression and anxiety.

**Nonrandomized Studies**

There has also been interest in the use of sacral nerve neuromodulation as a treatment of interstitial cystitis, a condition characterized by painful urinary urgency and frequency.[12-14] These studies reported a decrease in both urgency/frequency and pain. These patients would be considered candidates for sacral neuromodulation therapy based on the presence of urgency and frequency alone.

**Urinary Retention**

**Systematic Review**

A 2009 Cochrane review[15] described 8 randomized studies on implanted devices for urinary storage and voiding dysfunction in adults. In spite of methodologic problems (e.g., generally poor quality studies), the evidence “seems clear that continuous stimulation offers benefits for carefully selected people with overactive bladder syndrome and for those with urinary retention but no structural obstruction.” The authors concluded that while some people benefit, more research is needed to improve patient selection, to carry out the implant, and to find why so many fail.

In 2014, the Agency for Healthcare Research and Quality published a comparative effectiveness review focused on chronic urinary retention treatments.[16] The authors identified the previously described Cochran review as providing “low-strength evidence that neuromodulation improves the rate at which patients with Fowler’s syndrome can be catheter free after treatment,” but noted that there were few studies overall, and most were small and had other methodologic limitations.

**Randomized Controlled Trial**

In the randomized clinical study submitted to the FDA as part of the approval process, 177 of 581 patients had urinary retention.[7] Patients with urinary retention reported significant improvements in terms of volume catheterized per catheterization, a decrease in the number of catheterizations per day, and increased total voided volume per day. At 12 months post-implant, 61% of patients had eliminated the use of catheterization. Patients with implants also reported improved quality of life.

**Complications of SNM for Urinary Dysfunctions**

A large prospective series by White et al. focused on complications associated with SNM in 202 patients with urge incontinence, urinary urgency, or urinary retention.[17] At a mean follow-up of 37 months (range, 7-84), 67 patients (30%) had experienced adverse events that required either lead or implantable pulse generator revisions. Complications included pain (3%), device malfunction secondary to trauma (9%), infection (4%), postoperative hematoma (2%), and lead migration (6%). In addition, 5% of patients underwent elective removal, 4% had device removal due to lack of efficacy, and 2% required removal due to battery expiration. At the last follow-up, 172 patients (85%) had functional implanted units.
Conclusion

Data from RCTs and case series with long-term follow-up provides sufficient evidence to conclude that sacral nerve neuromodulation is effective and safe in selected patients with urge incontinence, urgency-frequency syndrome, and non-obstructive urinary retention.

Defecation Dysfunction

Fecal Incontinence

Systematic Reviews

A 2015 Cochrane review evaluated sacral nerve stimulation for fecal incontinence and constipation in adults.[18] This review included six trials assessing the effects of SNM for fecal incontinence. Two parallel group trials found that SNM reduced the number of incontinence episodes when compared with optimal medical therapy or percutaneous tibial nerve stimulation. Three of the four included crossover trials found reductions in incontinence episodes during the SNM “on” period relative to the “off” period; in the other crossover trial, participants did not experience any episodes of fecal incontinence during either period. The primary methodological quality issue noted was related to lack of clarity around randomization techniques and allocation concealment. The review authors concluded that there was limited evidence that SNM could improve continence in some patients with fecal incontinence.

In 2016, the Agency for Healthcare Research and Quality published a comparative effectiveness review on treatments for fecal incontinence.[19] There were 63 studies that met inclusion criteria for the review, and 53 surgical case series were reviewed for adverse events. There were 38 RCTs that assessed nonsurgical treatments and 12 that reviewed surgical interventions, including five studies of SNM. Regarding SNM, the authors concluded that the evidence was “insufficient because all five studies had moderate or high risk of bias, and none assessed the same treatment-outcome combination.”

In 2013, Thin et al. published a systematic review of randomized trials and observational studies on SNM for treating fecal incontinence.[20] A total of 61 studies met eligibility criteria; including at least 10 patients, having a clear follow-up interval and reporting the success rate of therapy based on a 50% or greater improvement in fecal incontinence episodes. Only 2 of the studies were RCTs,[21,22] and 50 were prospective case series. Data from 2 studies with long-term follow-up could be pooled to calculate median success rates using an intention-to-treat analysis. These median success rates were 63% in the short term (no more than 12 months’ follow-up), 58% in the medium term (12-36 months), and 54% in the long term (>36 months). The per-protocol short-, medium-, and long-term success rates were 79%, 80%, and 84%, respectively.

A 2009 Cochrane review reported on three cross-over studies, two for fecal incontinence (n=34 and n=2, respectively) and one for constipation (n=2).[23] This very limited evidence suggested that sacral nerve stimulation can improve continence in selected patients; however, it also reported that temporary, percutaneous stimulation for a 2-3 week period did not always successfully identify patients most likely to benefit from the stimulation. The authors concluded that larger, good quality randomized crossover trials are needed.

In 2011, Maeda et al. published a systematic review of studies on complications following permanent implantation of a SNM device for fecal incontinence and constipation.[24] The authors identified 94
articles. The vast majority of studies addressed fecal incontinence. A combined analysis of data from 31 studies on SNM for fecal incontinence reported a 12% suboptimal response to therapy (149 of 1,232 patients). A review of complications reported in the studies found that the most commonly reported complication was pain around the site of implantation, with a pooled rate of 13% (81/621 patients). The most common response to this complication was repositioning the stimulator, followed by explantation of the device and reprogramming. The second most common adverse event was infection, with a pooled rate of 4% (40/1025 patients). Twenty-five of the 40 infections (63%) led to explantation of the device.

In 2011, Tan et al. published a meta-analysis of randomized trials and observational studies published between 2000 and 2008 on SNM for treating fecal incontinence.[25] They identified a total of 34 studies that reported on at least one of their outcomes of interest and clearly documented how many patients underwent temporary and permanent SNM. Only one of these studies was an RCT; this was the study by Tjandra and colleagues, discussed earlier.[21] In the 34 studies, a total of 944 patients underwent temporary SNM and 665 subsequently underwent permanent SNM implantation. There were 279 patients who did not receive permanent implantation, and 154 of these were lost to follow-up. Follow-up in the studies ranged from 2 weeks to 35 weeks. In a pooled analysis of findings of 28 studies, there was a statistically significant decrease in incontinence episodes per week with SNM compared to maximal conservative therapy (weighted mean difference: -6.83; 95% confidence interval [CI]: -8.05 to -5.60, p<0.001). Fourteen studies reported incontinence scores, and when these results were pooled, there was also a significantly greater improvement in scores with SNM compared to conservative therapy (weighted mean difference: -10.57, 95% CI: -11.89 to -9.24, p<0.001).

A 2016 systematic review focused on the adverse events associated with SNM treatment of fecal incontinence.[26] A literature search of PubMed and Embase was performed for studies that included at least five patients with fecal incontinence treated with SNM. The researchers additionally searched the FDA’s Manufacturer and User Device Experience (MAUDE) database for reports from 2005 to October 2015. There were 45 articles included in the review that described distinct patient cohorts and provided information about adverse events. These included a total of 1,953 patients and a median follow-up time of 27 months. There were two studies with a total of 201 that provided the most detailed information.[27,28] In these two studies, approximately 20% of the patients had their devices explanted by the end of follow-up and a substantial number required additional surgeries. There were five more studies that reported adverse events with less detail, and these reported a significantly lower incidence of such events. Information on infectious complications was reported in 44 studies with 1,953 patients, and the pooled rate of these was 5.1%. There were 39 studies with 1,810 patients that reported explant rates, with an average rate of 10.0%. Increases in explant rates were seen with increased follow-up duration. An overall re-operation rate of 18.6% was seen, based on data from 1,784 patients. According to the MAUDE database, there was an average of ten incidents per month related to the Interstim device in 2005. This rose to approximately 100 incidents per month within the next three years and stabilized until the year prior to FDA approval of the device as a treatment for fecal incontinence, and have since tripled. From August 1 - October 31, there were 1,684 problem reports received by the FDA, with 652 reports mentioning gastrointestinal issues as indications for SNM treatment and 278 reports specifically referring to fecal incontinence or bowel dysfunction. Most adverse events were reported within two years after device implantation.

In 2015, a systematic review was published that evaluated the impact of SNM on clinical symptoms and gastrointestinal physiology in patients with fecal incontinence.[29] There were 81 studies included in the review, and the clinical outcomes assessed included frequency of fecal incontinence episodes, fecal incontinence severity score, and treatment success rates. A meta-analysis of the data from these studies was not possible, as most lacked a comparison group. Following SNM device implantation, ‘perfect’
continence was reported in 13%-88% of patients. The majority of studies found a reduction in incontinence episodes per week (mean, -7.0; range, -24.8 to -2.7) and Wexner scores. The studies did not demonstrate any consistent, statistically significant effects of SNM on physiological parameters or identify any clinicophysiological factors that predicted success.

**Randomized Controlled Trials**

No new RCTs for fecal incontinence were identified since the above systematic review was published.

**Nonrandomized studies**

In 2016, Patton et al. evaluated medium-term outcomes from SNM patients at a single institution.[30] Of the 166 patients that underwent preliminary nerve stimulation testing, 112 had a permanent device implanted, and an additional 15 patients received a device without an initial testing phase for a total of 127 patients with SNM devices. The mean follow-up was 2.7 years (range, 2 months – 8.5 years), and 14 patients had the device removed and four had died, leaving 109 patients. Of these, 91 (83%) responded to the follow-up survey. There were significant improvements from baseline in St Mark’s continence score (from 10.3 to 14.4, p < 0.01), bowel control score, and fecal incontinence quality of life measures. Complications from the device included 12 infections, five of which required surgery, 17 lead dislodgements, and five rotated SNM devices that required repositioning.

In 2016, Duelund et al. published the results of a two-center prospective registry study that included 164 fecal incontinence patients treated with SNM between 2009 and 2013.[31] The median follow-up in the study was 22 months (range, 1-50 months). There were improvements in Wexner incontinence scores and VAS impact on daily life. During follow-up, additional surgeries were required in 19.5% of patients. The most common complication was repositioning of the device due to pain or migration in 12.1% of patients, and infections leading to explantation were reported for 3% of patients. The same group also evaluated the effects of bilateral versus unilateral SNM for fecal incontinence treatment, and found no significant differences between groups.[32]

A 2014, study by Altomare et al. reported long-term outcomes (minimum of 60-month follow-up, median of 84-month follow-up) in patients implanted with a sacral nerve stimulator for fecal incontinence.[33] Patients were identified in a European registry and surveyed. Long-term success was defined as maintaining the temporary stimulation success criteria, i.e., at least 50% improvement in the number of fecal incontinence episodes (or fecal incontinence symptom score) at last follow-up, compared with baseline. A total of 272 patients underwent permanent implantation of an SNM device and 228 were available for follow-up. A total of 194 of the 272 (71.3%) implanted patients maintained improvement in the long term.

In 2013, Hull et al. reported outcomes in 72 patients (60% of the 120 implanted patients) who had completed a 5-year follow-up visit.[27] Sixty-four (89%) of the patients who contributed bowel diary data at 5 years had at least a 50% improvement from baseline in weekly incontinent episodes and 26 of the 72 patients (36%) had achieved total continence. It is uncertain whether outcomes differed in the 40% of patients who were missing from the 5-year analysis.

Mellgren et al. reported on the long-term effectiveness and safety of sacral nerve stimulation for fecal incontinence in a large prospective multicenter study.[34] One hundred thirty-three patients underwent test stimulation with a 90% success rate. Mean length of follow-up was 3.1 (range, 0.2-6.1) years, with 83 patients completing all or part of the 3-year follow-up assessment. At 3 years follow-up, 86% of
patients (P < .0001) reported ≥ 50% reduction in the number of incontinent episodes per week compared with baseline and the number of incontinent episodes per week decreased from a mean of 9.4 at baseline to 1.7. Perfect continence was achieved in 40% of subjects. Sacral nerve stimulation had a positive impact on the quality of life. There were no reported unanticipated adverse device effects associated with sacral nerve stimulation therapy.

In 2011, Maeda and colleagues in Denmark published a retrospective review of prospectively collected data from 176 patients who underwent permanent SNM for fecal incontinence. A total of 245 patients had initially undergone temporary stimulation. The review focused on reportable events, defined as suboptimal outcomes (lack of or loss of efficacy) or adverse events. At the time of data collection, a median of 47 months had elapsed since implantation of InterStim (n=106) and 21 months in patients implanted with InterStim II (n=70). A total of 592 reportable events were identified in 150 of the 176 (85.2%) patients after a median of 11 months using the implantable devices. Overall, interventions were able to successfully resolve 63 of 212 events (30%). The five-year follow-up results from this study was published in 2014. At this point, 60 of the 101 patients reported a favorable outcome and 41 reported an unfavorable outcome, with 24 of these patients having had their devices removed or permanently switched off. There were 521 reportable events recorded from 94 of the patients (93.1%)

Michelsen et al. reported on the outcome of percutaneous nerve evaluation tests and sacral nerve stimulation for the treatment of fecal incontinence from a single center covering a period of 6 years. A total of 177 patients with fecal incontinence underwent a percutaneous nerve evaluation test. Of these patients, 142 (80%) had a positive test, including 21 of 25 (84%) patients who required a repeat percutaneous nerve evaluation test. Because of a functional failure, 16 patients underwent a revision of the permanent electrode. Of 126 patients, 15 (12%) have undergone an explantation, with an infection rate of only 1.6%. Overall, after a median follow-up of 24 (range, 3-72) months, the median Wexner incontinence score decreased from 16 (range, 6-20) to 10 (range, 0-20) (P < .0001).

In 2010, Wexner and others determined the safety and efficacy of sacral nerve stimulation. A total of 133 patients underwent test stimulation with a 90% success rate, and 120 (110 females) of a mean age of 60.5 years and a mean duration of FI of 6.8 years received chronic implantation. Mean follow-up was 28 (range, 2.2-69.5) months. At 12 months, 83% of subjects achieved therapeutic success (95% confidence interval: 74%-90%; P < 0.0001), and 41% achieved 100% continence. Therapeutic success was 85% at 24 months. Incontinent episodes decreased from a mean of 9.4 per week at baseline to 1.9 at 12 months and 2.9 at 2 years. There were no reported unanticipated adverse device effects associated with InterStim Therapy.

Other small case series (n = 10-40) have reported the experiences of patients with fecal incontinence who were treated with sacral neuromodulation. These series are not summarized in depth here because methodological limitations do not permit conclusions on the safety and effectiveness of SNM for fecal incontinence. These limitations included patients with a variety of etiologies of fecal incontinence, including obstetric injury, spinal cord injury, prior surgery, sacral malformation, or idiopathic incontinence and the wide range of follow-up periods (e.g., 2 months– 9.5 years). Thus, it is difficult to determine the complication rates or the durability of any benefits initially reported.

**Conclusion**

With longer term results from 2 randomized controlled trials, prospective case series, and a pooled analysis of data from the RCTs and observational studies, evidence is considered sufficient to conclude
that sacral nerve neuromodulation/stimulation improves outcomes when used for the treatment for chronic fecal incontinence in well-selected patients who have failed conservative therapy.

Constipation

Systematic Review

The 2015 Cochrane review of SNM for fecal incontinence and constipation, described earlier, included two studies assessing SNM as a constipation treatment. One trial, which included only two participants, found that the participants experienced a greater number of bowel movements per week when the device was on. The other trial, a larger randomized trial by Dinning et al., found that SNM did not affect the frequency of bowel movements. The study included patients aged 18 to 75 years with slow transit constipation. Potentially eligible patients completed a three-week stool diary and, in order to continue participating, they needed to indicate in the diary that they had complete bowel movements less than three days per week for at least two of the three weeks. Patients with metabolic, neurogenic or endocrine disorders known to cause constipation were excluded. There were 57 patients that met eligibility criteria and had temporary percutaneous nerve evaluation (PNE), and 55 underwent permanent implantation. In random order, patients received active stimulation or sham stimulation. The primary outcome measure, determined by stool diaries, was a bowel movement with feelings of complete evacuation more than two days per week for at least two of three weeks; it was only assessed in phase 2. Compared with sham stimulation, 16 of 54 patients (29.6%) met the primary outcome during stimulation and 11 of 53 patients (20.8%) met it during sham stimulation; the difference was not statistically significant (p=0.23). Other outcomes did not differ significantly by group. The review authors concluded that SMN did not improve constipation symptoms and there were some adverse events associated with its use.

In 2013, Thomas et al. published a systematic review of controlled and uncontrolled studies evaluating sacral nerve stimulation for treatment of chronic constipation. The authors identified 11 case series and 2 blinded cross-over studies. Sample sizes in the case series ranged from 4 to 68 patients implanted with a permanent SNM device; in 7 of the 11 studies, fewer than 25 patients underwent SNM implantation. Among the 2 cross-over studies, one included 2 patients implanted with an SNM device. The other, a 2012 study by Knowles and colleagues, temporary stimulation was evaluated in 14 patients. Patients were included if they were diagnosed with evacuatory dysfunction and rectal hyposensitivity and had failed maximal conservative treatment. Patients were randomized to 2 weeks of stimulation with the SNM device turned on and 2 weeks with the SNM device turned off, in random order. There was no wash-out period between treatments. The primary efficacy outcome was change in rectal sensitivity and was assessed using 3 measures of rectal sensory thresholds. The study found a statistically significantly greater increase in rectal sensitivity with the device turned on in 2 of the 3 measures. Among the secondary outcome measures, there was a significantly greater benefit of active treatment on the percentage of successful bowel movements per week and the percentage of episodes with a sense of complete evacuation. In addition to its small sample size, the study was limited by the lack of a wash-out period between treatments i.e., there could have been a carry-over effect when the device was used first in the “on” position. Moreover, the authors noted that the patients were highly selected; only 14 of the approximately 1800 patients approached met the eligibility criteria and agreed to participate in the study.

Randomized Controlled Trials
One RCT has been published since the 2015 Cochrane review. This double-blind crossover trial, by Zerbib et al., included 36 patients (34 women) with refractory constipation, defined as at least two of the following criteria: fewer than three bowel movements per week, sensation of incomplete evacuation on more than a quarter of attempts, or straining to evacuate on more than a quarter of attempts. This study defined a positive response to therapy as a more than 50% improvement in symptoms and/or at least three bowel movements per week. Of the 36 patients, 20 responded to the initial peripheral nerve evaluation and had a permanent stimulator implanted. Positive responses were seen in 12 of the patients during the active stimulation period and 11 of the patients during the sham stimulation period. Adverse events noted by the researchers included device-related pain in five patients and wound infection or hematoma in three patients, leading to device removal in two patients. SNM did not have a significant effect on colonic transit time. The authors concluded that the results of the study did not support the placement of SNM devices in patients with refractory constipation. The improvements seen with sham stimulation highlight the importance of control groups for comparison in studies of this technology.

Additionally, longer-term follow-up results to the study by Dinning et al. were published in 2016. There were 53 patients that entered long-term follow-up, with one patient death. Adverse events or patient dissatisfaction lead to 44 patients withdrawing from the study by the end of the second year. Because of this, only ten patients met the primary outcome measure after one year, and only three patients met this measure after two years. There was no difference in colonic isotope retention at 72 hours at one-year follow-up.

**Nonrandomized Studies**

In 2010, Maeda and colleagues published a retrospective review of 38 patients with constipation who received permanent SNM after a successful trial period. The study focused on reportable events, defined as suboptimal outcomes (lack of or loss of efficacy) or adverse events. The authors did not report detailed criteria for temporary or permanent placement of an SNM device. At the time of chart review, a mean of 25.7 months had elapsed since implantation. A total of 58 reportable events were identified in 22 of the 38 (58%) patients. A median of 2 (range 1-9) events per patient were reported; 26 of 58 events (45%) were reported in the first 6 months after device implantation. The most common reportable events were lack or loss of efficacy (26 of 58 events, 45%), and pain (16 events, 28%). Twenty-eight (48%) of the events were resolved by reprogramming. Surgical interventions were required for 19 (33%) of the events, most commonly permanent electrode replacement (14 events). Three of 38 (8%) patients discontinued use of the device due to reportable events.

In 2010, Kamm and colleagues published findings on a prospective study that included patients who failed conservative treatment for intractable idiopathic constipation and underwent 21 days of test stimulation. Sixty-two patients who had idiopathic chronic constipation lasting at least 1 year and had failed medical and behavioral treatments were included. Forty-five of the 62 (73%) met criteria for permanent implantation during the 3-week trial period. After a median follow-up of 28 months (range 1-55 months) after permanent implantation, 39 of 45 (87%) patients were classified as treatment successes (i.e., met same improvement criteria as were used to evaluate temporary stimulation). There was a significant increase in the frequency of bowel movements from a median of 2.3 per week at baseline to 6.6 per week at latest follow-up (p<0.001). The frequency of spontaneous bowel movements (i.e., without use of laxatives or other stimulation) increased from a median of 1.7 per week at baseline to 4.3 per week at last follow-up; p=0.0004. A total of 101 adverse events were reported; 40 (40%) of these were attributed to the underlying constipation or an unrelated diagnosis. Eleven serious adverse events related to treatment were reported (the authors did not specify whether any patients experienced more...
than 1 serious event). The study has been criticized for including a large number of patients who had more than 2 bowel movements per week at study entry.

A prospective registry study published in 2016 evaluated the effects of SNM on antegrade continence enema use in pediatric patients with severe constipation.[45] There were 22 patients below age 21 included; 55% were male and the median age was 12 years. The median frequency of antegrade continence enema use dropped from seven per week to one per week at 12 months. The Fecal Incontinence Severity index improved after 6 months, while other outcomes, including laxative use, Gastrointestinal Symptom Scale, and Fecal Incontinence Quality of Life Scale did not change. Ten children received cecostomy/appendicostomy closure within two years.

Several small case series were identified that focused on patients with slow transit constipation.[46-48] While promising results were reported, these case series are inadequate to permit scientific conclusions due to methodological limitations such as lack of lack of randomization and blinding, and lack of an adequate comparison group.

Conclusion

Only 3 controlled cross-over studies are available; one study was very small and had only 2 patients, the second study had methodological limitations, and the third and largest study showed no statistical difference between sham and stimulation. In addition, there are several, mainly small, case series. This represents insufficient evidence to permit scientific conclusions about the efficacy and safety of sacral nerve neuromodulation/stimulation for patients with constipation.

Chronic Pelvic Pain

Systematic Review

Tirlapur et al. assessed the effectiveness of tibial and sacral nerve stimulation in the treatment of bladder pain syndrome (BPS) and chronic pelvic pain (CPP).[49] Authors included randomized and prospective quasi-randomized controlled studies vs. sham nerve stimulation treatment or usual care of patients with CPP and BPS who underwent sacral or tibial nerve stimulation were included. Three studies with 169 patients treated with tibial nerve stimulation were included; two for CPP and one for BPS. There were improvements in pain, urinary and quality of life scores. There were no reported data for sacral nerve stimulation. Authors concluded that due to the quality of the literature, a large multi-centered clinical trial investigating the effectiveness of electrical nerve stimulation to treat BPS and CPP is recommended.

Nonrandomized studies

Several case series have evaluated sacral neuromodulation for treating chronic pelvic pain. For example, in 2012 Martelluci and colleagues reported on 27 patients with chronic pelvic pain (at least 6 months) who underwent testing for SNM implantation[50]. After a 4-week temporary stimulation phase, 16 of 27 patients (59%) underwent implantation of an Interstim device. In the 16 implanted patients, mean pain on a visual analogue scale (VAS) was 8.1 prior to implantation and 2.1 at the 6- and 12-month follow-ups. An earlier study by Siegel and colleagues reported on 10 patients and stated that 9 of the 10 experienced a decrease in pain with SNM.[51]

Conclusion
Data from several small case series with heterogenous patients represents insufficient evidence that sacral nerve neuromodulation/stimulation is safe and effective for treating chronic pelvic pain. RCTs are needed, with sham control groups, to assess the efficacy of neuromodulation/stimulation as a treatment of chronic pelvic pain.

Clinical Practice Guidelines

American Urological Association (AUA) and the Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU)\[52\]

The 2014 joint AUA/SUFU guidelines for non-neurogenic OAB in adults considers SNM an option for third-line treatment in carefully selected patients who failed conservative therapies and are characterized by severe OAB symptoms or those not considered candidates for pharmacologic therapy. The recommendation was graded as an “option,” defined as a non-directive statement that leaves the decision up to the individual clinician and patient because the balance between benefits and risks/burdens appears equal or uncertain. The strength of evidence was given a Grade C defined as low quality/low certainty based on observational studies that are inconsistent, small, or have other limitations that potentially confound interpretation of the data.

Summary

There is enough research to show that sacral nerve neuromodulation/stimulation (SNM) can improve health outcomes and quality of life in some patients with urinary urge, urinary incontinence, urinary retention, or fecal incontinence. Therefore, SNM may be considered medically necessary for these conditions when the policy criteria are met.

There is not enough research to show that sacral nerve neuromodulation/stimulation (SNM) improves health outcomes for people with conditions other than urinary urge or urinary incontinence, urinary retention, and fecal incontinence. Therefore, SNM is considered investigational for other conditions, including but is not limited to chronic constipation, chronic pelvic pain, urinary stress incontinence, or urge incontinence due to neurologic conditions such as multiple sclerosis, spinal cord injury, diabetes-related peripheral nerve conditions, and detrusor hyperreflexia.

REFERENCES

2. BlueCross BlueShield Association Medical Policy Reference Manual "Sacral Nerve Neuromodulation/Stimulation for Pelvic Floor Dysfunction " Policy No. 7.01.69

October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.


These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.


**CROSS REFERENCES**

Pelvic Floor Stimulation as a Treatment of Urinary Incontinence, Allied Health, Policy No. 4

Transanal Radiofrequency Treatment of Fecal Incontinence, Surgery, Policy No. 129

Posterior Tibial Nerve Stimulation for Voiding Dysfunction, Surgery, Policy No. 154
<table>
<thead>
<tr>
<th>CODES</th>
<th>NUMBER</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>64561</td>
<td>Percutaneous implantation of neurostimulator electrode array; sacral nerve (transforaminal placement) including image guidance, if performed</td>
</tr>
<tr>
<td></td>
<td>64581</td>
<td>Incision for implantation of neurostimulator electrode array; sacral nerve (transforaminal placement)</td>
</tr>
<tr>
<td></td>
<td>64585</td>
<td>Revision or removal of peripheral neurostimulator electrode array</td>
</tr>
<tr>
<td></td>
<td>64590</td>
<td>Insertion or replacement of peripheral or gastric neurostimulator pulse generator or receiver, direct or inductive coupling.</td>
</tr>
<tr>
<td></td>
<td>64595</td>
<td>Revision or removal of peripheral or gastric neurostimulator pulse generator or receiver</td>
</tr>
<tr>
<td></td>
<td>95970</td>
<td>Electronic analysis of implanted neurostimulator pulse generator system (e.g., rate, pulse amplitude, pulse duration, configuration of wave form, battery status, electrode selectability, output modulation, cycling, impedance and patient compliance measurements); simple or complex brain, spinal cord, or peripheral (i.e., cranial nerve, peripheral nerve, sacral nerve, neuromuscular) neurostimulator pulse generator/transmitter, without reprogramming</td>
</tr>
<tr>
<td></td>
<td>95971</td>
<td>simple spinal cord, or peripheral (i.e., peripheral nerve, sacral nerve, neuromuscular) neurostimulator pulse generator/transmitter, with intraoperative or subsequent programming</td>
</tr>
<tr>
<td></td>
<td>95972</td>
<td>complex spinal cord, or peripheral (i.e., peripheral nerve, sacral nerve, neuromuscular) (except cranial nerve) neurostimulator pulse generator/transmitter, with intraoperative or subsequent programming</td>
</tr>
<tr>
<td>HCPCS</td>
<td>C1767</td>
<td>Generator, neurostimulator (implantable), nonrechargeable</td>
</tr>
<tr>
<td></td>
<td>L8679</td>
<td>Implantable neurostimulator, pulse generator, any type</td>
</tr>
<tr>
<td></td>
<td>L8680</td>
<td>Implantable neurostimulator electrode, each</td>
</tr>
<tr>
<td></td>
<td>L8681</td>
<td>Patient programmer (external) for use with implantable programmable neurostimulator pulse generator</td>
</tr>
<tr>
<td></td>
<td>L8682</td>
<td>Implantable neurostimulator radiofrequency receiver</td>
</tr>
<tr>
<td></td>
<td>L8683</td>
<td>Radiofrequency transmitter (external) for use with implantable neurostimulator radiofrequency receiver</td>
</tr>
<tr>
<td></td>
<td>L8684</td>
<td>Radiofrequency transmitter (external) for use with implantable sacral root neurostimulator receiver for bowel and bladder management, replacement</td>
</tr>
</tbody>
</table>

October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
<table>
<thead>
<tr>
<th>CODES</th>
<th>NUMBER</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>L8685</td>
<td>Implantable neurostimulator pulse generator, single array, rechargeable, includes extension</td>
</tr>
<tr>
<td></td>
<td>L8686</td>
<td>Implantable neurostimulator pulse generator, single array, non-rechargeable, includes extension</td>
</tr>
<tr>
<td></td>
<td>L8687</td>
<td>Implantable neurostimulator pulse generator, dual array, rechargeable, includes extension</td>
</tr>
<tr>
<td></td>
<td>L8688</td>
<td>Implantable neurostimulator pulse generator, dual array, non-rechargeable, includes extension</td>
</tr>
<tr>
<td></td>
<td>L8689</td>
<td>External recharging system for battery (internal) for use with implantable neurostimulator</td>
</tr>
</tbody>
</table>

October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage.

Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
Regence

Medical Policy Manual

**Topic:** Sacroiliac Joint Fusion  
**Date of Origin:** December 2014

**Section:** Surgery  
**Last Reviewed Date:** December 2016

**Policy No:** 193  
**Effective Date:** February 1, 2017

**IMPORTANT REMINDER**

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

**DESCRIPTION**

The sacroiliac (SI) joint is a strong weight bearing joint with a self-locking mechanism that provides stability with movement on the left and right side of the sacrum. Similar to other structures in the spine, it is assumed that the SI joint may be a source of low back pain but there are currently no reference standards for diagnosis. If conservative therapies fail to adequately treat symptoms, SI joint fusion may be used to stabilize the SI joint including open, percutaneous, and minimally invasive techniques.

**BACKGROUND**

The sacroiliac (SI) joint is a joint between the sacrum and ilium of the pelvis. The SI joint is a strong weight bearing joint with a self-locking mechanism that provides stability with movement on the left and right side of the sacrum. Similar to other structures in the spine, it is assumed that the SI joint may be a source of low back pain.

Currently, there are no reference standards for the diagnosis of SI joint pain. SI joint pain is typically without any consistent, demonstrable radiographic or laboratory features and most commonly exists in the setting of morphologically normal joints. Clinical tests for SI joint pain may include various movement tests, palpation to detect tenderness, and pain descriptions by the patient. Research into sacroiliac joint pain has been inhibited by the lack of any criterion standard to measure its prevalence and against which various clinical examinations can be validated. Further confounding study of the SI
joint is that multiple structures, such as posterior facet joints and lumbar discs, may refer pain to the area surrounding the SI joint.

There are many methods for the treatment of chronic SI joint pain including nonsurgical and surgical approaches. Conservative management may include nonsteroidal anti-inflammatory medications, prescription analgesics, spinal manipulation, physical therapy, a home exercise program, and evaluation and management of cognitive, psychological, or behavioral issues.

If conservative therapies fail to adequately treat symptoms, SI joint fusion may be used to stabilize the SI joint. Surgical approaches include open, percutaneous, and minimally invasive techniques. The open surgery technique involves the iliac crest bone and the sacrum being held together with plates and/or screws until fusion occurs between the two bones. The use of minimally invasive techniques to fuse the SI joint has increased over the last several years. Minimally invasive procedures use specially designed implants for the stabilization of the SI joint. Recently, there have been several publications and reports of a technique that places a series of triangular titanium implants across the SI joint.

**Regulatory Status**

Several percutaneous or minimally invasive fixation/fusion devices have received marketing clearance by the Food and Drug Administration. These include the SI-FIX Sacroiliac Joint Fusion System (Medtronic), the IFUSE® Implant System (SI Bone), the Slmmetry® Sacroiliac Joint Fusion System (Zyga Technologies), Silex™ Sacroiliac Joint Fusion System (X-Spine Systems) and the SI-LOK® Sacroiliac Joint Fixation System (Globus Medical). FDA Product Code: OUR.

Note: This policy does not address percutaneous sacroplasty which is addressed in the *Percutaneous Vertebroplasty and Kyphoplasty* policy (SUR107).

**MEDICAL POLICY CRITERIA**

I. Injection for the purpose of diagnosing sacroiliac joint pain may be considered medically necessary when all of the following criteria (I.A-C) have been met:

   A. Pain has failed to respond to 3 months of conservative management, which must include all of the following (I.A.1-3):
      1. Use of prescription strength analgesics (including anti-inflammatory medications if not contraindicated); and
      2. Documented participation in at least 6 weeks of physical therapy that must include active exercise or documentation of why the member could not tolerate PT; and
      3. Evaluation and appropriate management of associated rheumatologic issues when present

   B. Dual (controlled) diagnostic blocks with 2 anesthetic agents with differing duration of action are used; and

   C. The injections are performed under imaging guidance.
II. Sacroiliac joint fusion performed by an open procedure may be considered **medically necessary** when one of the following criteria is met:

   A. As an adjunct to sacrectomy or partial sacrectomy related to tumors involving the sacrum; OR

   B. As an adjunct to the medical treatment of sacroiliac joint infection (e.g., osteomyelitis, pyogenic sacroiliitis)/sepsis; OR

   C. As a treatment for severe traumatic injuries associated with pelvic ring fracture.

III. Sacroiliac joint fusion performed by an open procedure, for any other indication not listed above (IIA-C) is considered **not medically necessary**.

IV. Sacroiliac joint fusion performed by percutaneous or minimally invasive techniques is considered **investigational**.

**POLICY GUIDELINES**

A successful trial of controlled diagnostic SI joint or lateral branch blocks consists of two separate positive blocks on different days with local anesthetic only (no steroids or other drugs), or a placebo controlled series of blocks, under fluoroscopic guidance, that has resulted in a reduction in pain for the duration of the local anesthetic used (e.g., three hours longer with bupivacaine than lidocaine). There is not a consensus on whether a minimum of 50% or 75% reduction in pain would be required to be considered a successful diagnostic block, although evidence supports a criterion standard of 75% to 100% reduction in pain with dual blocks. No therapeutic intra-articular injections (i.e., steroids, saline, other substances) should be administered for a period of at least four weeks before the diagnostic block. The diagnostic blocks should not be conducted under intravenous sedation unless specifically indicated (e.g., the patient is unable to cooperate with the procedure).

**SCIENTIFIC EVIDENCE**

SI joint fusion performed by open procedure is considered standard of care to stabilize the sacroiliac joint due to trauma, infection, and tumors involving the sacrum. Therefore, the focus of the literature review is on the use of diagnostic blocks for the diagnosis of SI joint pain and the use of percutaneous or minimally invasive fusion techniques.

Due to the volume of published literature regarding minimally invasive sacroiliac joint fusion with varying study design and quality, the following is a summary of key references published to date. It is important to note that many of the systematic reviews include similar studies in addition to those studies being summarized below.

**Diagnostic Blocks**

The use of diagnostic blocks to evaluate SI joint pain builds on the experience of diagnostic block use in other joints to evaluate pain. Blinded studies with placebo controls (although difficult to conduct when dealing with invasive procedures) are ideally required for scientific validation of sacroiliac joint blocks,
particularly when dealing with pain relief well-known to respond to placebo controls. In the typical evaluation of a diagnostic test, the results of SI diagnostic block would then be compared with a criterion standard. However, there is no current criterion standard for SI joint injection. A search for systematic reviews, randomized controlled trials, and comparative studies on diagnostic blocks was conducted. Two systematic reviews [1,2] are summarized below. A systematic review by Rupert[3] was excluded due to the inclusion of the same studies as the more recent 2012 systematic review[1].

Systematic Reviews

A 2012 systematic review[1] evaluated the accuracy of diagnostic sacroiliac joint interventions. The methodological quality of the studies was evaluated and only the studies meeting at least 50% of the applicable appraisal inclusion criteria were included. A total of 17 studies met inclusion criteria with a range of diagnostic interventions and relief cutoff thresholds. Only one placebo-controlled study was identified with methodological limitations. The review concluded that there is good evidence for the use of controlled diagnostic local anesthetic blocks. Uncontrolled blocks had a false positive rate of approximately 20%. Overall, the systematic review concluded, based on what the authors determined to be good evidence, “there was no significant difference when 70% or greater relief is utilized as the criterion standard with dual blocks.” In addition, the systematic review concluded that “there is no evidence to support the use of ultrasound or landmark-guided injections for sacroiliac joint pain. These injections must be performed under fluoroscopic or radiologic guidance.” Limitations of this systematic review include the lack of high quality evidence, significant variation in interventions, and discrepancies in a gold standard to measure against.

A systematic review was commissioned by the American Pain Society and conducted by the Oregon Evidence-based Practice Center in 2009.[2] The systematic review concluded that no studies were identified that evaluated validity or utility of diagnostic sacroiliac joint block as a diagnostic procedure for low back pain with or without radiculopathy.

Randomized Controlled Trials

No randomized controlled trials have been published.

Conclusion

There is no current criterion standard for SI joint injections to diagnose sacroiliac joint pain limiting the conclusions that can be drawn. The available evidence supports the use of controlled diagnostic local anesthetic blocks. Uncontrolled blocks had a false positive rate of 20%. The prevalence rate of SI joint pain is lower when the cutoff thresholds are higher (> 50%) with the use of dual blocks.

Sacroiliac Joint Fusion

Systematic Reviews

Zaidi (2015) conducted a systematic review of the evidence evaluating SI joint fusion interventions for treating SI joint pain or dysfunction.[4] A comprehensive literature search was conducted and the authors included five case series, eight retrospective studies, and three prospective studies with at least two patients (N=430). The mean duration of follow-up was 60 months with the most common pathology being SI joint degeneration/arthrosis followed by SI joint dysfunction, postpartum instability among other less common pathologies. Study participants reported satisfaction after the procedures which
varied widely. The rates of reoperation for open surgery were 5% to 65% (mean 15%) and for minimally invasive 0% to 17% (mean 6%). Major complications ranged from 5% to 20% with one study reporting a 56% adverse event rate. The authors concluded that surgical intervention is beneficial for a subset of patients and that serious consideration of alternatives should be considered prior to surgery.

Lingutla (2016) published a systematic review with meta-analysis evaluating SI joint fusion for low back pain where it has been determined that the cause of the pain is originating from the sacroiliac joint and not the lumbar spine.[5] Six nonrandomized studies were included with a mean follow-up of 17.6 months. The authors concluded that all outcome measures showed a statistical improvement for alleviating pelvic girdle pain. However, the review consisted of nonrandomized studies with some methodological limitations. More research is needed for this patient population.

A systematic review was conducted by Heiney (2015) that evaluated minimally invasive sacroiliac joint fusion utilizing a lateral transarticular technique.[6] A total of 12 unique studies were included and concluded for this particular technique that minimally invasive SI joint fusion that patients reported improvements in pain, disability, and quality of life scores.

A 2012 systematic review found that the quality of evidence for surgical treatment (débridement, fusion) compared to injection treatment (corticosteroid, botulinum toxin, prolotherapy) for chronic sacroiliac pain was very low.[7] No studies were identified that directly compared surgery to injection therapy. Seven case series using a range of surgical techniques that evaluated a range of surgical treatments were included and summarized. The literature was considered heterogeneous and insufficient to evaluate the comparative effectiveness of surgical treatments compared to other treatments. Several surgical studies reported complications including but not limited to infections, nonunion, further surgery, and intraoperative fracture. Studies had small sample sizes and provided little information on determining successful fusion.

In 2010, Ashman[8] conducted a systematic review comparing fusion to denervation for chronic SI joint pain. Six case series on fusion were identified that evaluated a single treatment. As a result, no conclusions could be drawn for the comparative efficacy of the treatments.

Randomized Controlled Trials

In 2015, Whang et al reported an industry-sponsored nonblinded RCT of the iFuse Implant System in 148 patients.[9] Twelve-month follow-up to this RCT was reported by Polly et al in 2015.[10] However, by 12 months, almost all patients in the control group had crossed over to SI JOINT fusion. Two-year follow-up of this trial was reported by Polly et al in 2016.[11] This last publication will be discussed in the case series section of this report. Trial inclusion was based on a determination of the SI JOINT as a pain generator from a combination of a history of SI JOINT-localized pain, positive provocative testing on at least three of five established physical tests, and at least a 50% decrease in SI JOINT pain after image-guided local anesthetic injection into the SI JOINT. The duration of pain before enrollment averaged 6.4 years (range, 0.47-40.7 years). A large proportion of subjects (37%) had previously undergone lumbar fusion, steroid SI JOINT infections (86%), and RFA (16%).

Patients were assigned 2:1 to minimally invasive SI JOINT fusion (n=102) or to nonsurgical management (n=46). Nonsurgical management included a stepwise progression of nonsurgical treatments, depending on individual patient choice. During follow-up, control patients received physical therapy (97.8%), intra-articular steroid injections (73.9%), and RFA of sacral nerve roots (45.7%). The primary outcome measure was 6-month success rate, defined as the proportion of treated subjects with a
20-mm improvement in SI JOINT pain in the absence of severe device-related or neurologic adverse events or surgical revision. Patients in the control arm could crossover to surgery after six months. Baseline scores indicated that the patients were severely disabled, with VAS pain scores averaging 82.3 out of 100 and ODI scores averaging 61.9 out of 100 (0=no disability, 100=maximum disability).

At six months, success rates were 23.9% in the control group versus 81.4% in the surgical group (posterior probability of superiority >0.999). A clinically important (≥15-point) improvement in ODI score was found in 27.3% of controls compared with 75.0% of fusion patients. Measures of QOL (36-Item Short-Form Health Survey, EuroQol-5D) also improved to a greater extent in the surgery group. Of the 44 nonsurgical management patients still participating at six months, 35 (79.5%) crossed over to fusion. Compared to baseline, opioid use at six months decreased from 67.6% to 58% in the surgery group, and increased from 63% to 70.5% in the control group (p=0.082). At 12 months, opioid use was similar between groups (55% vs 52%, p=0.61). Although these results generally favored fusion, the trial is limited due to the high number of patients that crossed over from the control group to the fusion group. This limits the comparative long-term conclusions that can be drawn.

In 2016, Sturesson et al reported another industry-sponsored nonblinded RCT of the iFuse Implant System in 103 patients. Selection criteria were similar to those of the Whang trial, including at least 50% pain reduction on SI JOINT block. Mean pain duration was 4.5 years. Thirty-three percent of patients had undergone prior lumbar fusion. Nonsurgical management included physical therapy and exercises at least twice per week; interventional procedures (eg, steroid injections, RFA) were not allowed. The primary outcome was change in VAS pain score at six months.

Of 109 randomized subjects, six withdrew before treatment. All patient assigned to iFuse underwent the procedure, and follow-up at six months was in 49 of 51 patients in the control group and in all 52 patients in the iFuse group. At six months, VAS pain scores improved by 43.3 points in the iFuse group and by 5.7 points in the control group (p<0.001). ODI scores improved by 25.5 points in the iFuse group and by 5.8 points in the control group (p=0.001, between groups). QOL outcomes showed a greater improvement in the iFuse group than in the control group. Changes in pain medication use are not reported. Although these results favored fusion, with magnitudes of effect in a range similar to the Whang RCT, this trial was also not blinded and lacked a sham control. Outcomes were only assessed to six months. Six-month results for the Whang and Sturesson trials are shown in Table 1.

### Table 1. Summary of 6-Month iFuse Results From Whang et al[9] and Sturesson et al[12]

<table>
<thead>
<tr>
<th>Results</th>
<th>VAS Score</th>
<th>Success End Point</th>
<th>ODI Score</th>
<th>SF-36 PCS Score</th>
<th>EQ-5D TTO Index</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ctrl</td>
<td>iFuse</td>
<td>Ctrl</td>
<td>iFuse</td>
<td>Ctrl</td>
</tr>
<tr>
<td>Baseline</td>
<td>82.2</td>
<td>82.3</td>
<td>61.1</td>
<td>62.2</td>
<td>30.8</td>
</tr>
<tr>
<td>Follow-up</td>
<td>70.4</td>
<td>29.8</td>
<td>23.9%</td>
<td>81.4%</td>
<td>56.4</td>
</tr>
<tr>
<td>Change</td>
<td>-12.1</td>
<td>-52.6*</td>
<td>-4.9</td>
<td>-30.3*</td>
<td>1.2</td>
</tr>
<tr>
<td>Sturesson et al (2016)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>73.0</td>
<td>77.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up</td>
<td>67.8</td>
<td>34.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change</td>
<td>-5.7</td>
<td>-43.3</td>
<td>-5.8</td>
<td>-25.5</td>
<td>0.11</td>
</tr>
</tbody>
</table>

The success end point was defined as a reduction in pain VAS score of ≥20, absence of device-related events, absence of neurologic worsening, and absence of surgical intervention.

Ctl: control; EQ-5D TTO: EuroQoL Time Tradeoff Index; ODI: Oswestry Disability Index; SF-36 PCS: 36-Item Short-Form Health Survey Physical Component Summary; VAS: visual analog scale. 

* p<0.001.

### Nonrandomized Studies

**Case Series With Good Reported Follow-Up Rates**
Case series with good follow-up rates are more likely to provide valid estimates of outcomes. Series with good follow-up rates (>80%) are reported in this section.

In 2012, Rudolf retrospectively analyzed his first 50 consecutive patients treated with the iFuse Implant System.\[13\] There were 10 perioperative complications, including implant penetration into the sacral neural foramen (two patients) and compression of the L5 nerve (1 patient); these three patients required surgical retraction of the implant. At three years postsurgery, 1 patient required additional implants due to worsening symptoms. At a minimum of 24 months of follow-up (mean, 40 months), the treating surgeon was able to contact 45 patients. The mean pain score was two (1 to 10 scale), and 82% of patients had attained the minimal clinically important difference in pain score (defined as ≥ 2 of 10).

In 2016, results from a case series of 172 patients undergoing SI JOINT fusion reported to two years were published by Duhon et al.\[14,15\] Patients were formally enrolled in a single-arm trial (NCT01640353) with planned follow-up for 24 months. Success was defined as a reduction of VAS pain score of 20 mm (out of 100 mm), absence of device-related adverse events, absence of neurologic worsening, and absence of surgical reintervention. Enrolled patients had a mean VAS pain score of 79.8, a mean ODI score of 55.2, and had a mean pain duration of 5.1 years. At six months, 136 (80.5%) of 169 patients met the success end point, which met the prespecified Bayesian probability of success rate. Mean VAS pain scores were 30.0 at six months and 30.4 at 12 months. Mean ODI scores were 32.5 at six months and 31.4 at 12 months. At two years, 149 (87%) of 172 patients were available for follow-up. VAS pain score at two years was 26.0 and ODI score was 30.9. Thus, 1-year outcomes were maintained at two years. Other outcomes (eg, QOL scores) showed similar maintenance or slight improvement compared to 1-year outcomes. Use of opioid analgesics decreased from 76.2% at baseline to 55% at two years. Over the 2-year follow-up, 8 (4.7%) patients required revision surgery.

In 2016, Polly et al reported 2-year outcomes from the RCT of SI JOINT fusion.\[11\] When reported, without an untreated control group, the study was a case series. Of 102 subjects originally assigned to SI JOINT fusion and treated, 89 (87%) were evaluated at two years. Although the clinical trial used a different composite end point, in this report, clinical outcomes were based on the amount of improvement in SI JOINT pain and in ODI scores. Improvement was defined as a change of 20 points in SI JOINT pain score and 15 points in ODI score. Substantial improvement was defined as a change in in 25 points in SI JOINT pain score or a score of 35 or less and an improvement of 18.8 points in ODI score. At 24 months, 83.1% and 82% had improvement and substantial improvement in SI JOINT pain score, and 68.2% and 65.9% had improvement and substantial improvement in ODI. By 24 months, the proportion taking opioids was reduced from 68.6% at baseline to 48.3%.

A 2014 report by Rudolph and Capobianco described 5-year follow-up for 17 of 21 consecutive patients treated at their institution between 2007 and 2009.\[16\] Of the four patients lost to follow-up, two had died and one had become quadriplegic due to severe neck trauma. For the remaining patients, mean VAS score (range, 0-10) improved from 8.3 before surgery to 2.4 at five years; 88.2% of patients had substantial clinical benefit, which was defined as a 2.5-point decrease in VAS score or a raw score less than 3.5. Mean ODI score at five years was 21.5. Imaging by radiograph and computed tomography showed intra-articular bridging in 87% of patients with no evidence of implant loosening or migration.

**Case Series With Unknown Follow-Up Rates**

The following case series did not report follow-up rates or study methodologies did not permit calculation of the complete number of patients treated.
In 2013, Smith et al retrospectively compared open with minimally invasive SI JOINT fusion. Because all patients received fusion, this study should be interpreted as a case series, with attention paid to the minimally invasive fusion group. Only patients with medical records documenting 12- or 24-month pain scales were included, resulting in 114 patients selected for the minimally invasive group. Losses to follow-up could not be determined. At 12 months, VAS pain scores decreased to a mean of 2.3 from a baseline of 8.1. At 24 months, mean VAS pain score was 1.7, but data for only 38 patients were analyzed. These improvements in VAS pain score were greater than those for open fusion, but conclusions of comparative efficacy should not be made given this type of study. Implant repositioning was performed in 3.5% of patients in the minimally invasive group.

A large (N=144) industry-sponsored, multicenter retrospective series was reported by Sachs et al in 2014. Consecutive patients from 6 sites were included if preoperative and 12-month follow-up data were available. No information was provided on the total number of patients treated during the same time interval. Mean baseline pain score was 8.6. At a mean 16-month follow-up, VAS score was 2.7 (10), an improvement of 6.1. Ten percent of patients reported an improvement of 1 point or less. Substantial clinical benefit, defined as a decrease in pain score by more than 2.5 points or a score of 3.5 or less, was reported in 91.9% of patients.

In 2016, Sachs et al reported outcomes of 107 patients with a minimum follow-up of 3 years. The number of potentially eligible patients was not reported, so the follow-up rate is unknown. Pain scores improved from a mean of 7.5 at baseline to 2.5 at a mean follow-up time of 3.7 years. ODI score at follow-up was 28.2, indicating moderate residual disability. Overall satisfaction rate was 87.9% (67.3% very satisfied, 20.6% somewhat satisfied). Revision surgery was reported in five (4.7%) patients. Without knowing the number of eligible patients, the validity of this study cannot be determined.

Adverse Events

From January 2010 through August 2016, a total of 438 MAUDE database injury reports were identified (product code OUR): 355 mentioned revision, 188 malposition, 32 radicular pain, 24 impingement or impingement, and 14 infection.

Summary

For individuals who have SI joint pain who receive SI joint fusion, the evidence includes two RCTs of minimally invasive fusion and a number of case series. Relevant outcomes are symptoms, functional outcomes, quality of life, medication use, and treatment-related morbidity. Both nonblinded RCTs reported superior short-term results for fusion, but more long term data is needed. Several case series have reported follow-up out to five years and report good outcomes, however, they are limited by study design and lack of a comparator group. More studies are needed that measure objective outcomes in order to evaluate the long-term effectiveness and safety of SI joint fusion.

Clinical Practice Guidelines

North American Spine Society

The North American Spine Society (NASS) published coverage recommendations for percutaneous sacroiliac joint fusion in 2015. NASS indicated that there was relatively moderate evidence. In the absence of high-level data, policies reflect the multidisciplinary experience and expertise of the
committee members in order to present reasonable standard practice indications in the United States. NASS recommended coverage when all of the following criteria are met:

1. “[Patients] have undergone and failed a minimum 6 months of intensive nonoperative treatment that must include medication optimization, activity modification, bracing and active therapeutic exercise targeted at the lumbar spine, pelvis, SI JOINT and hip including a home exercise program.
2. Patient’s report of typically unilateral pain that is caudal to the lumbar spine (L5 vertebra), localized over the posterior SI JOINT, and consistent with SI JOINT pain.
3. A thorough physical examination demonstrating localized tenderness with palpation over the sacral sulcus (Fortin’s point, ie, at the insertion of the long dorsal ligament inferior to the posterior superior iliac spine or PSIS) in the absence of tenderness of similar severity elsewhere (eg, greater trochanter, lumbar spine, coccyx) and that other obvious sources for their pain do not exist.
4. Positive response to a cluster of 3 provocative tests (eg, thigh thrust test, compression test, Gaenslen’s test, distraction test, Patrick’s sign, posterior provocation test). Note that the thrust test is not recommended in pregnant patients or those with connective tissue disorders.
5. Absence of generalized pain behavior (eg, somatoform disorder) or generalized pain disorders (eg, fibromyalgia).
6. Diagnostic imaging studies that include ALL of the following:
   a. Imaging (plain radiographs and a CT [computed tomography] or MRI [magnetic resonance imaging]) of the SI joint that excludes the presence of destructive lesions (eg, tumor, infection) or inflammatory arthropathy that would not be properly addressed by percutaneous SI JOINT fusion.
   b. Imaging of the pelvis (AP [anteroposterior] plain radiograph) to rule out concomitant hip pathology.
   c. Imaging of the lumbar spine (CT or MRI) to rule out neural compression or other degenerative condition that can be causing low back or buttock pain.
   d. Imaging of the SI joint that indicates evidence of injury and/or degeneration.
7. At least 75% reduction of pain for the expected duration of the anesthetic used following an image-guided, contrast-enhanced intra-articular SI joint injection on 2 separate occasions.
8. A trial of at least one therapeutic intra-articular SI joint injection (ie, corticosteroid injection).”

International Society for the Advancement of Spine Surgery

The International Society for the Advancement of Spine Surgery (ISASS) published a policy statement on minimally invasive sacroiliac joint fusion. These recommendations were updated in 2016.[21] ISASS lists criteria for determining a patient’s eligibility regarding minimally invasive SI joint fusion. However, the statement has several limitations including but not limited to the literature review methods are not transparent, there is no formal assessment of the quality of the evidence, and there is not a clear link between the recommendations and supporting evidence. ISASS recommendations state that patients who have all of the following criteria may be eligible for minimally invasive SI joint fusion:

- “Significant SI joint pain … or significantly limitations in activities of daily living because of pain from the SI joint(s).
- “SI joint pain confirmed with … at least three positive physical provocation examination maneuvers that stress the SI joint.
- “Confirmation of the SI joint as a pain generator with ≥ 75% acute decrease in pain immediately following fluoroscopically guided diagnostic intra-articular SI joint block using local anesthetic.
“Failure to respond to at least six months of non-surgical treatment consisting of non-steroidal anti-inflammatory drugs and/or … one or more of the following: … physical therapy…. Failure to respond means continued pain that interferes with activities of daily living and/or results in functional disability;

“Additional or alternative diagnoses that could be responsible for the patient’s ongoing pain or disability have been considered, investigated and ruled out.”

American Society of Interventional Pain Physicians (ASIPP)

The ASIPP guidelines published in 2013 have a recommendation for diagnostic sacroiliac joint injections which were based on a systematic review of the evidence.[22] The guideline indicates that sacroiliac joint blocks appear to be the evaluation of choice to provide appropriate diagnosis, due to the inability to make the diagnosis of sacroiliac joint-mediated pain with noninvasive tests. The ASIPP guidelines conclude and recommend the following for diagnostic sacroiliac joint blocks:

- The evidence for diagnostic intraarticular sacroiliac joint injections is good with 75% to 100% pain relief as the criterion standard with controlled local anesthetic or placebo blocks, and fair due to the limitation of the number of studies with 50% to 74% relief with a dual block.
- Controlled sacroiliac joint blocks with placebo or controlled comparative local anesthetic blocks are recommended when indications are satisfied with suspicion of sacroiliac joint pain.

American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine Practice

In 2010, the American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine Practice updated their guidelines for chronic pain management.[23] The guidelines recommend that diagnostic sacroiliac joint injections or lateral branch blocks may be considered for the evaluation of patients with suspected sacroiliac joint pain.

American Pain Society (APS)

The 2009 practice guidelines from the APS were based on a systematic review that was commissioned by the APS and conducted at the Oregon Evidence-based Practice Center.[2,24] The APS guideline states that there is insufficient evidence to evaluate the validity or utility of diagnostic sacroiliac joint block as a diagnostic procedure for low back pain with or without radiculopathy.

Summary

Based on the established use of injections to diagnose pain in other joints and clinical practice guideline recommendations, controlled diagnostic injections (two blocks with anesthetics of different duration) in select patients may be considered medically necessary for the diagnosis of sacroiliac joint pain when the policy criteria are met.

Sacroiliac joint fusion or fixation performed by open procedure is considered standard of care for traumatic injuries, tumors involving the sacrum, and SI joint infection/sepsis as outlined in the Medical Policy Criteria and therefore may be considered medically necessary. Sacroiliac joint fusion performed by an open procedure for any other indication is considered not medically necessary.
There is not enough research on percutaneous or minimally invasive sacroiliac joint fixation or fusion to permit conclusions regarding the effect of these procedures on health outcomes and safety. More research is needed that measures objective outcomes for a longer period of time. Therefore, these techniques are considered investigational for the treatment of SI joint pain.

REFERENCES


CROSS REFERENCES

Lumbar Spinal Fusion, Surgery Policy No. 187

Percutaneous Vertebroplasty, Kyphoplasty, Sacroplasty, and Coccygeoplasty, Surgery, Policy No. 107
<table>
<thead>
<tr>
<th>CODES</th>
<th>NUMBER</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>22899</td>
<td>Unlisted procedure, spine</td>
</tr>
<tr>
<td></td>
<td>27096</td>
<td>Injection procedure for sacroiliac joint, anesthetic/steroid, with image guidance (fluoroscopy or CT) including arthrography when performed</td>
</tr>
<tr>
<td></td>
<td>27279</td>
<td>Arthrodesis, sacroiliac joint, percutaneous or minimally invasive (indirect visualization), with image guidance, includes obtaining bone graft when performed, and placement of transfixing device</td>
</tr>
<tr>
<td></td>
<td>27280</td>
<td>Arthrodesis, open, sacroiliac joint, including obtaining bone graft, including instrumentation, when performed</td>
</tr>
<tr>
<td></td>
<td>27299</td>
<td>Unlisted procedure, pelvis or hip joint</td>
</tr>
<tr>
<td>HCPCS</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage.

Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
Spinal Cord and Dorsal Root Ganglion Stimulation

Effective: June 1, 2017

Next Review: April 2018
Last Review: May 2017

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Standard and high-frequency spinal cord stimulation, as well as dorsal root ganglion stimulation, delivers electrical stimulation to the spinal cord using implanted electrodes to block pain sensation. Dorsal root ganglion stimulation is different from spinal cord stimulation in terms of the placement of the electrodes.

MEDICAL POLICY CRITERIA

Notes:

- This policy only applies to the initial placement of the device. This policy does not apply to revision(s) or replacement(s) after the device has been placed.
- Please see the Regulatory Status section for a list of standard (non-high frequency), high-frequency, and dorsal root ganglion devices.

I. An initial trial period of spinal cord stimulation (standard or high frequency) including with temporarily implanted electrodes may be considered medically necessary when all of the following criteria (I. A – E) are met:

   A. Presence of severe and chronic refractory pain of the trunk or limbs, other than
critical limb ischemia.

B. The treatment is used only as a last resort; other treatment modalities (pharmacological, surgical, psychological, or physical, if applicable) have been tried and failed or are judged to be unsuitable or contraindicated.

C. Trunk and limb pain is neuropathic in nature (i.e. resulting from actual damage to the peripheral nerves). Common indications include, but are not limited to, the following:
   1. Failed back surgery syndrome
   2. Complex regional pain syndrome (i.e., reflex sympathetic dystrophy)
   3. Arachnoiditis
   4. Radiculopathies
   5. Phantom limb/stump pain
   6. Peripheral neuropathy

D. No serious untreated drug habituation exists.

E. Patient has been carefully screened, evaluated, and diagnosed by appropriate consultants of different specialties, who document agreement with application of these therapies or, at a minimum, do not object to application of these therapies.

II. Following an initial trial period of spinal cord stimulation (standard or high frequency) in patients meeting criteria I. A.-E. above, permanent implantation of electrodes for ongoing spinal cord stimulation may be considered medically necessary when at least 50% pain relief has been demonstrated during the trial therapy.

III. Spinal cord stimulation is considered investigational for all other indications, including but not limited to treatment of the following:
   A. Cancer-related pain
   B. Central deafferentation pain (related to CNS damage from a stroke or spinal cord injury)
   C. Chronic pelvic pain
   D. Chronic refractory angina pectoris
   E. Critical limb ischemia to forestall amputation
   F. Headache, including but not limited to chronic cluster headaches
   G. Heart failure
   H. Nociceptive pain (resulting from irritation, not damage to the nerves)
   I. Postherpetic neuralgia
   J. Visceral pain
   K. Vulvodynia; vulvar vestibulitis

IV. Dorsal root ganglion stimulation is considered investigational for all indications.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.
CROSS REFERENCES
1. Electrical Stimulation Devices Index, Durable Medical Equipment, Policy No. 83
2. Deep Brain Stimulation, Surgery, Policy No. 84
3. Occipital Nerve Stimulation, Surgery, Policy No. 174

BACKGROUND

Spinal cord stimulation (SCS; also called dorsal column stimulation) involves the use of low-level epidural electrical stimulation of the spinal cord dorsal columns. The neurophysiology of pain relief after SCS is uncertain but may be related to either activation of an inhibitory system or to blockage of facilitative circuits. SCS has been used in a wide variety of chronic refractory pain conditions, including pain associated with cancer, failed back pain syndromes, arachnoiditis, and complex regional pain syndrome (i.e., chronic reflex sympathetic dystrophy). There has also been interest in SCS as a treatment of critical limb ischemia, primarily in patients who are poor candidates for revascularization and in patients with refractory chest pain.

SCS devices consist of several components: (1) the lead that delivers the electrical stimulation to the spinal cord; (2) an extension wire that conducts the electrical stimulation from the power source to the lead; and (3) a power source that generates the electrical stimulation. The lead may incorporate from 4 to 8 electrodes, with 8 electrodes more commonly used for complex pain patterns. There are two basic types of power source. One type, the power source (battery), can be surgically implanted. The other, a radiofrequency receiver, is implanted, and the power source is worn externally with an antenna over the receiver. Totally implantable systems are most commonly used.

The patient’s pain distribution pattern dictates at what level in the spinal cord the stimulation lead is placed. The pain pattern may influence the type of device used; for example, a lead with 8 electrodes may be selected for those with complex pain patterns or bilateral pain. Implantation of the spinal cord stimulator is typically a 2-step process. Initially, the electrode is temporarily implanted in the epidural space, allowing a trial period of stimulation. Once treatment effectiveness is confirmed (defined as at least 50% reduction in pain), the electrodes and radio-receiver/transducer are permanently implanted. Successful SCS may require extensive programming of the neurostimulators to identify the optimal electrode combinations and stimulation channels.

Traditional SCS devices use electrical stimulation with a frequency on the order of 100 to 1000 Hz. In 2015, an SCS device, using a higher frequency of electrical stimulation (10,000 Hz) than predicate devices was approved by the U.S. Food and Drug Administration (FDA) through the premarket approval process. The high-frequency stimulation is proposed to be associated with fewer paresthesias, which are a recognized effect of SCS. In addition, in 2016, FDA approved a clinician programmer “app” that allows an SCS device to provide stimulation in “bursts” rather than at a constant rate. Burst stimulation is proposed to provide pain relief with fewer paresthesias. The burst stimulation device works in conjunction with standard SCS devices. With the newly approved app, stimulation is provided in five 500-Hz burst spikes at a rate of 40 Hz, with a pulse width of 1 ms.

Another variation on SCS stimulation is the wireless injectable stimulator. These miniaturized neurostimulators are transforaminally placed at the dorsal root ganglion (DRG) and are used to treat pain. DRG are located between spinal nerves and the spinal cord on the posterior root.
and are believed to play an important role in neuropathic pain perception. Two systems have received approval or clearance from FDA.

**REGULATORY STATUS**

A large number of neurostimulator devices, some used for spinal cord stimulation (SCS), have been approved by the U.S. Food and Drug Administration (FDA) through the premarket approval (PMA) process. Examples of fully implantable SCS devices approved through the PMA process include the Cordis programmable neurostimulator (Cordis Corp., Downers Grove, IL), approved in 1981, the Itrel™ (Medtronic, Minneapolis, MN), approved in 1984, the Genesis and Eon devices (St Jude Medical) in 2001 and the Precision Spinal Cord Stimulator (Advanced Bionics, Switzerland), approved in 2004. FDA product code: LGW.

In May 2015, the Nevro Senza™ Spinal Cord Stimulator (Nevro Corp., Menlo Park, CA), a totally implantable neurostimulator device, was approved by FDA for the following indications: chronic intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with the following: failed back surgery syndrome (FBSS), intractable low back pain, and leg pain. This device uses a higher frequency of electrical stimulation (10 kHz) than standard devices.

Two wireless injectable neurostimulators have been approved or cleared by FDA. In February 2016, FDA approved the Axium Neurostimulator System (Spinal Modulation, Menlo Park, CA) through the PMA process. The device is indicated as an aid the management of moderate-to-severe intractable pain of the lower limbs in adults with complex regional pain syndrome types 1 and II. In August 2016, the Freedom Spinal Cord Stimulator (Stimwave Technologies, Fort Lauderdale, FL) was cleared by FDA through the 510(k) process for treating chronic, intractable pain of the trunk and/or lower limbs.

In October 2016, FDA approved BurstDR stimulation (St Jude Medical, Plano, TX), a clinician programmer application that provides intermittent “burst” stimulation for patients with certain St Jude SCS devices.

**EVIDENCE SUMMARY**

The principal outcomes for treatment of pain are symptom relief and improved functional level. Relief of pain is a subjective outcome and can be influenced by nonspecific effects, placebo response, the natural history of the disease, and regression to the mean. Therefore, randomized controlled trials (RCTs) are important to control for nonspecific effects and to determine whether any treatment effect provides a significant advantage over the placebo/sham treatment or other treatments. Appropriate comparison groups depend on the condition being treated and may include placebo/sham stimulation, or medical or surgical management.

In the evaluation of the risks for implantable devices, observational studies can provide data on the likelihood of potential complications. The following complications for spinal cord stimulation (SCS) have been reported:\[^1\]

- Lead migration, connection failure, generator failure, and/or lead breakage
- Superficial and deep infection with or without abscess
- Hematoma
- Nerve injury

[^1]: These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
The following evidence summary focuses on the investigational indications noted in criteria III, as listed above.

**CANCER-RELATED PAIN**

In 2015, Peng et al. published an update to their 2013 systematic review, to evaluate the effectiveness of SCS for cancer-related pain compared with standard care using conventional analgesic medication.[2,3] The literature search yielded 430 initial articles; however, just 18 were deemed relevant to include in the review. No RCTs were identified that evaluated the efficacy of SCS in adult patients with cancer-related pain. No new publications were identified, since the four case series[4-7] using a before-after design, with a total of 92 patients, included in the original review. In the absence of randomized controlled studies, the efficacy of SCS for treating cancer-related pain cannot be determined.

**CHRONIC REFRACTORY ANGINA**

Two populations of patients have been studied: 1) patients who were not considered candidates for a revascularization procedure due to comorbidities or other factors, where SCS was compared to continued medical management; or 2) patients who would be considered candidates for a revascularization procedure for the purpose of symptom relief only, where SCS was compared to coronary artery bypass grafting. Aggregating results across these different patient populations may yield misleading conclusions about treatment effect or patient selection criteria as these patient populations may not be interchangeable (both sets of patients may not be eligible for both procedures). Therefore, the trials included in this review for each of these distinct patient populations are discussed separately below.[8-13]

**Systematic Reviews**

In 2016, Pan identified 12 RCTs that evaluated SCS in patients with refractory angina pectoris.[14] Most studies had small sample sizes (ie <50 patients) and together there were a total of 476 patients. Reviewers did not report the control interventions reported in the RCTs. Pooled analyses favored the SCS group in most cases for exercise time after intervention, pain level (VAS score) and angina frequency, but there was not a significant difference between intervention and control groups on physical limitation and angina stability.

A 2015 systematic review by Tsigaridas et al. included nine RCTs evaluating SCS for refractory angina, seven of which compared SCS to low or no stimulation and two of which compared SCS to alternative medical or surgical therapy for angina.[15] Similar to the Taylor et al. review described below, the authors found that most RCTs were small and variable in quality based on assessment with the modified Jadad score. The authors reported: “two of the RCTs were of high quality; two were of low quality and the remaining ones were of intermediate quality.” Most trials which compared SCS to low or no stimulation, found improvements in outcomes with SCS; however, given limitations in the evidence base, the authors concluded that larger multicenter RCTs are needed to assess the efficacy of SCS for angina.

In 2009 Taylor and colleagues published a systematic review of five randomized controlled trials comparing active SCS with placebo (four studies) or no treatment (one study).[16] The studies included for analysis were judged to be of moderate or poor quality (based on a lack of reported treatment randomization and/or treatment blinding among cited limitations). Follow-up ranged from 48 hours to two-months and study size ranged from 22 to 30 patients. Primary
outcomes identified by the review included impact on health-related quality of life, functional class and exercise capacity. Of these outcomes, active treatment was significantly associated with improvement in exercise capacity and health-related quality of life. No other differences between groups were identified. However, these results are limited by the moderate to poor quality of the reviewed studies which, because of their small sample sizes and limited follow-up duration, do not answer questions about the long-term durability of this type of treatment. In addition, the lack of distinction between placebo- and natural history-controlled groups does not allow for isolation of any treatment benefit of SCS over and beyond that conferred by placebo alone.

In 2008, a systematic review of the literature based on the Swedish Council on Technology Assessment in Health Care report on SCS in severe angina pectoris was published.[17] Seven controlled studies (five randomized), two follow-up reports, and a preliminary report, as well as two nonrandomized studies determined to be of medium-to-high quality were included in the review.

- The largest RCT[11-13] included 104 subjects and compared SCS and coronary artery bypass graft (CABG) in patients accepted for CABG and who were considered to have only symptomatic indication (i.e., no prognostic benefit) for CABG, according to the American College of Cardiology/American Heart Association guidelines, to run an increased risk of surgical complications, and to be unsuitable for percutaneous transluminal coronary angioplasty. Between-group differences on nitrate consumption, anginal attack frequency, and self-estimated treatment effect were not statistically significant at the 6-month follow-up. At the 5-year follow-up, significantly fewer patients in the CABG group were taking long-acting nitrates, and between-group differences on quality of life and mortality were not significant.

- A 2006 report by McNab et al. compared SCS and percutaneous myocardial laser revascularization (PMR) in a study with 68 subjects.[10] Thirty subjects in each group completed a 12-month follow-up, and differences on mean total exercise time and mean time to angina were not significant. Eleven participants in the SCS group and 10 in the PMR group had no angina during exercise.

- The remaining RCTs included in the systematic review included 25 or fewer subjects.

**Randomized Controlled Trials**

In another small pilot RCT, conducted by Eldabe et al. in 2016 to address uncertainties related to recruitment, outcome measures, and care standardization for a larger trial comparing SCS to usual care for refractory angina, enrollment was planned for 45 patients, but the trial failed to meet its enrollment target.[18] Among the 29 patients randomized to SCS (n=15) or usual care (n=14), there were no significant differences in primary or secondary outcomes between groups, but the trial was underpowered.

In 2012 Zipes and colleagues published the results from a multi-center, single-blind RCT (n=68) which compared high SCS (two-hours of stimulation four times per day) versus sham SCS (one-minute of stimulation once per day) among patients with angina who were not candidates for revascularization.[19] The study was terminated (at 6 months) due to slow enrollment and per the Data Safety Monitoring Board recommendation that the study be terminated for futility based on an interim data analysis. The 68 subjects who underwent SCS implantation were randomized to either high stimulation (n=32) or low stimulation (control group; n=36). The low-stimulation control was designed so that patients would feel
paresthesia, but the effect of stimulation would be subtherapeutic. Major adverse cardiac events (MACE) and rate of angina attacks were the primary outcomes of interest, along with total exercise time and exercise time to onset of angina. At 6 months an intention-to-treat analysis was conducted; data was available only for 58 of the 68 subjects (85%). No differences were found between groups in any of the outcomes, prompting the researchers to conclude the SCS was not more effective than placebo. However, long-term differences between groups are still not known as the study was terminated early. In addition, the small sample size may have been underpowered for assessing clinically meaningful differences.

In 2011 Lanza and colleagues reported on a small RCT in which 25 patients were randomly assigned to 1 of 3 treatment groups: SCS with standard levels of stimulation (n=10), SCS with low-level stimulation (75% to 80% of the sensory threshold) (n=7), or SCS with very low intensity stimulation (n=8).[20] Thus, patients in groups 2 and 3 were unable to feel sensation during stimulation. After a protocol adjustment at 1 month, patients in the very low intensity group were re-randomized to one of the other groups after which there were 13 patients in the standard stimulation group and 12 patients in the low-level stimulation group. At the 3-month follow-up (2 months after re-randomization), there were statistically significant between-group differences in 1 of 12 outcome variables. There were a median of 22 angina episodes in the standard stimulation group and 10 in the low-level stimulation group (p=0.002), indicating evidence for a significantly higher rate of angina episodes with standard SCS treatment. Non-significant variables included use of nitroglycerin, quality of life (VAS), Canadian Cardiovascular Society angina class, exercise-induced angina, and five sub-scales of the Seattle angina questionnaire. The small sample size and short-term follow-up does not permit conclusions about the long-term safety and effectiveness of SCS in these patients.

**Section Summary**

Numerous small RCTs have evaluated SCS as a treatment for refractory angina. While some studies have reported benefit, most have not. In two of the larger, more recent RCTs that enrolled more than 100 patients reported no benefit on the primary outcomes. Overall, this evidence is mixed and is not sufficient to allow conclusions on whether health outcomes are improved.

**CRITICAL LIMB ISCHEMIA**

Critical limb ischemia (CLI) is described as pain at rest or the presence of ischemic limb lesions. If the patient is not a suitable candidate for limb revascularization (typically due to insufficient distal run-off), it is estimated that amputation will be required in 60-80% of these patients within a year. Spinal cord stimulation has been investigated in this small subset of patients as a technique to relieve pain and decrease the incidence of amputation.

**Systematic Reviews**

In 2015, Aub Dabrh et al. conducted a systematic review of nonrevascularization-based treatments, including SCS, for patients with critical limb ischemia also included five RCTs.[21] In pooled analysis, the authors found that SCS was associated with reduced risk of amputation (odds ratio [OR], 0.53; 95% CI, 0.36 to 0.79). However, the reviewers concluded that there was “relatively low quality of the evidence mainly due to imprecision (ie, small sample size and wide CIs) and the risk of bias.”

A 2013 update of a systematic review from the Cochrane group on use of SCS in non-
reconstructible chronic critical leg ischemia (NR-CCLI) included 10 articles of six studies with a total of 444 patients.[22] None of the studies were blinded due to the nature of the treatment. One of the studies was non-randomized and one included only patients with ischemic ulcers. Treatment groups received SCS along with the same standard nonsurgical treatment as the control groups. At 12, 18 and 24 months follow-up individual studies showed a trend toward a better limb salvage that did not reach statistical significance. However, when results were pooled, a small but significant decrease in amputations was found for the SCS group at 12 months follow-up (pooled risk difference (RD): -0.11, 95% confidence interval: -0.20 to -0.02). The 11% difference in the rate of limb salvage means that 9 patients would need to be treated to prevent one additional amputation (number needed to treat [NNT]: 9, 95% CI: 5 to 50). Upon excluding results from the non-randomized trial from the analysis, the treatment difference for the group treated with SCS was no longer significant (pooled RD: -0.09, 95% confidence interval: -0.19 to 0.01). When results from the study with patients in Fontaine stage IV (the most severe stage of critical limb ischemia) were excluded, the direction of treatment benefit switched (from negative to positive, RD: 0.13, 95% CI 0.02 to 0.23), indicating evidence for increased risk of amputation following treatment with SCS.

Outcomes for pain relief and ulcer healing could not be pooled and the researchers reported mixed findings. Quality of life was unchanged in both control and treatment groups. The overall risk of complications or additional SCS treatment was 17%. Nevertheless, the report concluded that “There is evidence that SCS is better than conservative treatment alone to achieve amputation risk reduction, pain relief and improvement of the clinical situation” in patients with chronic critical leg ischemia. This seemingly incongruous conclusion may be explained by the authors’ conclusion that, “The benefits of SCS against the possible harm of relatively mild complications and costs must be considered.” A potential conflict of interest was noted for the principal investigator, who was part of the non-randomized study included in the analysis. Published comments by Klomp and Steyerberg strongly criticized the inclusion of this non-randomized trial, along the exclusion of data from a randomized study from the pooled analysis, stating:[23]

The same meta-analysis, performed with a different amputation data input of five randomized studies [instead of 4 RCTs and a non-randomized study], generated a risk difference of -0.07 (95% CI: -0.17 to +0.03) instead of -0.13 (95% CI: -0.22 to -0.04). The main conclusion, that spinal cord stimulation is better than conservative treatment alone in achieving a reduction in amputation risk, is not justified. If SCS is beneficial, the magnitude of the effect is very small.

In 2009, Klomp and colleagues published a meta-analysis of the same five RCTs identified in the 2013 Cochrane review.[24] The authors did not find a statistically significant difference in the rate of amputation in the treatment and control groups. There was a relative risk of amputation of 0.79 and a risk difference of -0.07 (p=0.15). They found insufficient evidence that SCS is more efficacious than best medical treatment alone. They also conducted additional analyses of data from their 1999 RCT to identify factors associated with a better or worse prognosis. They found that patients with ischemic skin lesions had a higher risk of amputation compared to patients with other risk factors. There were no significant interactions between this or any other prognostic factor. The analyses did not identify any subgroup of patients who might benefit from SCS.

In 2009, Simpson et al. systematic review described above also reviewed studies on SCS for treatment of inoperable critical limb ischemia.[25] Four RCTs met inclusion criteria; comparators were conventional medical management (CMM)[26-29], oral analgesics[30], or prostaglandin E1...
injection\textsuperscript{[31]}. The authors concluded that evidence for a treatment difference was found in reduction of analgesics up to 6 months, but not at 18 months. However, no between-group differences were found in pain relief, limb survival, health-related quality of life, or any other outcomes.

**Randomized Controlled Trials**

There have been no new randomized trials published since those included in the systematic reviews summarized above.

**Conclusion**

A number of small RCTs of SCS versus usual care have been completed on patients with critical limb ischemia. In pooled analyses of these RCTs, SCS did not result in a significantly lower rate of amputation, although one systematic review and meta-analysis did report a significant difference. This evidence is not sufficient to conclude that SCS improves outcomes for patients with critical limb ischemia.

**HEART FAILURE**

**Randomized Controlled Trials**

In 2016, Zipes et al. reported the results of the DEFEAT-HF trial, a prospective, multicenter, single-blind RCT trial comparing SCS with active stimulation to sham control in patients with New York Heart Association functional class III heart failure with a left ventricular ejection fraction of 35\% or less.\textsuperscript{[32]} Sixty-six patients were implanted with an SCS and randomized in a 3:2 manner to SCS ON (n=42) or SCS OFF (sham; n=24). For the study’s primary end point (change in left ventricular end systolic volume index from baseline to 6 months), there was no significant difference between groups (p=0.30). Other end points related to heart failure hospitalization and heart failure-related QOL scores and symptoms did not differ significantly between groups. After completion of the 6 month randomization period, all subjects received active SCS stimulation. From baseline to 12 months of follow-up, there were no significant echocardiographic treatment effects in the overall patient population in echocardiographic parameters (p=0.36). The study was originally powered based on a planned enrollment of 195 implanted patients, but enrollment was stopped early due to enrollment futility. The nonsignificant difference between groups may have been the result of underpowering. However, the absence of any treatment effects or between-group differences are further suggestive of a lack of efficacy of SCS for heart failure.

Findings of a small pilot crossover RCT evaluating SCS for heart failure were published in 2014 by Torre-Amione et al.\textsuperscript{[33]} Eligibility included symptomatic heart failure despite optimal medical therapy, left ventricular ejection fraction less than 30\%, hospitalization or need for intravenous inotropic support in the past year, and inability to walk more than 450 meters on a 6-minute walk test. All patients had an implanted heart device. Nine patients underwent SCS implantation. The efficacy of SCS therapy was assessed by changes in patient symptoms, LV function, and BNP level. In all cases, ICD sensing, detection, and therapy delivery were unaffected by SCS. Symptoms were improved in the majority of patients with SCS, while markers of cardiac structure and function were, in aggregate, unchanged. Two patients had minor implant-related events and no reported implant-related HF exacerbations or hospitalizations. These small, preliminary pilot studies were intended to report first-in-human feasibility and safety to support further study. RCTs with large sample sizes and long-term
follow-up are needed to draw conclusions on the safety and effectiveness of the therapy for this indication.

**Nonrandomized Studies**

In 2015 Tse et al. performed a small, nonrandomized, prospective, multicenter pilot trial in male patients with New York Heart Association (NYHA) class III HF, left ventricular ejection fraction (LVEF) 20%-35%, and implanted defibrillator device who were prescribed stable optimal medical therapy.[34] Seventeen patients underwent implantation of a SCS device (cases) and four patients who did not fulfill the study criteria served as nontreated controls. At six-month follow up, no deaths or device-device interactions were reported. Composite score improved by 4.2 ± 1.3 in all cases, and 11 cases (73%) showed improvement in ≥4 of 6 efficacy parameters, including NYHA class (p = 0.002); peak maximum oxygen consumption (p = 0.013); LVEF (p<0.001); and LV end-systolic volume (p = 0.002). No improvements were observed in the four controls.

**DORSAL ROOT GANGLION STIMULATION**

**Systematic review**

A systematic review, published in 2013 by Pope et al., evaluated therapeutics for chronic pain that target the dorsal root ganglion.[35] This review focused on ganglionectomy, and radiofrequency treatment of the dorsal root ganglion, with discussion of electrical stimulation of the DRG as an emerging therapy. Three studies of electrical DRG stimulation were included in the review, two case reports and one nonrandomized feasibility trial. The Deer et al. feasibility trial (described below) prospectively followed 10 patients with chronic, intractable neuropathic pain, over four weeks.[36] Eight of the nine patients who completed the trial experienced a clinically meaningful (>30%) reduction in pain, as measured using a visual analog scale, with an average pain reduction of 70%. Seven of the nine reduced their utilization of pain medication. There were no adverse events reported. The two case studies included in the review described successful treatment of cervicogenic headache, post-herpetic neuralgia, and discogenic pain.

**Randomized Controlled Trials**

One RCT, the ACCURATE study, compared wireless injectable neurostimulators and standard SCS.[37] The trial, published by Deer et al in 2016, was a multicenter unblinded noninferiority trial. Eligibility criteria included chronic (≥6 months) intractable (failed ≥2 drugs from different classes) neuropathic pain of the lower limbs associated with a diagnosis of CRPS or causalgia and no previous neurostimulation. Patients were randomized to receive DRG stimulation with the Axium device or standard SCS. They first underwent a temporary trial of stimulation lasting 3 to 30 days, depending on the protocol at each site. Patients who had 50% or greater reduction in lower limb pain after the temporary trial were eligible for permanent stimulation. Those who failed temporary stimulation exited the trial but were included in the analysis as treatment failures. Implanted patients were followed for 12 months, with assessments at 3, 6, 9, and 12 months postimplant.

A total of 152 patients were randomized and 115 (n=61 DRG, n=54 SCS) had a successful temporary trial and continued to permanent implantation. Twelve-month data were available for 105 patients (55 patients in the DRG group, 50 in the SCS group). The primary outcome was a composite measure of treatment success. Success was defined as: (1) 50% or greater
reduction in VAS score from baseline to the end of the trial phase; (2) VAS at 3 months that was 50% or greater lower than baseline; and (3) no stimulation-related neurologic deficits experienced during the study. The noninferiority margin was set at 10%; the trial was designed such that, if the noninferiority end point was met, a superiority analysis was also performed. Treatment success at 3 month was achieved by 55 (81.2%) of 69 patients in the DRG arm and 39 (55.7%) of 70 in the SCS arm. The noninferiority margin was met, and DRG was found to be statistically superior to SCS (p<0.001). At the 12-month follow-up, the primary end point was achieved by 49 (74.2%) of 66 in the DRG group and 35 (53%) of 66 in the SCS group and, again, DRG was considered noninferior to SCS and also superior (p<0.001). In terms of paresthesias, at 3 months and 12, SCS patients were significantly more likely to report paresthesias in nonpainful areas than DRG patients. At 3 months, 84.7% of DRG patients and 65% of SCS patients reported paresthesias only in their painful areas; at 12 months, these percentages were 94.5% and 61.2%, respectively. Twenty-one serious adverse events occurred in 19 patients (8 in the DRG group, 11 in the SCS group; difference between groups, p=NS). A limitation of the study was that it was unblinded and industry-sponsored, which could potentially bias outcome assessment and reporting.

Nonrandomized Studies

Several case series have been published.[38-40] The largest of them are summarized below. Liem (2015) reported on the outcomes of an industry-sponsored multicenter, prospective trial of DRG stimulation at six months[41] and one year.[38] The trial consisted of a run-in period in which 51 participants received DRG stimulation via leads connected to an external stimulator, followed by surgical placement of a fully-implanted neurostimulator in 32 of the 39 patients that achieved 50% or greater pain relief during the run-in period. More than half of the patients with fully implanted DNG stimulators reported at least 50% relief in pain, as measured by visual analog scale. Average pain ratings were 58% lower than baseline at six months and 56% lower at 12 months post-implantation. Patients also reported improved quality of life and mood by questionnaire (EQ-5D-3L and POMS). Over 12 months, there were 86 adverse events reported in 29 patients, including temporary motor stimulation (12 events), CSF leak (7 events) and infection (7 events). Approximately half of these events were judged by the investigators to be related to the device. Seven subjects had their devices removed and were withdrawn from the study.

A subgroup analysis of the Liem et al. study examined positional effects on paresthesia during DRG stimulation in the 32 patients with implanted neurostimulators.[42] Paresthesia and pain relief achieved with spinal cord stimulation can change as patients change position from upright to prone or supine, causing uncomfortable sensations. This study found no statistically significant difference in paresthesia intensity by body position. In order to truly determine the efficacy and safety of DRG stimulation well designed comparative studies with long-term follow-up must be performed to compare it to standard spinal cord stimulation.

Schu et al. reported on an industry-sponsored multicenter European case series of 29 patients treated with DRG stimulation for chronic neuropathic groin pain.[39] Of the 29 patients who underwent a 30-day trial period, 25 (86.2%) underwent implantation with the Axium DRG device. Final lead placement between T12 and L4 was determined based on patient feedback during paraesthesia mapping. Data analysis was based on the results of 23 patients with a mean follow-up of 27.8 weeks. The average pain reduction was 71.4 ± 5.6%, and 82.6% (19/23) of patients experienced a > 50% reduction in their pain at the latest follow-up. Adverse events were not reported. The authors stated that paraesthesia was largely unaffected by
positional changes. Limitations of this study include small sample size, lack of comparative data, and potential bias inherent in pain as a subjective outcome measure.

In 2013 Deer et al. conducted an industry-sponsored case series to evaluate the efficacy and safety of the Axium DRG system in ten patients with chronic intractable pain of the trunk and/or limbs.[36] The study was conducted across four centers for a period of four weeks. The study protocol and lead implantation procedures were similar to those reported by Liem et al. above; however, only results of trial DRGs over a period of three to seven days were reported. On average, there was a 70% reduction in pain following stimulation (p = 0.0007). Eight of the nine patients experienced a clinically meaningful (>30%) reduction in pain, and seven of the nine reduced their pain medication utilization. The study did not consider longer term effects with a permanently implanted device. Seventeen adverse events occurred of which 14 were considered to be device-related; none were thought to be serious.

PRACTICE GUIDELINE SUMMARY

AMERICAN SOCIETY OF INTERVENTIONAL PAIN PHYSICIANS (ASIPP)[43]

In 2013, the ASIPP updated their evidence-based guidelines for interventional techniques in the management of chronic spinal pain. The guidelines included the statement that there is fair evidence in support of SCS in managing patient with failed back surgery syndrome.

AMERICAN COLLEGE OF CARIOLOGY FOUNDATION AND THE AMERICAN HEART ASSOCIATION (ACCF/AHA)

Guidelines from the American College of Cardiology Foundation (ACCF) and the American Heart Association (AHA) published in 2007 with focused updates in 2011[44] and 2012[45] for the management of patients with unstable angina/non ST-Elevation myocardial infarction state:

“Transcutaneous electrical nerve stimulation and spinal cord stimulation for continued pain despite the implementation of Class I measures may be considered for patients with syndrome X. (Level of Evidence: B).”[46] However, the level of evidence indicates that the “treatment usefulness/ efficacy [is] less well established” and that this recommendation may be based on a single randomized controlled trial or one or more non-randomized studies.

The 2012 updated joint ACCF/AHA guidelines recommend that SCS may be considered for relief of refractory angina in patients with stable ischemia heart disease (Level of evidence: C, defined as very limited populations evaluated and/or only consensus opinion of experts, cases studies, or standard of care).[47] The guidelines conclude:

“Studies of spinal cord stimulation suggest that this technique might have some use as a method to relieve angina in patients with symptoms that are refractory to standard medical therapy and revascularization. There is a paucity of data on the mechanisms and long-term risks and benefits of this therapeutic approach, however.”

NEUROPATHIC PAIN SPECIAL INTEREST GROUP OF THE INTERNATIONAL ASSOCIATION FOR THE STUDY OF PAIN[48]

In 2013, the Neuropathic Pain Special Interest Group of the International Association for the Study of Pain (NeuPSIG) published consensus recommendations on management of neuropathic pain. The recommendations supporting the use of SCS for failed back surgery syndrome and for complex regional pain syndrome we rated as weak (quality of evidence
moderate to low; strength of recommendation weak to inconclusive). The recommendation for SCS for postherpetic neuralgia was also rated as weak (quality of evidence low; strength of recommendation inconclusive).

**SUMMARY**

**CHRONIC PAIN OF THE TRUNK AND LIMBS**

There is enough research to show that spinal cord stimulation (SCS) including high frequency SCS for the treatment of chronic trunk or limb pain, when all other treatment modalities have failed to adequately reduce symptoms may improve health outcomes. In addition, practice guidelines recommend SCS for select patients. Therefore, SCS may be considered medically necessary for treatment of chronic refractory pain of the trunk or limbs when policy criteria are met. Following the initial trial period of SCS, if the patient doesn’t experience at least 50 percent pain relief, then the treatment for permanent implantation is considered investigational.

**ALL OTHER CONDITIONS NOT RELATED TO CHRONIC PAIN OF THE TRUNK AND LIMBS**

There is not enough research to show that spinal cord stimulation (SCS), including standard or high frequency, in the treatment of conditions not related to severe and chronic refractory pain of the trunk or limbs improves health outcomes or is more effective than standard of care. Therefore, the use of SCS, including standard or high frequency is investigational for the treatment of all other conditions not related to severe and chronic refractory pain of the trunk or limbs.

**DORSAL ROOT GANGLION STIMULATORS**

There is not enough research to show that dorsal root ganglion (DRG) stimulation is safer and/or more effective than standard spinal cord stimulation for any indication, including the treatment of chronic pain. In addition, there are no practice guidelines that address the use of dorsal root ganglion stimulation for any indication. Therefore, the use of dorsal root ganglion stimulation is investigational for any indication, including the treatment of chronic pain.

**REFERENCES**


developed in collaboration with the American College of Emergency Physicians, the
Society for Cardiovascular Angiography and Interventions, and the Society of Thoracic
Surgeons endorsed by the American Association of Cardiovascular and Pulmonary
2007 Aug 14;50(7):e1-e157. PMID: 17692738

Guideline for the diagnosis and management of patients with stable ischemic heart
disease: a report of the American College of Cardiology Foundation/American Heart
Association Task Force on Practice Guidelines, and the American College of
Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular
Nurses Association, Society for Cardiovascular Angiography and Interventions, and
Society of Thoracic Surgeons. J Am Coll Cardiol. 2012 Dec 18;60(24):e44-e164. PMID:
23182125


Stimulation." Policy No. 7.01.25

<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>63650</td>
<td>Percutaneous implantation of neurostimulator electrode array; epidural</td>
</tr>
<tr>
<td></td>
<td>63655</td>
<td>Laminectomy for implantation of neurostimulator electrodes, plate/paddle, epidural</td>
</tr>
<tr>
<td></td>
<td>63661</td>
<td>Removal of spinal neurostimulator electrode percutaneous array(s), including fluoroscopy, when performed</td>
</tr>
<tr>
<td></td>
<td>63662</td>
<td>Removal of spinal neurostimulator electrode plate/paddle(s) placed via laminotomy or laminectomy, including fluoroscopy, when performed</td>
</tr>
<tr>
<td></td>
<td>63663</td>
<td>Revision including replacement, when performed, of spinal neurostimulator electrode percutaneous array(s), including fluoroscopy, when performed</td>
</tr>
<tr>
<td></td>
<td>63664</td>
<td>Revision including replacement, when performed, of spinal neurostimulator electrode plate/paddle(s) placed via laminotomy or laminectomy, including fluoroscopy, when performed</td>
</tr>
<tr>
<td></td>
<td>63685</td>
<td>Insertion or replacement of spinal neurostimulator pulse generator or receiver, direct or inductive coupling</td>
</tr>
<tr>
<td></td>
<td>63688</td>
<td>Revision or removal of implanted spinal neurostimulator pulse generator or receiver</td>
</tr>
<tr>
<td></td>
<td>95970</td>
<td>Electronic analysis of implanted neurostimulator pulse generator system (e.g., rate, pulse amplitude, pulse duration, configuration of wave form, battery status, electrode selectability, output modulation, cycling, impedance and patient compliance measurements); simple or complex brain, spinal cord, or peripheral (i.e., cranial nerve, peripheral nerve, sacral nerve, neuromuscular) neurostimulator pulse generator/transmitter, without reprogramming</td>
</tr>
<tr>
<td></td>
<td>95971</td>
<td>simple spinal cord, or peripheral (ie, peripheral nerve, sacral nerve, neuromuscular) neurostimulator pulse generator/transmitter, with intraoperative or subsequent programming</td>
</tr>
<tr>
<td></td>
<td>95972</td>
<td>complex spinal cord, or peripheral (ie, peripheral nerve, sacral nerve, neuromuscular) (except cranial nerve) neurostimulator pulse</td>
</tr>
</tbody>
</table>

Codes do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCPCS</td>
<td>C1820</td>
<td>Generator, neurostimulator (implantable), with rechargeable battery and charging system</td>
</tr>
<tr>
<td></td>
<td>C1822</td>
<td>Generator, neurostimulator (implantable), high frequency, with rechargeable battery and charging system</td>
</tr>
<tr>
<td></td>
<td>L8679</td>
<td>Implantable neurostimulator, pulse generator, any type</td>
</tr>
<tr>
<td></td>
<td>L8680</td>
<td>Implantable neurostimulator electrode, each</td>
</tr>
<tr>
<td></td>
<td>L8685</td>
<td>Implantable neurostimulator pulse generator, single array, rechargeable, includes extension</td>
</tr>
<tr>
<td></td>
<td>L8686</td>
<td>Implantable neurostimulator pulse generator, single array, nonrechargeable, includes extension</td>
</tr>
<tr>
<td></td>
<td>L8687</td>
<td>Implantable neurostimulator pulse generator, dual array, rechargeable, includes extension</td>
</tr>
<tr>
<td></td>
<td>L8688</td>
<td>Implantable neurostimulator pulse generator, dual array, nonrechargeable, includes extension</td>
</tr>
</tbody>
</table>

*Date of Origin: January 1996*
Surgical Treatments for Hyperhidrosis

Effective: May 1, 2017

Next Review: March 2018
Last Review: March 2017

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based on all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

This policy addresses surgical treatments for hyperhidrosis, excessive sweating beyond a level required to maintain normal body temperature.

MEDICAL POLICY CRITERIA

NOTE: This policy only addresses the surgical treatment of hyperhidrosis.

I Surgical treatment of hyperhidrosis, including gustatory hyperhidrosis, via endoscopic transthoracic sympathectomy or excision of axillary sweat glands may be considered medically necessary when there is clinical documentation that all of the following criteria are met:

A Primary medical conditions causing secondary hyperhidrosis have been identified and treated where possible

B The hyperhidrosis is persistent and severe, and has resulted in significant medical complications such as:

1. Acrocyanosis of the hands

2. Recurrent skin maceration with secondary bacterial or fungal infection
3. Recurrent secondary infections

4. Persistent eczematous dermatitis in spite of medical treatments with topical dermatologics or systemic anticholinergics

   C A trial of nonsurgical treatments has failed or is contraindicated.

II Tympanic neurectomy may be considered medically necessary for the treatment of severe gustatory hyperhidrosis if a trial of nonsurgical treatments failed or is contraindicated.

III Surgical treatment of hyperhidrosis via endoscopic transthoracic sympathectomy, excision of axillary sweat glands, or tympanic neurectomy is considered not medically necessary when the criteria in I. or II. above are not met.

IV All other surgical treatments of hyperhidrosis are considered investigational, including but not limited to the following:

   A Lumbar sympathectomy
   B Axillary liposuction or curettage performed alone or in combination with any other procedure
   C Subdermal laser-assisted axillary hyperhidrosis treatment
   D Percutaneous radiofrequency sympathicolysis or sympathectomy
   E Radiofrequency ablation for palmar hyperhidrosis.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

CROSS REFERENCES

1. Botulinum toxin Type A injection, Medication Policy Manual, Drugs, Policy No. 006

BACKGROUND

HYPERHIDROSIS

Hyperhidrosis may be defined as excessive sweating, beyond a level required to maintain normal body temperature in response to heat exposure or exercise. Hyperhidrosis can be classified as either primary or secondary.

Primary Hyperhidrosis

Primary localized hyperhidrosis is idiopathic in nature, typically involving the hands (palmar), feet (plantar), or underarms (axillae).

Primary focal hyperhidrosis is defined as bilateral, relatively symmetric, excessive sweating of at least six months’ duration induced by sympathetic hyperactivity in selected areas that is not associated with an underlying disease process. The most common locations are underarms (axillary hyperhidrosis), palms (palmar hyperhidrosis), soles of the feet (plantar hyperhidrosis) or face and scalp (craniofacial hyperhidrosis). The second (T2) and third (T3) thoracic ganglia
are responsible for palmar hyperhidrosis, the fourth (T4) thoracic ganglia controls axillary hyperhidrosis, and the first (T1) thoracic ganglia controls facial hyperhidrosis.

Secondary Hyperhidrosis

Secondary hyperhidrosis is usually generalized or craniofacial sweating. It can result from a variety of drugs, [e.g., tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs)], olfactory stimuli, or underlying diseases/conditions, such as febrile diseases, diabetes mellitus, anxiety, menopause, neurologic lesions, intrathoracic neoplasms, Raynaud’s disease, and Frey’s syndrome.

Secondary gustatory hyperhidrosis is excessive sweating on ingesting highly spiced foods. This trigeminovascular reflex typically occurs symmetrically on scalp or face and predominately over forehead, lips and nose.

Secondary facial gustatory sweating, in contrast, is usually asymmetrical and occurs independently of the nature of the ingested food. This phenomenon frequently occurs after injury or surgery in the region of the parotid gland.

Frey’s syndrome is an uncommon type of secondary gustatory hyperhidrosis that arises from injury to, or surgery near, the parotid gland resulting in damage to the secretory parasympathetic fibers of the facial nerve. After injury, these fibers regenerate and miscommunication occurs between them and the severed postganglionic sympathetic fibers that supply the cutaneous sweat glands and blood vessels. The aberrant connection results in gustatory sweating and facial flushing with mastication. Aberrant secondary gustatory sweating follows up to 73% of surgical sympathectomies and is particularly common after bilateral procedures.

The consequences of hyperhidrosis are primarily psychosocial in nature. Excessive sweating may be socially embarrassing or may interfere with certain professions. Symptoms such as fever, night sweats, or weight loss require further investigation to rule out secondary causes. Sweat production can be assessed with the minor starch iodine test, which is a simple qualitative measure to identify specific sites of involvement.

A variety of medical therapies have been investigated for treating primary hyperhidrosis, including topical therapy with aluminum chloride or tanning agents, oral anticholinergic medications, iontophoresis, intradermal injections of botulinum toxin, microwave treatment. Treatment of secondary hyperhidrosis naturally focuses on treatment of the underlying cause.

SURGICAL TREATMENT

This medical policy addresses only surgical treatment of hyperhidrosis. Surgical treatments for axillary hyperhidrosis include transthoracic sympathectomy and surgical excision of axillary sweat glands. Transthoracic sympathectomy may also be used for palmar hyperhidrosis. Surgical removal of axillary sweat glands has been performed in patients with severe isolated axillary hyperhidrosis. Removal may involve removal of the subcutaneous sweat glands without removal of any skin, limited excision of skin and removal of surrounding subcutaneous sweat glands, or a more radical excision of skin and subcutaneous tissue en bloc.
A variety of approaches have been reported for sympathectomy. For transthoracic sympathectomy, transthoracic endoscopic techniques have emerged as minimally invasive alternatives to transaxillary, supraclavicular, or anterior thoracic approaches. Percutaneous radiofrequency (RF) sympathicolysis has also been proposed as a sympathectomy technique in which RF lesions are made in the thoracic sympathetic chain under fluoroscopic guidance without the need for general anesthesia, intubation, or lung collapse. Lumbar sympathectomy may be performed as a surgical treatment of plantar hyperhidrosis and may also be done endoscopically.

While accepted as an effective treatment, sympathectomy is not without complications. In addition to the immediate surgical complications of pneumothorax or temporary Horner's syndrome, compensatory sweating on the trunk can occur in up to 55% of patients, reducing patient satisfaction with the procedure. Gustatory sweating may also occur. Sympathectomy also results in cardiac sympathetic denervation, which in turn can lead to a 10% reduction in the heart rate. In addition to the complications associated with transthoracic sympathectomy, lumbar sympathectomy for plantar hyperhidrosis may have the additional risk of permanent sexual dysfunction in men and women. Medical researchers have investigated whether certain approaches, e.g., T3 versus T4 sympathectomy, result in less compensatory sweating, but there remains a lack of consensus about which approach best minimizes the risk of this side effect.

Tympanic neurectomy is a surgical technique that may be used for treatment of severe gustatory hyperhidrosis. The nerves are transected in the middle ear through a flap created in the ear drum. Possible risks from this surgery include rupture of the tympanic membrane, infection, hearing loss, and loss of taste in certain parts of the tongue.

**EVIDENCE SUMMARY**

In order to determine whether surgical treatment of hyperhidrosis results in sustained improvements in clinically meaningful health outcomes, comparisons to conventional therapies in well-designed comparative studies (ideally randomized controlled trials) are needed using standardized functional measurement tools.

Since tympanic neurectomy for the treatment of severe gustatory hyperhidrosis when a trial of nonsurgical treatments failed, and excision of sweat glands have evolved into a standard of care, the focus of the following evidence summary is on systematic reviews (SRs), technology assessments (TAs), randomized controlled trials (RCT), and comparative nonrandomized studies for the investigational indications listed in the policy criteria.

**ENDOSCOPIC TRANSTHORACIC SYMPATHECTOMY**

**Systematic Reviews**

Deng (2011) published a meta-analysis of data from randomized controlled trials and observational studies published to 2010 evaluating thoracoscopic sympathectomy for patients with palmar hyperhidrosis.[1] The authors pooled outcome data from different approaches to sympathectomy, i.e., single-ganglia blockage (T2, T3, or T4), and multi-ganglia blockage (T2-3, T2-4, or T3-4). (Note: T refers to rib). Based on these analyses, they concluded that T3 (11 studies) and T3-4 (2 studies) had the “best” clinical efficacy i.e., postoperative resolution of
symptoms. The T3 approach resulted in a 97.9% pooled efficacy rate, and the T3-4 approach resulted in a 100% pooled efficacy rate. In the studies for which data were available, the pooled rate of postoperative compensatory sweating was 40% after T3 surgery. Data on compensatory sweating after T3-4 surgery was only available from one study with 60 patients; a pooled analysis could not be performed.

**Randomized Controlled Trials**

Youssef (2015) published results from a randomized controlled trial (RCT) that analyzed outcomes for unilateral sequential endoscopic transthoracic sympathectomy (S-ETS) in comparison with simultaneous bilateral endoscopic transthoracic sympathectomy (B-ETS) in treating patients with palmar hyperhidrosis (PH) and compensatory hyperhidrosis (CH). [2] Four hundred seven patients with intractable PH were randomly assigned to the two groups: 203 patients in the S-ETS group, and 204 patients in the B-ETS group. Three hundred sixty-four patients completed the study, and the authors report complication rates were comparable for both groups. Treatment success on the two month follow-up was 97.2% for S-ETS and 96.7% for B-ETS. The incidence of CH was decreased substantially from 131 (71.1%) patients in the B-ETS group compared to 22 (12.2%) patients in the S-ETS group (P<.001). Eighty-four (58.3%) patients in the S-ETS group had simultaneous disappearance or decreased perspiration on the soles. Finally, the authors reported that all patients in the S-ETS group were satisfied, whereas 37.9% of B-ETS patients were unsatisfied with their operation, mostly because of CH and recurrences. The author concluded that although both methods were safe, effective, and minimally invasive methods of treatment for PH.

Heidemann (2013) published results from an RCT that described two groups of consecutive patients with isolated axillary hyperhidrosis who underwent thoracoscopic sympathectomy (n = 49) or local axillary surgery (n = 47) at the same university hospital over a nine-year period, depending on referral or preference. [3] Patients received identical questionnaires to investigate local effect and side effects after surgery. Outcome after surgery for isolated axillary hyperhidrosis was significantly better after local surgical treatment compared with sympathectomy. Local effect was better and side effects fewer, but milder recurrent symptoms were more frequent. Authors suggest that local axillary surgery is preferable for isolated axillary hyperhidrosis and that R2-R3 or R2-R4 sympathicotomy should be discouraged.

Yuncu (2013) published an RCT which compared surgery at the T3 and T3-4 levels. The trial included 60 patients with axillary hyperhidrosis; 17 were assigned to T3-4 surgery and 43 to T3 surgery. [4] There were no significant differences between groups in postoperative satisfaction. At the 1-year follow-up, the incidence of compensatory sweating was lower in the T3 group (79%) than the T3-4 group (100%).

Ibrahim (2013) evaluated the operative and postoperative results of two-stage unilateral vs one-stage bilateral thoracoscopic sympathectomy. [5] Two hundred and seventy patients with severe palmar and/or axillary hyperhidrosis were included in the study. One hundred and thirty patients received one-stage bilateral, single-port video-assisted thoracoscopic sympathectomy (one-stage group) and 140, two-stage unilateral, single-port video-assisted thoracoscopic sympathectomy, with a mean time interval of four months between the procedures (two-stage group). The mean postoperative follow-up period was 12.5 (range: 1-24 months). Sixteen (12%) patients of the one-stage group and 15 (11%) of the two-stage group suffered from mild/moderate pain (P = 0.8482). Pneumothorax occurred in 8 (6%) patients of the one-stage
group and in 11 (8%) of the two-stage group. Compensatory sweating occurred in 25 (19%) patients of the one-stage group and in 6 (4%) of the two-stage group (P = 0.0001). The authors concluded that both two-stage unilateral and one-stage bilateral single-port video-assisted thoracoscopic sympathectomies were effective, safe and minimally invasive procedures.

A 2011 study by Baumgartner and colleagues included 121 patients with disabling palmoplantar hyperhidrosis. Patients were randomized to receive bilateral sympathectomy over T2 (n=61 patients) or T3 (n=60 patients). Six of 121 (5%) patients, three in each group, were considered treatment failures, (i.e., had recurrent palmar sweating to a bothersome level). There were no significant differences between groups in the reported subjective change in plantar or axillary sweating after surgery. At six months, the mean level of compensatory sweating (0 to 10 severity scale) was 4.7 (standard deviation [SD]=2.7) for the T2 group and 3.8 (SD=2.8) for the T3 group (p=not significant). Similarly, at 1 year, the mean severity rating of compensatory sweating was 4.7 (SD=2.5) in the T2 group and 3.7 (SD=2.8) in the T3 group; p=0.09.

In 2011, an additional study was published by Ishy et al. in Brazil in which surgery at the T3 and T4 levels was compared. This study included 20 patients with palmar hyperhidrosis. All patients experienced complete bilateral remission of palmary sweating after 1 year of follow-up. The level of compensatory sweating did not differ significantly between groups at 1 week, 1 month, or 6 months, but at 1 year, there was a significantly higher rate in the T3 compared to the T4 group (20/20, 100% in the T3 group and 15/20, 75% in the T4 group, p=0.47).

Inan (2011) published results from an additional RCT comparing different surgical techniques for hyperhidrosis. The authors reported primary success rates of 96.3% for isolated palmar hyperhidrosis, 95.7% for palmar and axillary hyperhidrosis, and 66.7% for palmar and face/scalp hyperhidrosis. Complication rates were similar among the groups and included pneumothorax which required no intervention. RCTs continue to be published comparing levels of sympathectomy. Large case series on endoscopic transthoracic sympathectomy (ETS) have reported success rates for of up to 98% for treatment of axillary and/or palmar hyperhidrosis.

**COMPLICATIONS**

A 2013 series reported on complications after thoracic sympathectomy in 1731 patients with palmar, axillary or craniofacial hyperhidrosis. Thirty days after surgery, 1531 (88.4%) of patients reported compensatory sweating. Among the 1531 patients, compensatory sweating was mild in 473 (31%), moderate in 642 (42%) and severe in 416 (27%). Gustatory sweating was reported by 334 of the 1731 (19%) patients.

**PLANTAR HYPERHIDROSIS**

**Systematic Reviews**

No SRs were identified

**Randomized Controlled Trials**

No RCTs were identified
Nonrandomized Studies

Case series have found lower rates of efficacy for plantar compared to axillary or palmar hyperhidrosis. In a retrospective analysis of prospectively collected data on patients who underwent ETS for primary focal hyperhidrosis, Wait et al. reported complete resolution of symptoms in 19 of 197 (9.6%) plantar hyperhidrosis patients compared to 99.7% and 73% for palmar and axillary hyperhidrosis, respectively.[17] In addition to low success rates, concerns have been reported for side effects in sexual functioning in both males and females.

LUMBAR SYMPATHECTOMY

Systematic Review

No SRs were identified.

Randomized Controlled Trials

No RCTs were identified.

Nonrandomized Studies

The evidence is limited to several case series trials that are unreliable due to the following: lack of randomization, lack of a control group for comparison, heterogeneous patient characteristics, lack of long-term follow-up, subjective outcomes, and the use of different surgical techniques.[20-25]

SURGICAL REMOVAL OF AXILLARY SWEAT GLANDS (INCLUDING LIPOSUCTION AND CURETTAGE)

There is sufficient evidence to suggest that excisional removal of sweat glands may be safe and effective as a treatment of severe, refractory axillary hyperhidrosis and this technique is considered a standard of care for surgical candidates.

There is insufficient evidence to determine whether liposuction or curettage of sweat gland is safe or effective as a treatment of axillary hyperhidrosis. Although this procedure has been performed for several decades, only scattered reports regarding its effectiveness were identified in a PubMed literature search.[26-31]

AXILLARY SUBDERMAL LASER TREATMENT

Systematic Reviews and Technology Assessments

In 2015, the Canadian Agency for Drugs and Technologies in Health (CADTH) published a rapid response review on the clinical effectiveness of laser therapy in axillary hyperhidrosis.[32] Five publications were included in the review, three RCTs and two nonrandomized studies. No relevant evidence-based guidelines were identified for inclusion. The authors reported that although the evidence suggests laser therapy may reduce sweating in cases of axillary hyperhidrosis, these results should be interpreted with caution due to the methodological limitations of the studies, which include but are not limited to, small sample sizes, a lack of reporting on efficacy and safety outcomes, potential selection bias, and a lack of long term follow-up data.
Randomized Controlled Trials
No RCTs were identified.

Nonrandomized Studies
No studies were identified.

PERCUTANEOUS RADIOFREQUENCY (RF) SYMPATHICOLYSIS

Systematic Reviews
No SRs were identified

Randomized Controlled Trials
No RCTs were identified.

Nonrandomized Studies
No studies were identified.

PRACTICE GUIDELINE SUMMARY

In 2011, an expert consensus statement on the surgical treatment of hyperhidrosis was published by a task force of the Society of Thoracic Surgeons.[33] The document stated that endoscopic thoracic sympathectomy is the treatment of choice for patients with primary hyperhidrosis. They further recommend the following treatment strategies (with R referring to rib and the number to the specific rib):

- R3 interruption for palmar hyperhidrosis; an R4 interruption is also reasonable. The authors note a slightly higher rate of compensatory sweating with an R3, but R3 is also more effective at treating hyperhidrosis.
- R4 or R5 interruption for palmar-axillary, palmar-axillary-plantar or axillary hyperhidrosis alone; R5 interruption is also an option for axillary hyperhidrosis alone.
- R3 interruption for craniofacial hyperhidrosis without blushing; an R2 and R3 procedure is an option but may lead to a higher rate of compensatory sweating, and also increases the risk of Horner’s syndrome.

SUMMARY

There is enough research to show that surgical treatment, including gustatory hyperhidrosis, via endoscopic transthoracic sympathectomy or excision of axillary sweat glands improves health outcomes for people with primary hyperhidrosis and certain medical complications. In addition, tympanic neurectomy for the treatment of severe gustatory hyperhidrosis if a trial of nonsurgical treatments failed and excision of sweat glands have evolved into a standard of care. Clinical guidelines based on research recommend surgical treatment for primary hyperhidrosis. Therefore, surgical treatments for people with hyperhidrosis may be considered medically necessary when policy criteria are met. There is not enough research to show surgical treatment for hyperhidrosis improves health outcomes for all other
conditions and/or complications. Therefore, surgical treatment for hyperhidrosis is considered not medically necessary when policy criteria are not met.

There is not enough research to show that surgical treatments of hyperhidrosis including, but not limited to lumbar sympathectomy, axillary liposuction or curettage performed alone or in combination with any other procedure, subdermal laser-assisted axillary hyperhidrosis treatment, percutaneous radiofrequency sympathicolysis or sympathectomy and radiofrequency ablation for palmar hyperhidrosis improves health outcomes for people with hyperhidrosis. Therefore, these techniques are considered investigational.

REFERENCES


<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>32664</td>
<td>Thoracoscopy, surgical; with thoracic sympathectomy</td>
</tr>
<tr>
<td></td>
<td>64818</td>
<td>Sympathectomy, lumbar</td>
</tr>
<tr>
<td></td>
<td>69676</td>
<td>Tympanic neurectomy</td>
</tr>
<tr>
<td>HCPCS</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

*Date of Origin: November 1999*
**DESCRIPTION**

Gastroesophageal reflux disease, or GERD, is a condition characterized by heartburn and other symptoms related to reflux of stomach acid into the esophagus. Non-surgical treatments include lifestyle modifications, which may vary for the individual patient (i.e., dietary changes, smoking cessation, avoidance of foods that may trigger reflux symptoms, sitting upright following a meal, etc.) or pharmacologic acid therapies such as antacids or proton pump inhibitors (PPIs). However, for some patients, these treatments may not be effective or tolerated, at which time, other anti-reflux options may be considered. Among them, transesophageal endoscopic therapies are minimally invasive antireflux procedures being investigated as alternatives to medical management or fundoplication surgery in the treatment of GERD.
## MEDICARE ADVANTAGE POLICY CRITERIA

<table>
<thead>
<tr>
<th>Procedure(s):</th>
<th>CPT and/or HCPCS codes</th>
<th>CMS Coverage Manuals, National Coverage Determinations (NCD), Noridian Local Coverage Determinations (LCD) and Articles (LCA)</th>
<th>Medical Policy Manual</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transesophageal radiofrequency energy</td>
<td>43257</td>
<td>Non-Covered Services (L35008)</td>
<td></td>
</tr>
<tr>
<td><strong>Examples:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• CSM Stretta™ System, or the Stretta procedure</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Transoral incisionless fundoplication (TIF) | 43210 | Non-Covered Services (L35008) | |
| **Examples:** | | | |
| • EsophyX | | (See also LCA for Non-coverage of Transoral Incisionless Fundoplication (A52885) regarding non-coverage of TIF). | |

| Endoscopic injection of a bulking agent | 43192, 43201, 43236, 43499 | None | |
| **Examples:** | | | |
| • pyrolytic carbon-coated zirconium oxide spheres (Durasphere®) | | | |

| Endoscopic submucosal implantation or injection of a biocompatible polymer | | | |
| **Examples:** | | | |
| • Enteryx, | | | |
| • polymethylmethacrylate [PMMA] beads(1) | | | |
| • the Gatekeeper Reflux Repair system | | | |

---

*These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage.*

*Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.*
Transesophageal endoscopic gastroplasty

Examples:
- EndoCinch
- Plicator
- StomaphyX

<table>
<thead>
<tr>
<th>Procedure</th>
<th>CPT Code</th>
<th>Coverage</th>
<th>Medicare Coverage Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medicare coverage guidance is not available in the health plan’s service area for transesophageal endoscopic gastroplasty for GERD. Therefore, the health plan’s medical policy is applicable.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Transesophageal Endoscopic Therapies for Gastroesophageal Reflux Disease (GERD), Surgery, Policy No. 110 (see “Note” below)

**NOTE:** If a procedure or device lacks scientific evidence regarding safety and efficacy because it is investigational or experimental, the service is noncovered as not reasonable and necessary to treat illness or injury. (Medicare IOM Pub. No. 100-04, Ch. 23, §30 A). According to Title XVIII of the Social Security Act, §1862(a)(1)(A), only medically reasonable and necessary services are covered by Medicare. In the absence of a NCD, LCD, or other coverage guideline, CMS guidelines allow a Medicare Advantage Organization (MAO) to make coverage determinations, applying an **objective, evidence-based process, based on authoritative evidence.** (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5). The Medicare Advantage Medical Policy - Medicine Policy No. M-149 - provides further details regarding the plan’s evidence-assessment process (see Cross References).
CROSS REFERENCES

Investigational (Experimental) Services and New and Emerging Medical Technologies and Procedures, Medicine, Policy No. M-149

Gastroesophageal Reflux Surgery, Surgery, Policy No. M-186

REFERENCES

1. FDA Website for Soft Tissue Fillers (Dermal Fillers)
2. NCD for Endoscopy (100.2)

CODING

<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>43192</td>
<td>Esophagoscopy, rigid, transoral; with directed submucosal injection(s), any substance</td>
</tr>
<tr>
<td></td>
<td>43201</td>
<td>Esophagoscopy; rigid or flexible; with directed submucosal injection(s), any substance</td>
</tr>
<tr>
<td></td>
<td>43210</td>
<td>Esophagogastroduodenoscopy, flexible, transoral; with esophagogastric fundoplasty, partial or complete, includes duodenoscopy when performed</td>
</tr>
<tr>
<td></td>
<td>43236</td>
<td>Esophagogastroduodenoscopy, flexible, transoral, with direct submucosal injections, any substance</td>
</tr>
<tr>
<td></td>
<td>43257</td>
<td>; with delivery of thermal energy to the muscle of lower esophagus sphincter and/or gastric cardia, for treatment of gastroesophageal reflux disease</td>
</tr>
<tr>
<td></td>
<td>43499</td>
<td>Unlisted procedure, esophagus</td>
</tr>
<tr>
<td>HCPCS</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

*IMPORTANT NOTE: Medicare Advantage medical policies use the most current Medicare references available at the time the policy was developed. Links to Medicare references will take viewers to external websites outside of the health plan’s web control as these sites are not maintained by the health plan.
Vagus Nerve Stimulation

Effective: June 1, 2017

Next Review: April 2018
Last Review: April 2017

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Vagus nerve stimulation (VNS) involves implantation of an infraclavicular pulse generator that sends weak electric impulses to the left vagus nerve within the carotid sheath in the neck. This implantable generator is used as a treatment for a number of conditions.

MEDICAL POLICY CRITERIA

Notes:

- This policy does not apply to vagus nerve blocking therapy. See cross references.
- This policy only applies to the initial placement of the device. This policy does not apply to revision(s) or replacement(s) after the device has been placed.

I. Vagus nerve stimulation (VNS) may be considered medically necessary as a treatment of medically refractory seizures. Patients must have tried and been unresponsive to or intolerant of four antiepileptic drugs.

II. VNS is considered investigational for all other indications, including but not limited to the following:

A. Anxiety disorders
### II. Indications

B. Bulimia  
C. Chronic refractory hiccups  
D. Cognitive impairment associated with Alzheimer's disease  
E. Depression  
F. Essential tremors  
G. Fibromyalgia  
H. Headaches  
I. Heart failure  
J. Obesity  
K. Traumatic brain injury  
L. Tinnitus

### III. Non-implantable vagus nerve stimulation devices are considered **investigational** for all indications.

**NOTE:** A summary of the supporting rationale for the policy criteria is at the end of the policy.

### CROSS REFERENCES

1. Gastric Electrical Stimulation; Surgery, Policy No. 111  
2. Vagus Nerve Blocking Therapy for Obesity; Surgery, Policy No. 200

### BACKGROUND

An implanted VNS device delivers mild electronic impulses via two electrodes connected to the generator and wrapped around the vagus nerve. The stimulator may be programmed in advance or may be activated on demand by placing a magnet against the generator implantation site.

While the mechanisms for the therapeutic effects of vagal nerve stimulation are not fully understood, the basic premise of VNS in the treatment of various conditions is that vagal visceral afferents have a diffuse central nervous system projection, and activation of these pathways has a widespread effect on neuronal excitability. Electrical stimulus is applied to axons of the vagus nerve, which have their cell bodies in the nodose and junctional ganglia and synapse on the nucleus of the solitary tract in the brainstem. From the solitary tract nucleus, vagal afferent pathways project to multiple areas of the brain. There are also vagal efferent pathways that innervate the heart, vocal cords, and other laryngeal and pharyngeal muscles, and provide parasympathetic innervation to the gastrointestinal tract that may also be stimulated by VNS.

VNS was originally approved for the treatment of medically-refractory epilepsy. Significant advances have occurred in surgical treatment for epilepsy and in medical treatment of epilepsy with newly developed and approved medications. Despite these advances, however, 25% to 50% of patients with epilepsy experience breakthrough seizures or suffer from debilitating adverse effects of antiepileptic drugs. VNS has been used as an alternative to or adjunct to epilepsy surgery or medications as a therapy for refractory seizures.
Based on observations that patients treated with VNS experienced improvements in mood, VNS has been evaluated for the treatment of refractory depression. VNS has been investigated for multiple other conditions which may be affected by either the afferent or efferent stimulation of the vagus nerve, including headaches, tremor, obesity, heart failure, fibromyalgia, tinnitus, and traumatic brain injury.

Recently, less-invasive, non-surgical means of transcutaneous VNS have been developed; however, these non-implantable methods have not yet received approval from the U.S. Food and Drug Administration (FDA) as a treatment for any condition.

REGULATORY STATUS

Implantable VNS Devices

Several VNS therapy systems by Cyberonics Inc. have pre-market approval (PMA) from the U.S. Food and Drug Administration (FDA) for treatment of refractory partial-onset seizures and chronic or recurrent depression, when certain criteria are met. For example, in 1997, the NeuroCybernetic Prosthesis (NCP®) system was approved for use in conjunction with drugs or surgery “as an adjunctive treatment of adults and adolescents over 12 years of age with medically refractory partial onset seizures.” The VNS Therapy™ System was approved in 2005 “for the adjunctive long-term treatment of chronic or recurrent depression for patients 18 years of age or older who are experiencing a major depressive episode and have not had an adequate response to four or more adequate antidepressant treatments.”

Non-implantable VNS Devices

Cerbomed has developed a transcutaneous VNS (t-VNS®) system, NEMOS®, that uses a combined stimulation unit and ear electrode to stimulate the auricular branch of the vagus nerve, which supplies the skin over the concha of the ear. Patients self-administer electric stimulation for several hours a day; no surgical procedure is required. The device has not been FDA approved for use in the US.

electroCore, LLC has developed a non-invasive VNS (gammaCore®) released for use by the FDA in April of 2017. The device intended for non-invasive vagus nerve stimulation on the side of the neck to treat cluster headache and to reduce the frequency of cluster headache attacks. Product code: PKR

EVIDENCE SUMMARY

In order to assess the safety and effectiveness of vagus nerve stimulation (VNS), particularly for indications in which the primary outcomes are subjective (e.g., pain reduction, improved mood, improved functioning), well-designed, randomized controlled trials (RCTs) are necessary. Such trials include double-blinding, appropriate randomization, an appropriate control group (i.e., sham VNS or standard medical treatment), large study populations, adequate follow-up time, and adverse events reporting.

MEDICALLY REFRACTORY SEIZURES

The criteria for VNS for seizures are based on a 1998 BlueCross BlueShield Association (BCBSA) Technology Evaluation Center (TEC) assessment[1], a 2015 Cochrane review[2] which included the three published double-blind randomized controlled trials (RCTs)[3-5], and numerous case series, retrospective reviews, and other non-randomized studies on adult[6-11],

The two RCTs were large, well-designed multicenter trials that reported an approximate 25% reduction in partial-onset seizure frequency following three months of VNS. Adverse effects were mild and consisted primarily of hoarseness or voice change during “on” periods of stimulation. The remaining literature is limited to numerous non-randomized trials. Although evidence from non-randomized studies are generally considered unreliable for assessing the safety and effectiveness of VNS, the findings from these numerous studies have consistently shown significantly reduced seizure activity in patients with drug-resistant epilepsy. In addition, clinical practice guidelines from the American Academy of Neurology stated that “…sufficient evidence exists to rank VNS for epilepsy as effective and safe…”[26] Thus, despite the lack of RCTs in the published clinical evidence, VNS has become a recognized standard of care for treatment in selected patients with medically refractory seizures.

More recently, a 2014 RCT reported long-term quality of life outcomes for 112 patients with pharmaco-resistant focal seizures, which supported the beneficial effects of VNS for this group.[27]

REFRACTORY DEPRESSION

Technology Assessments

A 2006 BCBSA TEC Assessment[28], evaluated the effectiveness of VNS in the treatment of refractory depression compared with continued medical management. The evidence consisted of one case series, one observational study, and one randomized controlled trial. The assessment found that “overall, the evidence supporting efficacy of VNS is not strong.”

The randomized controlled trial (RCT) of 221 patients that compared VNS with a sham control (implanted but inactivated VNS) did not show a statistically significant difference between VNS and continued medical therapy in relieving depression symptoms.[29-31] The trial was short and possibly underpowered to detect a smaller amount of VNS benefit. In addition the adequacy of blinding was questionable. The observational study included a subset of 205 VNS treated patients from the RCT described above who were followed long-term. A separately recruited control group of 124 patients received ongoing treatment for depression.[29,32] Although the study findings favored the VNS therapy group, this evidence is considered unreliable due to significant methodological limitations including but not limited to the following: 1) Non-randomized allocation of treatment does not control for possible between-group differences in individual patient characteristics; thus, it cannot be ruled out that these differences, rather than the treatments received, were responsible for the observed outcomes; 2) The lack of a sham study group does not control for the expected placebo effects; 3) The inadequate, non-concurrent comparison group does not permit conclusions on the efficacy of VNS compared with placebo or other treatment options, 4) The differences in sites of care between VNS treated patients and controls may introduce response bias. (Analysis performed on subsets of patients cared for in the same sites, and censoring observations after treatment changes, generally showed diminished differences in apparent treatment effectiveness.); and 5) Differences in concomitant therapy changes cannot be ruled out as an explanation of the observed outcomes.

The case series (Study D-01) was a feasibility study of 60 patients receiving VNS; improvement was reported in depression scores.[33] It is uncertain whether loss to follow-up...
was addressed adequately in the analysis. In addition, the case series is limited by the lack of an appropriate comparison group.

Systematic Reviews

In a meta-analysis that included 14 studies, Martin and Martin-Sanchez reported that among the uncontrolled studies in their analysis, 31.8% of subjects responded to VNS treatment.[34] However, results from a meta-regression to predict each study’s effect size suggested that 84% of the observed variation across studies was explained by baseline depression severity (p<0.0001). The authors concluded that current data was insufficient to determine whether VNS is an effective treatment for depression and noted that positive results from uncontrolled studies may be due to placebo effect.

A 2008 systematic review and meta-analysis for VNS of treatment-resistant depression identified no new RCTs since the pivotal RCT described above, which the authors determined to be inconclusive.[35] As noted above, RCTs are considered the appropriate design for studying VNS for any indication. However, this review also included 17 nonrandomized, open studies which found VNS to be associated with a reduction in depressive symptoms. The authors concluded that, while open studies have reported promising results, further clinical trials are needed to study the mechanism of action and cost-effectiveness, and to confirm the efficacy of VNS in treatment-resistant depression.

Randomized Controlled Trials

Since the BCBSA TEC Assessment and the 2008 systematic review, a single randomized controlled trial was identified that evaluated the effectiveness of VNS for treatment of refractory depression. Aaronson et al. randomized 331 patients with treatment-resistant depression (TRD) into one of three VNS dose groups: LOW (0.25 mA current, 130 μs pulse width), MEDIUM (0.5-1.0 mA, 250 μs), or HIGH (1.25-1.5 mA, 250 μs).[34] Patients were included that had a history of failure to respond to at least 4 adequate dose/duration of antidepressant treatment trials from at least 2 different treatment categories. After 22 weeks, the current dose could be adjusted in any of the groups. At follow up visits at weeks 10, 14, 18, and 22 after enrollment, there was no statistically significant difference between the dose groups for the study’s primary outcome, defined as a change in the Inventory of Depressive Symptomatology (IDS) score from baseline. However, the mean IDS score improved significantly for each of the groups from baseline to the 22 week follow up. At 50 weeks of follow up, there were no significant differences between the treatment dose groups for any of the depression scores used. Most patients completed the study; however, there was a high rate of reported adverse events, including voice alteration in 72.2%, dyspnea in 32.3%, and pain in 31.7%. Interpretation of the IDS improvement over time is limited by the lack of a no treatment control group. Approximately 20% of the patients included had a history of bipolar disorder; and therefore, the results may not be representative of most patients with treatment resistant unipolar depression. The lack of a placebo comparison group within this study limits conclusions regarding the isolated treatment effect of VNS in this patient population.

Nonrandomized Studies

Numerous non-randomized studies evaluated the effectiveness of VNS for the treatment of refractory depression.[33,35-41] It is not possible to reach reliable conclusions from these studies as they fail to control for the biases discussed above.
TREATMENT OF CHRONIC HEART FAILURE

Randomized Controlled Trials

In 2015, Zannad and colleagues reported results from the NECTAR-HF trial, a randomized, sham-controlled trial to outcomes from VNS in patients with severe left ventricular (LV) dysfunction despite optimal medical therapy. Ninety-six patients were implanted with VNS and randomized in a 2:1 manner to VNS ON or VNS OFF for 6 months. Programming of the generator was performed by a physician un-blinded to treatment assignment, while all other investigators and site study staff involved in endpoint data collection were blinded to randomization. Sixty-three patients were randomized to the intervention, of whom 59 had paired pre-post data available, while 32 were randomized to control, of whom 28 had paired data available. The analysis was a modified intention-to-treat. For the primary endpoint of change in left ventricular end systolic diameter (LVESD) from baseline to 6 months, there were no significant differences between groups (P=0.60 between-group difference in LVESD change). Other secondary efficacy endpoints related to LV remodeling parameters, LV function, and circulating biomarkers of heart failure, did not differ between groups, with the exception of SF-60 physical component score, which showed greater improvement in the VNS ON group than in the control group (from 36.3 to 41.2 in the VNS ON group vs from 37.7 to 38.4 in the control group; P=0.02). Subject blinding was found to be imperfect, which may have biased the subjective outcome data reporting.

In the ANTHEM-HF study, 60 patients with heart failure with reduced ejection fraction were implanted with VNS, randomly assigned to right- or left-sided implantation (n=29 and 31, respectively), and followed for 6 months. Overall, from baseline to 6 month follow-up, LV ejection fraction improved by 4.5% (95% CI 2.4 to 6.6), left ventricular end systolic volume (LVESV) improved by -4.1 mL (95% CI -9.0 to 0.8), LVESD improved by -1.7 mm (95% CI -2.8 to -0.7), heart rate variability improved by 17 ms (95% CI 6.5 to 28), and 6-minute walk distance improved by 56 m (95% CI 37 to 75). Given there was no sham comparator group, it is unclear if the observed improvements may be attributed to VNS or some other confounding factor.

Nonrandomized Studies

Several small case series describe VNS treatment outcomes in patients with heart failure; however, for the reasons noted above, evidence from non-randomized studies is considered unreliable in the study of VNS as a treatment for any indication.

OTHER INDICATIONS

Nonrandomized Studies

Small case series (n ≤ 40 patients) and one non-randomized comparison study described experiences with VNS in patients with bulimia, anxiety, Alzheimer’s disease, migraine headaches, obesity, essential tremor, and eating disorders including obesity and food cravings. For the reasons noted above, evidence from non-randomized studies is considered unreliable in the study of VNS as a treatment for any indication.

TRANSCUTANEOUS VAGUS NERVE STIMULATORS

Only conditions for which there is at least one RCT will be discussed, as case series are inadequate to determine the effect of the technology.
Refractory Epilepsy

Aihua et al reported results from a series of 60 patients with pharmaco-resistant epilepsy treated with a transcutaneous VNS (t-VNS) device, who were randomly assigned to receive stimulation over the earlobe (control group) or the Ramsay-Hunt zone (treatment group), which includes the external auditory canal and the conchal cavity and is considered to be the somatic sensory territory of the vagus nerve.[52] Thirty patients were randomized to each group; 4 subjects from the treatment group were excluded from analysis due to loss to follow-up (n=3) or adverse effects (n=1), while 9 subjects from the control group were excluded from analysis due to loss to follow-up (n=2) or increase or lack of decrease in seizures or other reasons (n=7). In the treatment group, compared with baseline, the median monthly seizure frequency was significantly reduced after 6 months (5.5 vs 6.0; p<0.001) and 12 months (4.0 vs 6.0; p<0.001) of t-VNS therapy. At 12-month follow-up, t-VNS group subjects had a significantly lower median monthly seizure frequency compared with the control group (4.0 vs 8.0; p<0.001).

Two small case series were identified that used a t-VNS device for treatment of medication-refractory seizures. In a small case series of 10 patients with treatment-resistant epilepsy, Stefan et al reported that 3 patients withdrew from the study, while 5 of 7 patients reported a reduction in seizure frequency.[53] In another small case series, He et al reported that among 14 pediatric patients with intractable epilepsy who were treated with bilateral t-VNS, of the 13 patients who completed follow-up, mean reduction in self-reported seizure frequency was 31.8% after 8 weeks, 54.1% from week 9 to 16, and 54.2% from week 17 to 24.[54]

Psychiatric Disorders

Hein et al reported results of 2 pilot RCTs of a t-VNS device for the treatment of depression, 1 which included 22 subjects and 1 with 15 subjects.[55] In the first study, 11 subjects each were randomized to active or sham t-VNS. At 2 weeks follow-up, Beck Depression Inventory (BDI) self-rating scores in the active-stimulation group decreased from 27.0 to 14.0 points (p<0.001), while the sham-stimulated patients did not show significant reductions in the BDI (31.0 to 25.8 points). In the second study, 7 patients were randomized to active t-VNS and 8 patients were randomized to sham t-VNS. In this study, BDI self-rating scores in the active stimulation group decreased from 29.4 to 17.4 points (p<0.05) after 2 weeks, while the sham-stimulated patients did not show significant change in BDI (28.6 to 25.4 points). The authors do not report direct comparisons in BDI change between the sham- and active-stimulation groups.

Hasan et al reported a randomized trial of t-VNS for the treatment of schizophrenia.[56] Twenty patients were assigned either to active t-VNS or to sham treatment for 12 weeks. There was no statistically significant difference in the improvement of schizophrenia status during the observation period.

Shiozawa et al conducted a systematic review of studies evaluating the evidence related to transcutaneous stimulation of the trigeminal or vagus nerve for psychiatric disorders.[57] They found 4 studies that addressed t-VNS for psychiatric disorders and included a total of 84 subjects. Three of the 4 studies evaluated physiologic parameters in healthy patients and 1 evaluated pharmaco-resistant epilepsy (Stefan et al, previously described[53]). The authors also include a fifth study in a data table, although not in their text or reference list (Hein et al, previously described[55]). Overall, the studies included were limited by small size and poor generalizability.
Headache

Goadsby et al reported results from an open-label pilot study of t-VNS for the treatment of migraine with or without aura.[58] Eighty migraine attacks were self-treated by 27 patients, of an initial sample of 30 patients (2 patients treated no migraine attacks with the device, 1 patient treated only an aura). Of 54 moderate or severe attacks treated, 12 subjects (22%) were pain-free at 2 hours posttreatment. Thirteen subjects reported adverse events, which were all considered mild or moderate.

Impaired Glucose Tolerance

Huang et al reported results of a pilot RCT of a t-VNS device that provides stimulation to the auricle for the treatment of impaired glucose tolerance.[59] The study included 70 patients with impaired glucose tolerance who were randomized to active or sham t-VNS, along with 30 controls who received no t-VNS treatment. After 12 weeks of treatment, patients who received active t-VNS were reported to have significantly lower 2-hour glucose tolerance test results than those who received sham t-VNS (7.5 mmol/L vs 8 mmol/L; p=0.004).

ADVERSE EVENTS

The most commonly reported adverse effects of VNS have been mild and consist primarily of hoarseness of voice during "on" periods of stimulation, transient throat pain, and coughing. More serious adverse events reported include, but are not limited to direct delivery of the current to the nerve due to generator malfunction; modified synchronization between cardiac and respiratory activity affecting the oxygen delivery to tissues; heart block with ventricular standstill; bradyarrhythmias and severe asystolia; and changes in respiration during sleep.[1,29,35,60-63]

NON-IMPLANTABLE VAGUS NERVE STIMULATORS FOR CLUSTER HEADACHE

The only FDA released device is the gammaCore®, which is intended for non-invasive vagus nerve stimulation (nVNS) on the side of the neck to treat cluster headache and to reduce the frequency of cluster headache attacks.

In 2017, Silberstein et al reported results from the manufacturer funded ACT1 study – a randomized, double-blind, sham-controlled study of nVNS as a treatment for cluster headache (CH). One hundred fifty subjects were randomized to receive sham control or nVNS treatment for less than or equal to one month; completers could enter a 3-month nVNS open-label phase. A considerable proportion of patients correctly guessed their treatment allocation after their first treatment, though blinding was found to have improved by the end of the one-month period. The primary end point was response rate, defined as the proportion of subjects who achieved pain relief (pain intensity of 0 or 1) at 15 minutes after treatment initiation for the first CH attack without rescue medication use through 60 minutes. Secondary end points included the sustained response rate (15-60 minutes). Subanalyses of episodic cluster headache (eCH) and chronic cluster headache (cCH) cohorts were prespecified.

During the randomized phase of one month, 14 participants discontinued participation from the treatment group, and 8 in the control group discontinued. In the three-month open label period, 17 and 11 discontinued from the treatment and control groups, respectively. Application site reactions and nervous system AEs occurred more frequently with sham treatment than with nVNS in the double-blind phase. Adverse device effects (ADEs) were reported by 35/150...
(nVNS, 11; sham, 24) subjects in the double-blind phase and 18/128 subjects in the open-label phase.

Intent-to-treat analysis included 133 subjects: 60 nVNS-treated (eCH, n = 38; cCH, n = 22) and 73 sham-treated (eCH, n = 47; cCH, n = 26). Authors reported a response in 26.7% of nVNS-treated subjects and 15.1% of sham-treated subjects. Response rates were significantly higher with nVNS than with sham for the eCH cohort (nVNS, 34.2%; sham, 10.6%; \( p = 0.008 \)) but not the cCH cohort (nVNS, 13.6%; sham, 23.1%; \( p = 0.48 \)). Sustained response rates were significantly higher with nVNS for the eCH cohort and total population.

Gaul et al (2016, 2017) reported the results of a randomized open-label study of nVNS as a prophylactic therapy for chronic cluster headache (CH) in patients diagnosed at least one year prior to enrollment.\[64,65\] The study was funded by the device manufacturer. In a two-week baseline period, all 97 participants received only their individualized standard of care (SoC). Patients were then randomized to a four-week period of SoC with nVNS (n=48) or SoC alone, i.e., control (n=49). Four participants from the SoC with nVNS chose to withdraw; one control participant was removed from the study for failing to meet enrollment criteria. In an optional four-week period following, all participants received SoC with nVNS (n=92); 70 completed the optional period (11 controls discontinued from each group).

Efficacy was evaluated by the mean number of CH attacks per week, defined as the number of attacks during the last two weeks of the randomized phase minus the number of attacks during baseline divided by two. Safety and tolerability were assessed in those who were assigned treatment; and the intent-to-treat (ITT) population was those who had more than one efficacy recording in their home diary after randomization.

In the ITT population (n=45 SoC plus nVNS, n=48 in control) authors reported a mean therapeutic gain of 3.9 fewer CH attacks per week (95% confidence interval (CI): 0.5, 7.2; \( p = 0.02 \)). However, the proportion of participants receiving SoC plus nVNS in the ITT population from the randomized phase with more than 50% response to treatment was 40.0, and in controls who went on to receive treatment in the extension phase, the proportion was 16.7.

During the randomization phase, 38% participants in the SoC plus nVNS group experienced adverse events (AEs), and 27% of controls experienced AEs. In the extension phase, 25% and 24% experienced AEs, respectively. Overall, the most common AEs for any treatment were CH attacks, headache, nasopharyngitis, dizziness, oropharyngeal pain, and neck pain. No serious AEs were considered related to the nVNS device.

The study is limited by a sham placebo control group, which may result in placebo response in the nVNS group.

**PRACTICE GUIDELINE SUMMARY**

**AMERICAN PSYCHIATRIC ASSOCIATION**

The American Psychiatric Association (APA) (2010, reaffirmed 2015) has level III* recommendations regarding the use of vagus nerve stimulation (VNS) for patients with major depressive disorder.\[66\] Strategies to address nonresponse during an acute phase of depression include VNS as an additional option for individuals who have not responded to at least four adequate trials of antidepressant treatment, including ECT (electroconvulsive...
therapy). Maintenance treatment with VNS is also appropriate for individuals whose symptoms have responded to this treatment modality.

* [III] May be recommended on the basis of individual circumstances (As opposed to level I or II which are recommended with substantial and moderate clinical confidence, respectively.)

**AMERICAN ACADEMY OF NEUROLOGY**

The American Academy of Neurology (AAN) 2013 consensus statement states VNS may be considered for seizures in children, for LGS (Lennox-Gastaut-syndrome)- associated seizures, and for improving mood in adults with epilepsy; and VNS may be considered to have improved efficacy over time.[67] These statements are based on Level C evidence, which is defined as, “possibly effective, ineffective or harmful (or possibly useful/predictive or not useful/predictive) for the given condition in the specified population.”

### SUMMARY

Although the current evidence is limited, vagus nerve stimulation (VNS) has evolved to a standard of care as a treatment of medically refractory seizures. Therefore, VNS for medically refractory seizures may be considered medically necessary for patients who have had inadequate response to or are intolerant of at least four antiepileptic drugs.

The evidence is insufficient to permit conclusions about the benefit of VNS as a treatment for conditions other than medically refractory seizures. Therefore, VNS is considered investigational for all indications other than selected patients with refractory seizures.

There is not enough research to know if transcutaneous vagus nerve stimulation (tVNS) improves health outcomes as a treatment for any condition. In addition, no tVNS devices have received approval from the U.S. Food and Drug Administration (FDA). Therefore, transcutaneous vagus nerve stimulation is considered investigational as a treatment for all indications.

There is not enough research to know if or how well non-invasive vagus nerve stimulation (nVNS) works to treat people with any condition, including but not limited to cluster headache. This does not mean that it does not work, but more research is needed to know. No clinical guidelines based on research recommend nVNS for people with cluster headache or any other condition. Therefore, non-invasive vagus nerve stimulation is considered investigational as a treatment for all indications.

### REFERENCES


October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.


### CODES

<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>61885</td>
<td>Insertion or replacement of cranial neurostimulator pulse generator or receiver, direct or inductive coupling; with connection to a single electrode array</td>
</tr>
<tr>
<td></td>
<td>61886</td>
<td>Insertion or replacement of cranial neurostimulator pulse generator or receiver, direct or inductive coupling; with connection to two or more electrode arrays</td>
</tr>
<tr>
<td></td>
<td>61888</td>
<td>Revision or removal of cranial neurostimulator pulse generator or receiver</td>
</tr>
<tr>
<td></td>
<td>64553</td>
<td>Percutaneous implantation of neurostimulator electrode array; cranial nerve</td>
</tr>
<tr>
<td></td>
<td>64568</td>
<td>Incision for implantation of cranial nerve (e.g., vagus nerve) neurostimulator electrode array and pulse generator</td>
</tr>
<tr>
<td></td>
<td>64569</td>
<td>Revision or replacement of cranial nerve (e.g., vagus nerve) neurostimulator electrode array, including connection to existing pulse generator</td>
</tr>
<tr>
<td></td>
<td>64570</td>
<td>Removal of cranial nerve (e.g., vagus nerve) neurostimulator electrode array and pulse generator</td>
</tr>
<tr>
<td></td>
<td>95970</td>
<td>Electronic analysis of implanted neurostimulator pulse generator system (e.g., rate, pulse amplitude, pulse duration, configuration of wave form, battery status, electrode selectability, output modulation, cycling, impedance and patient compliance measurements); simple or complex brain, spinal cord, or peripheral (i.e., cranial nerve, peripheral nerve, sacral nerve, neuromuscular) neurostimulator pulse generator/transmitter, without reprogramming</td>
</tr>
<tr>
<td></td>
<td>95971</td>
<td>; simple spinal cord, or peripheral (i.e., peripheral nerve, sacral nerve, neuromuscular) neurostimulator pulse generator/transmitter, with intraoperative or subsequent programming</td>
</tr>
<tr>
<td></td>
<td>95974</td>
<td>Electronic analysis of implanted neurostimulator pulse generator system (e.g., rate, pulse amplitude, pulse duration, configuration of wave form, battery status, electrode selectability, output modulation, cycling, impedance and patient compliance measurements); complex cranial nerve neurostimulator pulse generator/transmitter, with intraoperative or subsequent programming, with or without nerve interface testing, first hour</td>
</tr>
<tr>
<td></td>
<td>95975</td>
<td>; complex cranial nerve neurostimulator pulse generator/transmitter, with intraoperative or subsequent programming, each additional 30 minutes after first hour (list separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td></td>
<td>0466T</td>
<td>Insertion of chest wall respiratory sensor electrode or electrode array, including connection to pulse generator (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>HCPCS</td>
<td>L8679</td>
<td>Implantable neurostimulator, pulse generator, any type</td>
</tr>
<tr>
<td></td>
<td>L8680</td>
<td>Implantable neurostimulator electrode, each</td>
</tr>
<tr>
<td></td>
<td>L8681</td>
<td>Patient programmer (external) for use with implantable programmable neurostimulator pulse generator, replacement only</td>
</tr>
<tr>
<td></td>
<td>L8682</td>
<td>Implantable neurostimulator radiofrequency receiver</td>
</tr>
<tr>
<td></td>
<td>L8683</td>
<td>Radiofrequency transmitter (external) for use with implantable neurostimulator radiofrequency receiver</td>
</tr>
</tbody>
</table>

October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage.

Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>L8685</td>
<td></td>
<td>Implantable neurostimulator pulse generator, single array, rechargeable, includes extension</td>
</tr>
<tr>
<td>L8686</td>
<td></td>
<td>Implantable neurostimulator pulse generator, single array, non-rechargeable, includes extension</td>
</tr>
<tr>
<td>L8687</td>
<td></td>
<td>Implantable neurostimulator pulse generator, dual array, rechargeable, includes extension</td>
</tr>
<tr>
<td>L8688</td>
<td></td>
<td>Implantable neurostimulator pulse generator, dual array, non-rechargeable, includes extension</td>
</tr>
<tr>
<td>L8689</td>
<td></td>
<td>External recharging system for battery (internal) for use with implantable neurostimulator, replacement only</td>
</tr>
</tbody>
</table>

*Date of Origin: February 1998*


Varicose Vein Treatment

Effective: September 1, 2017

Next Review: March 2018
Last Review: August 2017

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based on all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Varicose veins are dilated, tortuous veins that may cause pain or skin ulcers; however, the majority of treatment is done for cosmetic reasons. Invasive treatment may include surgical removal and/or destruction using lasers, heat, or injection of sclerosing solution.

MEDICAL POLICY CRITERIA

NOTES:

- Member contracts for covered services vary. Member contract language takes precedence over medical policy. In addition, when there is a contract denial for treatment of varicose veins, the denial not only includes treatment but also the associated duplex scans (i.e. CPT 93970 or 93971) for treatment planning.

POLICY CRITERIA

- This policy only addresses treatment of the superficial system veins of the lower extremity (e.g., long and short saphenous veins, saphenous tributaries, and associated lower extremity perforator veins) and upper extremity varices including sclerotherapy and vulvar varices.
Embolization, ablation, and sclerotherapy of the ovarian, internal iliac, or gonadal veins for treatment of pelvic congestion syndrome or varicoceles are addressed separately (see Cross References below).

I All of the following general criteria (see Policy Guidelines) must be met for varicose vein treatment to be considered for coverage:

A At least one or more of the following indications must be documented to be present:

1. Functional impairment, attributed to varicose veins, which limits performance of instrumental activities of daily living (ADL). Instrumental ADL are defined as feeding, bathing, dressing, grooming, meal preparation, household chores, and occupational tasks that are required as a daily part of job functioning. Clinical records must specifically document ALL of the following:
   a. The specific instrumental ADL that is impaired; and
   b. A description of how performance of the instrumental ADL is limited
2. Ultrasound documented recurrent attacks of superficial phlebitis.
3. Recurrent or persistent hemorrhage from ruptured varix.
4. Ulceration from venous stasis where incompetent varices are a significant contributing factor.

B There is clinical documentation that ongoing medically supervised conservative therapy, including use of compression (minimum 20 mmHg) stockings (or compression wrap when stockings cannot be utilized), has been utilized for a minimum of three months, is currently being utilized, and did not successfully treat the patient’s indication(s) or clinical condition. Clinical documentation must include all of the following:

1. History of present illness, physical examination, and conservative therapy treatment plan. Note: There are a number of different classification scales for compression stockings; for consistency, this policy requires that units of compression be documented in mmHg.
2. Progress notes from a treating provider of at least 1 office visit after at least 3 months of conservative therapy documenting patient compliance with conservative therapy, including the use of compression (minimum 20 mmHg) stockings, is currently being utilized, and the patient response. For example, compression stockings should be worn daily while the patient is out of bed. Unna boot or compression wrap may be utilized in lieu of compression stockings when there is documentation of an open venous stasis ulcer of the leg to be treated.
3. For requests for additional treatment sessions, three months of conservative therapy must have been utilized after the most recent varicose vein procedure, and have not successfully treated the patient’s symptoms.

C Incompetence in the superficial system veins (e.g., long and short saphenous veins, perforator veins, and saphenous tributaries) must be supported by
complete venous imaging study documentation obtained no more than 6 months prior to the request for coverage with the diameter of the vein and the reflux in seconds measured at multiple levels in the thigh and calf. *Note:* for requests for additional treatment sessions after previous varicose vein procedures, additional imaging is not required so long as imaging is submitted that was performed no more than 6 months prior to the current request for coverage. Remeasurement must be done as part of a complete venous study.

D Clear, interpretable photographs are required on any affected areas of the leg, e.g., protruding varicose veins or ulcers and must be consistent with the submitted clinical description

II Procedures

A Ligation/stripping and phlebectomy (i.e., stab, hook, transilluminated powered)

1. Ligation/stripping and phlebectomy of incompetent superficial system veins (including the long and short saphenous veins and saphenous tributaries including accessory saphenous veins) and varicose veins 4 mm or greater in diameter may be considered **medically necessary** when all of the following criteria are met:
   
   a. The incompetent superficial veins proximal to the vein to be treated either have been treated or are being treated concurrently.
   
   b. All of Criteria I. (A-D) above are met.
   
   c. For ligation/stripping of the long and short saphenous veins, significant incompetence exceeding 0.5 seconds is demonstrated at the saphenofemoral junction (SFJ) and thigh, or at the saphenopopliteal junction (SPJ) and calf.

2. If criteria II.A.1. above are not met, ligation/stripping or phlebectomy is considered **not medically necessary.**

B Endovenous ablation

1. Endovenous radiofrequency or laser ablation of incompetent long or short saphenous veins may be considered **medically necessary** when the all of the following are met:

   a. Minimum vein diameters where treatment is requested:

      i. Long saphenous vein diameter 5.5 mm or greater throughout the segment to be ablated, measured via ultrasound at the SFJ (or proximal thigh), mid-thigh, and knee (or above knee); (If below knee ablation requested mid-calf measurement also necessary); or

      ii. Short saphenous vein diameter is 4 mm or greater throughout the segment to be ablated, measured via ultrasound at the SPJ and mid-calf.

   b. Significant incompetence exceeding 0.5 seconds throughout the segment to be ablated, is demonstrated at the SFJ and thigh, or at the SPJ and calf.

   c. Clinical documentation that all incompetent segments of the same...
vein will be treated in the same session.

d. All of Criteria I. (A-D) above are met.

2. If criteria II.B.1. above are not met, endovenous radiofrequency or laser ablation of incompetent long or short saphenous veins is considered **not medically necessary**.

3. Endovenous laser or radiofrequency ablation of the entire incompetent saphenous vein usually can be accomplished in a single treatment session. Multiple separate sessions for ablation of segments of a continuous vein are considered **not medically necessary**. Although additional procedures, including ligation or sclerotherapy, performed in the same treatment session on the same ablated saphenous vein are considered included components of the ablation procedure, procedures on other saphenous venous systems may be distinct procedural services.

4. Endovenous laser or radiofrequency ablation is considered **investigational** for all of the following:
   
a. Cryoablation of any vein
   
b. Radiofrequency or laser ablation of veins other than the long or short saphenous veins, including but not limited to the following:
      i. accessory saphenous veins
      ii. branch tributaries
      iii. varicose veins
      iv. perforator veins
   
c. Ablation of saphenous and other veins (i.e., vulvar varices)
   
d. Mechanochemical ablation of any vein
   
e. Microwave ablation of any vein
   
f. Steam injection ablation of any vein

C Sclerotherapy

1. Sclerotherapy (liquid, foam, or microfoam) of the following superficial system veins, short saphenous vein, and saphenous tributaries including accessory saphenous veins, and varicose veins 4 mm or greater in diameter may be considered **medically necessary** when both of the following criteria are met:
   
a. If related superficial system veins proximal to the incompetent vein to be treated are incompetent, those incompetent proximal veins either have been treated or are being treated concurrently
   
b. All of Criteria I. (A-D) above are met.

2. If criteria II.C.1. above are not met, sclerotherapy is considered **not medically necessary**.

3. Ultrasound guidance (see Policy Guidelines) for liquid, foam, or microfoam sclerotherapy of varicose veins **other than** the following superficial system
veins; the short saphenous vein and saphenous tributaries including accessory saphenous veins is considered not medically necessary.

4. Sclerotherapy is considered investigational for the following:
   a. Vulvar, including labial and buttock varices
   b. Upper extremity varices
   c. The long saphenous vein
   d. The perforator veins

5. Sclerotherapy of small (less than 4 mm in diameter) superficial reticular veins and/or telangiectasias (spider veins) is considered cosmetic.

III Treatment sessions (see Policy Guidelines): the medical necessity of each treatment session must be established. Subject to other applicable criteria, treatment sessions may be considered medically necessary when one of the following criteria are met (A, B or C):

A Initial treatment, single session; OR
B Initial treatment including endovenous ablation: either a single bilateral session or two treatment sessions (a separate session for each of the right and left legs); OR
C Subsequent treatment when the clinical outcome of prior treatment(s) during three months subsequent to prior treatment(s) has been established and documented and criteria I.A.-D. are met in addition to either criteria 1. or 2. below:
   1. Single session; or
   2. For subsequent treatment including bilateral endovenous ablation, either a single bilateral session or two treatment sessions (a separate session for each of the right and left legs).

IV If Criteria I. A-D above are not met, varicose vein treatment is considered not medically necessary.

V Follow-up venous studies performed within 6 months following the most recent ipsilateral treatment, in the absence of complications, are considered not medically necessary, including but not limited to routine confirmation studies following endovenous ablation.

VI Use of endovenous glue/adhesive (e.g. cyanoacrylate adhesives) is considered investigational for all indications.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

POLICY GUIDELINES

It is critical that the list of information below is submitted for review to determine if the policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome.

- History of present illness, physical examination, and impact on activities of daily living (ADL) (including the specific ADL) impaired, how it impacts performance, and what is done to alleviate it)
- Complete duplex studies including vein names with measurements of seconds of reflux and average vein diameters. A complete venous study includes a minimum of the following:
  - Deep veins: common femoral, mid-femoral, and popliteal
  - Long saphenous vein: SFJ, mid-thigh, knee, and mid-calf
  - Short saphenous vein: SPJ, and mid-calf
  - Perforators: site with seconds of reflux and diameters
  - Branch tributaries: site with seconds of reflux and diameters
  - Varicose veins (varices): diameters
- Photos (clear and interpretable quality)
- Conservative therapy treatment plan (including units of compression stocking strength documented in mmHg)
- Results of monitoring conservative therapy, including documentation of medical supervision and timeframe of conservative therapy
- Procedures requested:
  - Specific veins to be treated
  - Number of treatment session(s) being requested
  - If bilateral endovenous ablation is requested, document whether a bilateral or two unilateral sessions are being requested
  - Specify the veins to be treated in each session
  - For ablations, specify how all incompetent segments of the same vein are to be treated

**Treatment Sessions**

Each treatment session should address as much abnormality as is appropriate and reasonable and may include more than one vein and/or modality.

### CROSS REFERENCES

1. [Cosmetic and Reconstructive Surgery](#), Surgery, Policy No. 12
2. [Ovarian Internal Iliac, and Gonadal Vein Embolization as a Treatment of Pelvic Congestion Syndrome](#), Surgery, Policy No.147

### BACKGROUND

The venous system of the lower extremities consists of the superficial system (e.g., long and short saphenous veins and accessory or tributary veins that travel in parallel with the long and short saphenous veins) and the deep system (e.g., popliteal and femoral veins). These two parallel systems are interconnected via perforator veins and at the saphenofemoral and the saphenopopliteal junctions.

**Note:** The long and short saphenous veins are also known as the great or greater and the small or lesser saphenous veins, respectively. This policy uses the nomenclature long saphenous vein and short saphenous vein as these terms are consistent with current CPT nomenclature.

One-way valves are present within all veins to direct the return of blood up the lower limb. Larger varicose veins, many protruding above the surface of the skin, typically are related to valve incompetence. As the venous pressure in the deep system is generally greater than that of the superficial system, valve incompetence leads to increased hydrostatic pressure...
transmitted to the unsupported superficial vein system. Backflow (venous reflux) with pooling of blood ultimately results in varicosities. In addition, clusters of varicosities may appear related to incompetent perforating veins, such as Hunter and Dodd, located in the mid- and distal thigh, respectively and/or associated with incompetence at the saphenofemoral junction. In some instances, the valvular incompetence may be isolated to a perforator vein, such as the Boyd perforating vein located in the anteromedial calf. These varicosities are often not associated with saphenous vein incompetence since the perforating veins in the lower part of the leg do not communicate directly with the saphenous vein.

Although many varicose veins are asymptomatic, when present, symptoms include itching, burning, heaviness, fatigue, and pain. In addition, chronic venous insufficiency secondary to venous reflux can lead to peripheral edema, hemorrhage, thrombophlebitis, venous ulceration, and chronic skin changes. In an effort to improve the consistency in diagnosing chronic venous disorders, particularly for patient selection in clinical trials, an international consensus committee developed CEAP classification.[1] In this system, classification is based on clinical manifestations (C), etiology (E), anatomical distribution (A), and underlying pathophysiology (P). (See Appendix 1)

Note: The term "varicose veins" does not apply to the telangiectatic dermal veins, which may be described as "spider veins" or "broken blood vessels." While abnormal in appearance, these veins typically are not associated with any symptoms, such as pain or heaviness, and their treatment is considered cosmetic.

TREATMENT OF SUPERFICIAL VARICOSE VEINS

Conservative Therapy

Treatment of venous reflux/venous insufficiency is aimed at reducing abnormal pressure transmission from the deep to the superficial veins. Varicose veins can usually be treated with non-surgical measures. Symptoms often decrease when the legs are elevated periodically, when prolonged standing is avoided, and when elastic compression stockings are worn.

Operative Therapy

If conservative treatment measures fail, additional treatment options typically focus first on identifying and correcting the site of reflux, and second on redirecting venous flow through veins with intact valves. Thus conventional surgical treatment of varicosities is based on the following three principles:

- Control of the most proximal point of reflux, typically at the saphenofemoral junction, as identified by preoperative Doppler ultrasonography. Surgical ligation and division of the saphenofemoral or saphenopopliteal junction is performed to treat the valvular incompetence.

- Removal or occlusion by ablation of the refluxing long and/or short saphenous vein from the circulation. The classic strategy for isolation is vein stripping in conjunction with vein ligation and division.

- Removal or occlusion of the refluxing varicose tributaries. Strategies for removal include phlebectomy (i.e., ligation/division/stripping, powered phlebectomy, or stab avulsion) or occlusion by injection sclerotherapy; either at the time of the initial treatment, or subsequently. Over the years various different minimally invasive alternatives to ligation...
and stripping have been investigated, including sclerotherapy and thermal ablation using radiofrequency energy (high frequency radiowaves), laser energy, or cryoablation (also called cryotherapy).

Endovenous Ablation

The objective of endovenous ablation techniques is to cause injury to the vessel, causing retraction and subsequent fibrotic occlusion of the vein.

Thermal Ablation

Three endovenous thermal ablation techniques have been investigated as minimally invasive alternatives to vein ligation and stripping.

- Radiofrequency (RF) ablation is performed by means of a specially designed catheter inserted through a small incision in the distal medial thigh to within 1-2 cm of the saphenofemoral junction. High frequency radio waves (200-300 kHz) are delivered through the catheter electrode and cause direct heating of the vessel wall, causing the vein to collapse. The catheter is slowly withdrawn, closing the vein.

- Laser ablation is performed similarly; a laser fiber is introduced into the saphenous vein under ultrasound guidance; the laser is activated and slowly removed along the course of the saphenous vein. Laser ablation may be referred to as endovenous laser ablation (EVLA) or endovenous laser treatment (EVLT).

- Cryoablation uses extreme cold to cause injury to the vessel. Technical developments since thermal ablation procedures were initially introduced include the use of perivenous tumescent anesthesia which allows treatment of veins larger than 12 mm in diameter and helps to protect adjacent tissue from thermal damage during treatment of the lesser saphenous vein.

- There are two technologies that are not available in the United States:
  - Microwave ablation is performed via endovenous catheter using microwave energy to heat the vessel walls.
  - Steam ablation is catheter-based endovenous thermal ablation that uses high pressure pulses of steam to heat the vein to 120°C.

Mechanochemical Ablation

Endovenous mechanochemical ablation (MOCA) utilizes both sclerotherapy and mechanical damage to the lumen. Following ultrasound imaging, a disposable catheter with a motor drive is inserted into the distal end of the target vein and advanced to the saphenofemoral junction. As the catheter is pulled back, a wire rotates at 3500 rpm within the lumen of the vein, abrading the lumen. At the same time, a liquid sclerosant (sodium tetradecyl sulphate) is infused near the rotating wire. It is proposed that mechanical ablation allows for better efficacy of the sclerosant, without the need for the tumescent anesthesia used in thermal ablation.

Cyanoacrylate Adhesive

Cyanoacrylate adhesive is a clear, free-flowing liqulate that polymerizes in the vessel via an anionic mechanism (i.e. polymerizes into a solid material upon contact with body fluids or
tissues). The adhesive is gradually injected along the length of the vein in conjunction with ultrasound and manual compression. The acute coaptation halts blood flow through the vein until the implanted adhesive becomes fibrotically encapsulated and establishes chronic occlusion of the treated vein. Cyanoacrylate glue has been used as a surgical adhesive and sealant for a variety of indications, including gastrointestinal bleeding, embolization of brain arteriovenous malformations, and to seal surgical incisions or other skin wounds.

**Sclerotherapy**

The objective of sclerotherapy is to destroy the endothelium of the target vessel by injecting an irritant solution (either a detergent, osmotic solution, or a chemical irritant), ultimately resulting in the complete obliteration of the vessel. The success of the treatment depends on accurate injection of the vessel, an adequate injectant volume and concentration of sclerosant, and post-procedure compression. Compression theoretically results in direct apposition of the treated vein walls to provide more effective fibrosis and may decrease the extent of the thrombosis formation.

Sclerotherapy is an accepted and effective treatment of telangiectatic vessels. Historically, larger veins and very tortuous veins were not considered to be good candidates for sclerotherapy. Technical improvements in sclerotherapy, including the routine use of Duplex ultrasound to target refluxing vessels, luminal compression of the vein with anesthetics, and foam sclerosant in place of liquid sclerosant, have improved its effectiveness in these veins. Other concerns have arisen with these expanded uses of sclerotherapy. For example, use of sclerotherapy in the treatment of varicose tributaries without prior ligation, with or without vein stripping creates issues regarding its effectiveness in the absence of the control of the point of reflux and isolation of the refluxing saphenous vein. Sclerotherapy of the long saphenous vein raises issues regarding appropriate volume and concentration of the sclerosant and the ability to provide adequate post-procedure compression. Moreover, the use of sclerotherapy, as opposed to the physical removal of the vein with stripping, raises the issue of recurrence due to recanalization.

**TREATMENT OF PERFORATOR VEINS**

Perforator veins cross through the fascia and connect the deep and superficial venous systems. Incompetent perforating veins were originally addressed with an open surgical procedure, called the Linton procedure, which involved a long medial calf incision to expose all posterior, medial, and paramedial perforators. While this procedure was associated with healing of ulcers, it was largely abandoned due to a high incidence of wound complications. The Linton procedure was subsequently modified by using a series of perpendicular skin flaps instead of a longitudinal skin flap to provide access to incompetent perforator veins in the lower part of the leg. The modified Linton procedure may be occasionally utilized for the closure of incompetent perforator veins that cannot be reached by less invasive procedures. Subfascial endoscopic perforator surgery (SEPS) is a less-invasive surgical procedure for treatment of incompetent perforators and has been reported since the mid-1980s. Guided by Duplex ultrasound scanning, small incisions are made in the skin and the perforating veins are clipped or divided by endoscopic scissors. The operation can be performed as an outpatient procedure. Endovenous ablation of incompetent perforator veins with sclerotherapy and radiofrequency has also been reported.

**OTHER**
Deep vein valve repair or reconstruction and replacement are being investigated.

Venous “glue” or “superglue” is not cleared for use in the United States. This is an adhesive delivered via endovenous catheter as a method for sealing the vein.

**REGULATORY STATUS**

The following devices have received specific U.S. Food and Drug Administration (FDA) marketing clearance for the endovenous treatment of superficial vein reflux:

- The VenaSeal™ (Medtronic) Closure System was FDA approved in 2015. The system includes a liquid adhesive, catheter, guidewire, dispenser gun and tips, and syringes. The clear liquid adhesive, cyanoacrylate adhesive, is injected into the diseased vein and polymerizes into a solid material to permanently seal the vein.

- The CERMAVEIN Steam Vein Sclerosis (SVS™) system is being studied outside of the United States but does not have FDA approval or clearance for marketing.

- The ClariVein® Infusion Catheter (Vascular Insights) received marketing clearance through the 510(k) process in 2008 (K071468). It is used for mechanochemical ablation. Predicate devices were listed as the Trellis® Infusion System (K013635) and the Slip-Cath® Infusion Catheter (K882796). The system includes an infusion catheter, motor drive, stopcock and syringe and is intended for the infusion of physician-specified agents in the peripheral vasculature.

- Polidocanol is an injectable sclerosing agent that may be used for intravenous treatment of varicose veins.
  
  o Varithena® (Biocompatibles, Inc, a BTG group company), formerly Varisolve®, is a polidocanol sclerosant microfoam made with a proprietary gas mix that is dispersed from a canister with a controlled density and more consistent bubble size. FDA approval in 2013 was for the treatment of incompetent great saphenous veins, accessory saphenous veins, and visible varicosities of the great saphenous vein system above and below the knee.

  o In 2010, Asclera® (Merz North America, Inc) is an injectable solution with FDA approval for the treatment of uncomplicated spider veins (varicose veins ≤ 1mm in diameter) and reticular veins (varicose veins 1-3 mm in diameter) in the lower extremities.

- A modified Erbe Erbokryo® cryosurgical unit (Erbe USA) received FDA clearance for marketing in 2005. A variety of clinical indications are listed, including cryostripping of varicose veins of the lower limbs.

- The Trivex system is a device for transilluminated powered phlebectomy that received FDA clearance through the 510(k) process in October 2003. According to the label, the intended use is for “ambulatory phlebectomy procedures for the resection and ablation of varicose veins.”

- In 2002, the Diomed 810 nm surgical laser and EVLT ™ (endovenous laser therapy) procedure kit received FDA clearance through the 510(k) process, "... for use in the
endovascular coagulation of the greater saphenous vein of the thigh in patients with superficial vein reflux."

- In 1999, the VNUS® Closure™ system (a radiofrequency device) received FDA clearance through the 510(k) process for "endovascular coagulation of blood vessels in patients with superficial vein reflux." The VNUS RFS and RFSFlex devices received FDA clearance in 2005 for "use in vessel and tissue coagulation including: treatment of incompetent (i.e., refluxing) perforator and tributary veins. The modified VNUS® ClosureFAST™ Intravascular Catheter received FDA clearance through the 510(k) process in 2008.

### EVIDENCE SUMMARY

Outcomes of interest for venous interventions include symptom control, healing and recurrence, recannulation of the vein, and neovascularization. Recannulation (recanalization) is the restoration of the lumen of a vein after it has been occluded; this occurs more frequently following treatment with endovenous techniques. Neovascularization is the proliferation of new blood vessels in tissue, and occurs more frequently following vein stripping. Direct comparisons of durability for endovenous and surgical procedures are complicated by these different mechanisms of recurrence. Relevant safety outcomes include the incidence of paresthesia, thermal skin injury, thrombus formation, thrombophlebitis, wound infection, and transient neurologic effects.

### ENDOVENOUS ABLATION

Endovenous ablation of varicose veins has been proposed as an alternative to ligation and/or stripping. Outcomes of interest include short and long term functional improvement and recurrence rates related either to recannulization of the saphenous vein or neovascularization. In terms of safety, relevant outcomes include the incidence of paresthesias, thermal skin or nerve injuries, thrombus formation, thrombophlebitis, and wound infection.

#### Vein Diameter

There is currently no standardized range for saphenous vein diameter most likely to be associated with severe symptoms or for which endovenous ablation is recommended. In studies of the correlation between long saphenous vein diameter and the presence or absence of reflux, the best cutoff measurement to predict reflux varied between studies from 5.05 mm to 7.3 mm.[2-5] Sensitivity and specificity ranged from 76% to 87% and 60% to 87%, respectively. It is important to note that there is heterogeneity among the populations included in the studies. In addition, there was heterogeneity between studies in measurement techniques (e.g., location, position).

#### Laser Ablation Compared to Radiofrequency Ablation

He (2017) conducted a systematic review which evaluated the effectiveness and safety of endovenous laser ablation compared to radiofrequency ablation for the treatment of varicose veins.[6] The systematic review included a total of 12 studies (N=1,577) (10 RCTs and 2 nonrandomized studies). The meta-analysis of the combined studies concluded that there were no significant differences in effectiveness and safety outcomes between the two groups.
An additional study by Woźniak (2016) also evaluated laser ablation compared to radiofrequency ablation.[7] The study included 510 adults with five year follow-up and reported similar conclusions to He (2017) summarized above.

Laser Ablation and Radiofrequency Ablation Compared to Ligation and Stripping

Systematic Reviews

A number of systematic reviews of randomized controlled trials (RCTs) comparing various types of ablation to surgical treatment have been published. These review consistently reported moderate quality of evidence. Most of the reviews compared endovenous laser ablation (EVLA), radiofrequency ablation (RFA), and surgical treatment of varicose veins. Overall, these techniques had similar, statistically significant improvement in function and in pain relief compared to preoperative scores. RFA and EVLA had low rates of technical procedure failure rates, and short-term recannulization rates. Adverse effects were generally minor for all techniques. Though intraoperative pain was not reported, EVLA consistently resulted in significantly greater pain and bruising when compared to RFA for one to two weeks following the procedure. RFA had significantly more occurrences of superficial phlebitis. Recanalization was similar for EVLA and RFA at one-year follow-up.

The primary limitation of the current evidence is the lack of long-term data on recanalization rates for ablation techniques and neovascularization rates for ligation and stripping. In addition, many of the available studies used first-generation technology and, therefore, do not provide data on newer devices. For example, newer laser technology may result in decreased pain during and after the procedure. Newer RFA technology (e.g., ClosureFast RF catheter) may result in higher rates of vein occlusion.

The most recent systematic review is an updated Cochrane review from 2014, which compared RFA, EVLA, and foam sclerotherapy versus ligation/stripping for saphenous vein varices.[8] Included in the review were 13 randomized studies with a combined total of 3081 patients. The overall quality of the evidence was moderate. For EVLA versus surgery, there were no significant differences between the treatment groups for clinician noted or symptomatic recurrence, or for recanalization. Neovascularization and technical failure were reduced in the laser group (OR=0.05, p<0.001; and OR=0.29, p<0.001, respectively). For RFA versus surgery, there were no significant differences between the groups in clinician noted recurrence, recanalization, neovascularization, or technical failure. The authors concluded that sclerotherapy, EVLA, and RFA were at least as effective as surgery in the treatment of long saphenous vein varicose veins.

Radiofrequency Ablation of Varicose Veins

Systematic Reviews

In 2016, Boersma et al. published results from a systematic review and meta-analysis that compared the anatomical success rates and complication rates of six treatment modalities for small saphenous vein incompetence: surgery, endovenous laser ablation (EVLA), radiofrequency ablation (RFA), ultrasound-guided foam sclerotherapy (UGFS), steam ablation, and mechanochemical endovenous ablation (MOCA).[9] Although the review included 49 articles (five RCTs and 44 cohort studies), nine were specific to RFA and were cohort studies. The pooled anatomical success rate for RFA in 386 incompetent small saphenous veins was 97.1% (95% CI 94.3% to 99.9%). RFA had a relatively low neurological complication rate
(mean 9.7%) when compared to the overall neurological complication rate (mean 19.6%) of the six treatment modalities.

In 2012, a systematic review of RCTs and meta-analysis was published that compared the clinical outcomes of endovenous laser ablation (EVLA), radiofrequency ablation (RFA).[10] The review included 28 RCTs and reported no significant difference in primary failure and clinical recurrence with EVLA and RFA compared with surgery. The advantages of the endovenous ablation techniques over surgery were a lower rate of wound infections and hematoma, and a shorter recovery period.

Randomized Controlled Trials (RCTs)

No new RCTs on RFA of varicose veins have been published since the systematic review.

Nonrandomized Trials

Several case series have reported on endoluminal radiofrequency ablation.[11-14] The largest was reported by Merchant and colleagues, who analyzed the four-year data collected in the ongoing Closure Study Group registry focusing on the treatment of reflux of the long saphenous vein.[11] Data were available on 890 patients and 1,078 limbs treated at 32 centers. Clinical and duplex ultrasound follow-up was performed at one-week, six-months, and yearly for four-years. The vein occlusion rates were 91% at one week and 88.8% at four-years, although only 98 limbs had been followed up to the four-year mark. These results suggest that radiofrequency ablation results in durable occlusion. Radiofrequency ablation has typically been limited to vessels less than 12 mm in diameter. The rationale behind this patient selection criterion is that the electrodes must remain in direct contact with the vein wall during treatment and the largest diameter of the deployed radiofrequency electrodes is 12 mm. The authors noted that exsanguinations, perivenous tumescent infiltration, and external compression may promote electrode and vessel wall contact such that larger veins can be treated. However, in this large case series, there were only 58 limbs with vein sizes larger than 12 mm, and only 29 available for follow-up at six-months or one-year. While the occlusion rate was similar to that seen in smaller vessels, long-term data are inadequate to determine if this effect is durable.

In 2005, Merchant and Pichot also reported the 5-year Closure Study Group registry data.[15] There were 1222 limbs in 1006 patients treated at 34 centers with radiofrequency ablation of various levels of the long saphenous vein, the short saphenous vein, and the accessory saphenous vein. At five-year follow-up using duplex ultrasound examination, 185 limbs were considered failures due to nonocclusion (12.4%), recanalization of a previously occluded vein (69.7%), or groin reflux of a vein with occluded trunk (17.8%). In the latter group, the groin reflux often involved an accessory vein. Logistic regression analysis of risk factors of gender, age, body mass index [BMI], vein diameter, and catheter pullback speed showed that each unit increase in BMI over 25 was associated with increasing risk of long-term failure. In addition, a catheter pull-back speed over the standard speed of 3 cm/min was associated with failure to occlude or recanalization. The authors pointed out that this anatomical failure did not necessarily result in clinical failure; most patients experienced initial symptom relief that was maintained over 5 years.

Laser Ablation of Varicose Veins

Systematic Reviews
In 2016 Boersma et al. published results from a systematic review and meta-analysis that compared the anatomical success rates and complication rates of six treatment modalities for small saphenous vein incompetence, as discussed above.\cite{9} The review included 28 articles specific to EVLA, and included both RCT’s and cohort studies. The pooled anatomical success rate for EVLA in 2,950 incompetent small saphenous veins was 98.5% (95% CI 97.7% to 99.2%). EVLA had a low neurological complication rate (mean 4.8%) when compared to the overall neurological complication rate (mean 19.6%) of the six treatment modalities. The authors concluded that EVLA should be a preferred treatment in small saphenous vein incompetence.

A systematic review of endovenous laser ablation (EVLA) versus surgery was published in 2009.\cite{16} Fifty-nine studies were included, with seven studies that directly compared EVLA and surgery. Randomized and nonrandomized studies directly comparing outcomes for EVLA or surgery were included for the assessment of safety or effectiveness, while case series with a minimum patient population of 100 were included for the assessment of safety alone. For all studies, it was calculated that 5,759 patients (6,702 limbs) were treated with EVLA and 6,395 patients (7,727 limbs) underwent surgery. Few differences were apparent between treatments with respect to clinical effectiveness outcomes, although long-term follow-up was lacking. Nonclinical effectiveness outcomes generally favored EVLA over surgery in the first two months after treatment. The authors concluded that while EVLA offers short-term benefits and appears to be as clinically effective as surgery up to 12 months after treatment, clinical trials with a minimum of three years of follow-up are required to establish the enduring effectiveness of EVLA.

Similarly, the 2012 systematic review with meta-analysis summarized above under radiofrequency ablation also reported no significant difference in primary failure and clinical recurrence with EVLA compared with surgery.\cite{10}

**Randomized Controlled Trials**

The following RCTs on EVLA of the long saphenous vein were published since the systematic reviews summarized above:

In 2015, van der Velden et al. published results from a five-year follow-up comparing conventional surgery, endovenous laser ablation, and ultrasound-guided foam sclerotherapy in patients with great saphenous varicose veins.\cite{17} A total of 224 legs were included (69 conventional surgery, 78 EVLA, and 77 UGFS), and 193 were evaluated at final follow up (86.2%). At the five year follow-up, the Kaplan-Meier analysis showed obliteration or absence of the great saphenous vein in 85% of patients who underwent conventional surgery and 77% of patients who underwent EVLA (not significantly different). Grade I neovascularization was higher in the conventional surgery group (27% vs 3%, p<0.001), while grade II neovascularization was similar in the two groups (17% vs 13%).

In 2014, Brittenden et al. reported a multicenter randomized trial that compared foam sclerotherapy, EVLA, and surgical treatment in 798 patients.\cite{18} The study was funded by U.K.’s Health Technology Assessment Programme of the National Institute for Health Research.\cite{19} Veins greater than 15 mm were excluded from the study. At the six week follow-up visit, patients who were assigned to treatment with foam or laser had the option of treatment with foam for any residual varicosities; this was performed in 38% of patients in the foam group and 31% of patients in the EVLA group. Six months after treatment, mean disease-specific quality of life was slightly worse after sclerotherapy than after surgery (p=0.006), and...
there were more residual varicose veins, although the differences were small. Disease-specific quality of life was similar for the laser and surgery groups. The frequency of procedural complications was similar for the foam sclerotherapy (6%) and surgery (7%) groups, but was lower in the laser group (1%). The rate of complications at 6 months (primarily lumpiness and skin staining), was highest for the sclerotherapy group.

In 2013, Biemans et al. published results from the MAGNA trial, which randomized 223 consecutive patients (240 legs) with long saphenous vein reflux to EVLA, ligation and stripping, or physician compounded foam sclerotherapy (1 ml aethoxysclerol 3#: 3ml air).[20] At one-year follow-up, the anatomic success rates were similar between EVLA and stripping (88.5% and 88.2%, respectively), which were superior to foam sclerotherapy (72.2%). Ten percent of the stripping group showed neovascularization. Health-related quality of life improved in all groups. The CEAP classification improved in all groups with no significant difference between the groups. Transient adverse events were reported in 11 patients after stripping, seven after EVLA, and five after sclerotherapy.

The ongoing, and largest randomized study on EVLA, comparing endovenous laser ablation with costectomy and stripping of the great saphenous vein (RELACS), schedule to follow patients for five years, randomized 400 patients to EVLA performed by a surgeon at one site or to ligation and stripping performed by a different surgeon at a second location.[21] Fifty-four patients withdrew from the study after receiving the randomization result (from an independent site), due primarily to preference for the other treatment. At the two year follow-up there was no significant difference between the groups for clinically recurrent varicose veins, medical condition on the Homburg Varicose Vein Severity Score, or disease-related quality of life. Saphenofemoral reflux was detected by ultrasonography more frequently after EVLA (17.8% vs 1.3%). At 5-year follow-up, Kaplan-Meier analysis showed obliteration or absence of the great saphenous vein in 85% of patients who underwent conventional surgery and 77% of patients who underwent EVLA (not significantly different). 15 Grade I neovascularization was higher in the conventional surgery group (27% vs 3%, p<0.001), while grade II neovascularization was similar in the 2 groups (17% vs 13%).

In 2012 Rasmussen et al. reported the five year follow-up data comparing EVLA (n=121) with ligation and stripping (n=68).[22] Data was available on 98% of the patients. There was no significant difference between the two groups for clinical recurrence (EVLA 36%, stripping 35%) or in the percentage of reoperations (EVLA 38.6%, stripping 37.7%).

Literature on isolated treatment of the anterior accessory saphenous vein is limited. In a 2009 study, outcomes from a cohort of 33 patients who underwent EVLA of the anterior accessory saphenous vein were compared with 33 matched controls undergoing EVLA of the greater saphenous vein.[23] In 21 of the patients (64%) in the accessory saphenous vein group there had been no previous treatment of the greater saphenous vein. At 12-month follow-up there was no evidence of reflux in these patients, and the treated accessory saphenous vein was not visible with ultrasound. The Aberdeen Varicose Vein Symptom Severity Score had improved in both groups, with no significant difference between the two groups. Patient satisfaction scores were also similar.

Nonrandomized Trials

The bulk of the clinical trials on laser ablation of varicose veins are case series[24-28] and registry data[15]. Using historical controls for comparison is difficult since treatment outcomes are variably reported. There are no consistent definitions of success versus failure, either
based on patient or clinical assessment. In general, recurrence rates after ligation and stripping are estimated at around 20%. Doppler or Duplex ultrasound are perhaps the most objective form of assessment of recurrence, but many of the reports of the long term outcomes of ligation and stripping did not use ultrasound studies for postoperative assessment. Only two studies have reported objective results of ligation and stripping at 12 and 24 months. Jones and colleagues reported on the results of a study that randomized 100 patients with varicose veins to undergo either ligation alone or ligation in conjunction with stripping.[29] The results of the ligation and stripping group are relevant to this discussion. At one year, reflux was detected in 9% of patients, rising to 26% at two years. Rutgers and Kitslaar reported on the results of a trial that randomized 181 limbs to undergo either ligation and stripping or ligation combined with sclerotherapy.[30] At two years, Doppler ultrasound demonstrated reflux in approximately 10% of patients, increasing to 15% at three years. Therefore, based on this crude assessment, the reflux rate of 13% for radiofrequency ablation at one year[31] and 6% for laser ablation at two years[24] is roughly comparable to the reflux rate of 9-10% reported by Jones et al and Rutgers and Kitslaar.

**Cryoablation**[32]

Disselhoff and colleagues reported two and five year outcomes from a randomized trial that compared cryoablation with EVLA.[33,34] One hundred and twenty patients were included with symptomatic uncomplicated varicose veins (CEAP C2) with saphenofemoral incompetence and greater saphenous vein reflux. At 10 days after treatment, EVLA had better results than cryoablation with respect to pain score over the first 10 days (2.9 vs. 4.4), resumption of normal activity (75% vs. 45%) and induration (15% vs. 52%). At the two year follow-up, freedom from recurrent incompetence was observed in 77% of patients after EVLA and 66% of patients after cryoablation (not significantly different). At five years, 36.7% of patients were lost to follow-up; freedom from incompetence and neovascularization was found in 62% of patients treated with EVLA and 51% of patients treated with cryoablation (not significantly different). Neovascularization was more common after cryoablation, but incompetent tributaries were more common after EVLA. There was no significant difference between groups in the Venous Clinical Severity Score or Aberdeen Varicose Vein Severity Score at either two or five years.

Klem and colleagues published results from a randomized trial in 2009 that found endovenous cryoablation (n=249) to be inferior to conventional stripping (n=245) for treating patients with symptomatic varicose veins.[35] The percentage of patients with greater saphenous vein remaining was 44% in the endovenous cryoablation group and 15% in the conventional stripping group. The Aberdeen Varicose Vein Questionnaire also showed better results for conventional stripping (score of 11.7) in comparison with cryoablation (score of 8.0). There were no differences between the groups in SF-36 subscores, and neural damage was the same (12%) in both groups.

**Cyanoacrylate Ablation**

Bozkurt (2016) conducted a one year prospective comparative study (n=310) evaluating cyanoacrylate glue compared to endovenous laser ablation for venous insufficiency.[36] The authors concluded that periprocedural pain, ecchymosis, permanent paresthesia were less in the cyanoacrylate ablation group. There were no significant differences in closure rates at 12 months follow-up. In addition, there were no significant differences in severity scores nor the
Aberdeen Varicose Vein Questionnaire. Additional studies are needed to evaluate the effectiveness and safety of this technique.

Mechanochemical Ablation

Systematic Review

In 2016 Boersma et al. published results from a systematic review and meta-analysis that compared the anatomical success rates and complication rates of six treatment modalities for small saphenous vein incompetence, as discussed above.[9] The review included just one study on mechanochemical ablation (MOCA), and although the authors reported an anatomical success rate of 94%, more research is needed to determine these effects.

Randomized Controlled Trials

In 2014, Bootun et al. published early one month results from an ongoing study comparing 119 patients randomized to mechanochemical ablation (MCA) (n=60) or RFA (n=59).[37] The maximum and average pain scores were significantly lower during MCA compared to RFA (p<0.001). At one month follow-up, both groups showed complete or proximal occlusion rates of 92%, though data were available for only 67% of participants. These preliminary outcomes do not permit conclusions due to methodological limitations including the short-term follow-up and incomplete data. The authors noted that data from longer follow-up is being collected.

Nonrandomized Studies

The remainder of the evidence on MCA of varicose veins is limited to nonrandomized series and cohort studies.[38-43] In the only comparative study, van Eekeren and colleagues compared postoperative pain and early quality of life in 68 patients treated with either RFA or MCA of great saphenous veins.[41] Patients who did not want to be treated with MCA were offered treatment with RFA; this study design could potentially lead to selection bias. There was no significant between-group difference in procedure-related pain. Compared with RFA, patients treated with MCA had a 14.3 mm reduction in pain measured on a 100 mm visual analog scale (VAS) measured over the first 3 postoperative days (6.2 vs. 20.5) and a 13.8 mm reduction in pain (4.8 vs. 18.6 mm; p<.001) over the first two weeks. MCA patients treated also had a significantly earlier return to normal activities (1.2 vs. 2.4 days) and return to work (3.3 vs. 5.6 days; p=.02). There was a similar improvement in quality of life for the two groups when measured at six weeks. Longer studies are required to determine the durability of these effects.

Microwave Ablation

This technique has not been approved or cleared for marketing by the FDA. Two clinical trial reports were found. The first, a preliminary randomized trial, compared endovenous microwave ablation (EMA) with high ligation and stripping (HLS).[44] At 24-months follow-up, there was no significant difference in outcomes between the two groups. The second, a retrospective comparison between laser (n=163 limbs in 138 patients) and microwave (n=143 limbs in 121 patients) ablation of the greater saphenous vein, found significantly lower ecchymosis, skin burn, and paresthesia in the laser ablation.[45] However, the recanalization rate was significantly higher in the laser ablation group at one week and six months postoperatively (p<0.01). Loss to follow-up at 24-months was about 19% in each group.

Steam Ablation
This technique has not been approved or cleared for marketing by the FDA. There is currently no published clinical trial evidence on this technique.

**SCLEROTHERAPY**

In general, reported outcomes of uncontrolled studies have varied for sclerotherapy, as have the periods of follow-up. In many studies the outcomes are reported in terms of cure rates, but the criteria for cure or failure are poorly defined. Studies have also reported subjective patient-assessed outcomes or physician assessment, both of which may be poorly defined. More recent studies included results of Doppler or duplex ultrasonography; however, the relationship between finding ultrasonographic evidence of recurrent reflux and clinical symptoms is uncertain. Finally, it should be noted that sclerotherapy of the long saphenous vein is a fundamentally different approach than stripping. With stripping, recurrences are likely related to an incomplete surgical procedure or to revascularization. With sclerotherapy, recurrences may be additionally related to recanalization of an incompletely fibrosed saphenous vein.

Below is a summary of articles that are representative of the current published evidence. The results of these studies have established ligation and stripping as the gold standard treatments for saphenofemoral incompetence, due to the improved long-term recurrence rates. Sclerotherapy is used primarily as an adjunct to treat varicose tributaries.

**Systematic Reviews**

In 2016 Boersma et al. published results from a systematic review and meta-analysis that compared the anatomical success rates and complication rates of six treatment modalities for small saphenous vein incompetence, as discussed above. The review included just six articles specific to ultrasound-guided foam sclerotherapy (UGFS). The pooled anatomical success rate for UGFS in 494 incompetent small saphenous veins was 63.6% (95% CI 47.1% to 80.1%); however, more research is needed to determine these effects.

As noted above, the updated 2014 Cochrane review included comparisons of sclerotherapy and ligation and stripping. There was no significant difference between sclerotherapy and surgery in the rate of recurrence as rated by clinicians (odds ratio [OR], 1.74; p=0.06) or for symptomatic recurrence (OR=1.28). The authors concluded that sclerotherapy, EVLA, and RFA were at least as effective as surgery in the treatment of long saphenous vein varicose veins.

A systematic review from 2008 found that foam sclerotherapy of varicose veins is associated with a higher recurrence rate in patients with saphenofemoral incompetence compared to the rates of endovenous laser therapy or radiofrequency obliteration, while a 2009 systematic review suggested that outcomes from sclerotherapy are worse than those of surgery (ligation and stripping) for saphenous vein reflux.

**Randomized Controlled Trials**

Several controlled trials comparing sclerotherapy of varicose tributaries or the saphenous vein, with and without associated ligation and stripping, have reported that the absence of ligation and stripping was associated with an increased frequency of recurrence. These trials are difficult to interpret due to the lack of clarity about which vein—either the varicose tributaries or the saphenous vein itself—have undergone sclerotherapy. Nonetheless, these trials established the importance of control of the site of reflux (ligation) and isolation of the refluxing portion of the saphenous vein (stripping). The following are examples of these studies:
Results from the five year follow up published by van der Velden at al. in 2015 study, as previously mentioned under EVLA, also examined ultrasound-guided foam sclerotherapy in 77 legs.[17] The authors found obliteration or absence of the greater saphenous vein was observed in only 23% of patients treated with sclerotherapy compared to 85% of patients who underwent conventional surgery and 77% of patients who underwent EVLA. Thirty-two percent of legs treated initially with sclerotherapy required one or more reinterventions during follow-up compared with 10% in the conventional surgery and EVLA groups. However, clinically relevant grade II neovascularization was higher in the conventional surgery and EVLA groups (17% and 13%, respectively), compared with the sclerotherapy group (4%). EuroQol-5D scores improved equally in all groups.

In 2015, King et al. published results from the VANISH-1 study, a manufacturer-funded multicenter placebo RCT undertaken to evaluate the efficacy of relief of symptoms and safety of Varithena (0.5%, 1%, and 2%) compared with 0.125% (control) and placebo.[48] Seven-hundred and eighty patients were screened; 279 patients met the study criteria and were treated with either placebo (n=56), or Varithena 0.125% (n=57), 0.5% (n=51), 1% (n=52), or 2% (n=63). Patients rated the duration and intensity of nine symptoms and activity levels during the previous 24 hours using the VVSymQscore instrument. At week eight VVSymQscores for pool Varithena (0.5%+1%+2%) patients were significantly superior to placebo (p=<.001), and VVSymQscores decreased significantly (p<.001) from baseline at eight weeks for all Varithena individual doses. There were no serious AE’s and no PE’s; however, patients receiving higher Varithena dose concentrations (1% and 2%) had higher rates of treatment-emergent AE’s, which occurred in ≥ 3% of patients. The most common kinds of treatment-emergent AE’s included pain, superficial thrombophlebitis, and hematoma at the injection site.

Microfoam sclerotherapy was studied in the 2014 VANISH-2 study, an ongoing five year manufacturer-funded pivotal double-blind RCT undertaken to obtain FDA marketing approval for Varithena microfoam (BTG).[49] The study compared 0.5% or 1.0% polidocanol microfoam with subtherapeutic foam dose (0.125%) and endovenous placebo in 232 patients. The authors reported early eight week follow-up data finding elimination of reflux and/or occlusion of the previously incompetent vein in 85.6% of the combined 0.5% and 1.0% groups, 59.6% in the 0.125% “subtherapeutic” group, and 1.8% of the placebo group. The improvement in the venous clinical severity score was significantly greater in the 0.5% and 1.0% groups (-5.10) compared with placebo (-1.52), but was not reported for the 0.125% group. The 1.0% dose of Varithena was selected for the 2013 FDA approval. Adverse events occurred in 60% of patients receiving foam sclerotherapy compared to 39% of placebo; 95% were mild or moderate and transient. The most common adverse events were retained coagulum, leg pain, and superficial thrombophlebitis. Deep vein thrombosis was detected by ultrasound in 2.8% of Varithena-treated patients with 1% having proximal symptomatic thrombi treated with anticoagulants. No pulmonary emboli were detected and no clinically significant cardiac or cardiopulmonary, neurologic, or visual adverse events were reported. In the short-term the rates of occlusion with this microfoam sclerotherapy were similar to those reported for EVLA or stripping. RCTs comparing EVLA or stripping with microfoam sclerotherapy with long-term outcomes are needed to evaluate comparative effectiveness. In 2015, Todd and Wright published an update to the VANISH-2 study and reported on findings at one year.[51] Results at year one showed symptoms improved when compared to week 8 (64% with total VVSymQ scores of 3 or less at week eight vs 85% at year one). Reductions from baseline in the individual symptom scores that compose the VVSymQ score were also demonstrated, with all five HASTI symptoms showing a continued decrease from over time. In addition,
improvements from baseline in appearance as assessed by both the patients themselves (PA-V score) and blinded experts reading standardized photographs (IPR-V score) were maintained, with a small trend toward further improvement between week eight and one year. Ten patients of the 232 in the total population had 12 AEs reported during the long-term follow-up period through year one, including one death; however, all were unrelated to treatment. Of the patients who had venous thrombus AEs during the main eight week trial, none had recurrent venous thrombus AEs, and all clots stabilized or resolved completely. No post-thrombotic syndrome or other clinically important sequelae were reported. No patient developed a new venous thrombus AE in the one year follow-up, and no pulmonary emboli were diagnosed at any time through the one year in this study.

A 2012 study was a noninferiority trial of foam sclerotherapy versus ligation and stripping in 430 patients.[52] Analysis was per protocol. Forty patients (17%) had repeat sclerotherapy. At two years, the probability of clinical recurrence was similar in the two groups (11.3% sclerotherapy vs 9.0% ligation and stripping), although reflux was significantly more frequent in the sclerotherapy group (35% vs 21%). Thrombophlebitis occurred in 7.4% of patients after sclerotherapy. There were two serious adverse events in the sclerotherapy group (deep venous thrombosis and pulmonary emboli) that occurred within one week of treatment.

In 2010 Blaise et al. reported three year follow-up from a multicenter double-blind randomized trial (143 patients) that compared treatment of the greater saphenous vein with either 1% or 3% polidocanol foam.[53] Additional treatment with foam sclerotherapy was carried out at six weeks, three and six months if required to abolish persistent venous reflux. There were 49 additional injections in the 1% polidocanol group and 29 additional injections in the 3% group. At the three year follow-up, venous reflux was observed in 21% of patients in the 1% group and 22% of patients in the 3% polidocanol group.

Neglen and colleagues reported on a "partially randomized" trial that compared the outcomes of three different treatment strategies: 1) sclerotherapy alone; 2) ligation and stripping, or 3) ligation combined with sclerotherapy.[54] It was difficult to determine the target of the sclerotherapy. As described in the article, sclerosant was injected into all points of control (presumably at the junction of the perforator veins) and, "if possible, into the main stem of the long saphenous vein." Thus, it seems that the intent of the sclerotherapy was not the obliteration of the long saphenous vein as an alternative to stripping, but as a treatment of the varicose tributaries. Therefore, among those patients who underwent ligation plus sclerotherapy, this trial tested whether or not stripping could be eliminated from the overall approach. In the group who received sclerotherapy alone, almost 70% of patients self-reported a cure immediately postoperatively, which declined to about 30% after five years. This gradual recurrence rate for sclerotherapy alone is similar to that reported in the above studies. For the ligation and sclerotherapy group, 70% reported a cure immediately postoperatively, dropping to 50% after five years. The best long-term results were reported for the ligation and stripping group, which reported an 80% immediate cure rate, dropping to 70% after five years. The physician assessment of treatment outcome showed greater differences among the three groups. For example, based on physician assessment (observation and foot volumetric measurements), only 5% of the sclerotherapy group were considered cured after 5 years, compared to 10% in the ligation and sclerotherapy group and 60% in the ligation and stripping group.

Rutgers and colleagues reported on a trial that randomized 156 patients with varicose veins and saphenofemoral incompetence to undergo either ligation and stripping or ligation and
sclerotherapy. The site of sclerotherapy was not described. At the three years follow-up, the cosmetic results were better in those limbs that had undergone stripping. Additionally, the clinical and Doppler ultrasound evidence of reflux was significantly less in those undergoing stripping.

Nonrandomized Studies

There has also been interest in injecting sclerosant into the saphenous vein either in conjunction with ligation as an alternative to stripping, as a stand-alone procedure, or as an alternative to both ligation and stripping.

Myers et al. published results from a three-year follow-up prospective observational study of sclerotherapy in 489 patients with refluxing saphenous veins and related tributaries. Out of 807 veins treated, 56% were associated with the great saphenous vein and 22% with the small saphenous vein; 22% were tributaries alone. Ultrasound at three to five days after each treatment showed successful occlusion in an average of 1.5 sessions for the group as a whole (65% in one session and 26% in two sessions). The Kaplan-Meier analysis showed three-year survival rates of 83% for tributaries, 53% for great saphenous veins, and 36% for small saphenous veins. These results do not support the use of sclerotherapy for refluxing saphenous veins.

Kanter and Thibault published result from a case series, which included 172 patients with 202 limbs who had varicose veins with associated saphenofemoral incompetence. Using ultrasound guidance, sclerosant was injected into the long saphenous vein 3-4 cm distal to the saphenofemoral junction. Injections were given at 30- to 90-second intervals, proceeding distally as previously injected segments were observed to spasm. Immediately after therapy, a thigh compression stocking was applied. Two weeks after the initial procedure, patients were reevaluated with Duplex ultrasound and were re-treated if found to have persistent reflux. There was a clinical recurrence rate of 22.8% at one year.

Ninja published two case series (1996; 1997) evaluating sclerotherapy for patients with symptomatic vulvar varicosities. The first study included seven women and the second study included five women. Both studies concluded that all patients noticed marked improvements in symptoms after treatment. However, the sample sizes in these two studies were very small and they lacked a comparator group.

Adverse Effects

Although long-term sequelae have not been reported with sclerotherapy, transient adverse effects have been found in up to 8% of patients, including cerebrovascular accidents, transient ischemic attacks, speech and/or visual disturbance, migraine, shortness of breath, dizziness, and numbness. Bubbles appear in the right side of the heart between 9 and 59 seconds after injection and emboli have been detected in the middle cerebral artery following sclerotherapy of saphenous trunks and varices. Deep venous occlusion after ultrasound-guided sclerotherapy has also been reported; risk was found to be greater when treating veins >5 mm in diameter (odds ratio of 3.7) and injecting 10 mL or more of foamed sclerosant (odds ratio of 3.6). A systematic review of visual disturbance following sclerotherapy found this adverse effect to be rare and transient; further research was recommended to clarify the mechanism of action of sclerosants.

Sclerotherapy and Endovenous Thermal Ablation

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
Randomized Controlled Trial

In 2015, Vasquez and Gasparis published results from a manufacturer sponsored multicenter randomized placebo-controlled study. The purpose of the study was to determine the efficacy and safety of Varithena (0.5%, 1.0%) and placebo, each administered with endovenous thermal ablation.[63] A total of 234 patients were screened; 117 patients met the study criteria and received treatment (38 placebo, 39 Varithena 0.5%, and 40 Varithena 1%). Patients were assessed using the Quality of Life/Symptoms (mVEINES-QOL/Sym) questionnaire, Patients Self-Assessment of Visible Varicose Veins (PA-V) and the Independent Photography Review-Visible Varicose Veins (IPR-V) instruments. Efficacy showed baseline scores were greater at week eight for pooled Variethena than for placebo for both IPR-V (−1.2 vs. −0.8 points, p = 0.001) and PA-V (−1.8 vs. −1.6 points, p = 0.16), however, only IPR-V change score reached statistical significance. The comparison of the individual dose concentrations of Variethena (0.5%, 1.0%) with placebo showed a similar pattern for both IPR-V and PA-V scores. Although no patients presented spontaneously with symptoms of thrombus, six patients were found to have venous thrombi, and all occurred during the first eight weeks post treatment. Through six months of follow-up, there were no reports of visual disturbance or migraine among Varithena recipients, no pulmonary emboli, and no AE-related study withdrawals. There was one serious AE, breast cancer, considered unrelated to the study drug.

Other Treatments

FDA approval of the VenaSeal™ Closure System, which uses adhesive, was based on three manufacturer-sponsored clinical studies, one of which was a randomized controlled noninferiority trial. In the VeClose Study, 222 subjects with symptomatic long saphenous vein incompetence were randomized to undergo either the VenaSeal closure (n=108) or RFA (n=114).[64] A three month follow-up was conducted during which no adjunctive procedures were allowed. There were a number of methodological limitations in this study, which include but are not limited to, a 14% loss of data, which was accounted for using various methods such as imputing missing data. While these analyses supported noninferiority, their reliability is unclear. These results require validation in large RCTs with lower rates of data loss and longer-term follow-up.

PRACTICE GUIDELINE SUMMARY

INTERSOCIETAL ACCREDITATION COMMISSION

In 2016, the Intersocietal Accreditation Commission (IAC) published standards and guidelines on vascular testing for accreditation.[65] The IAC has recommendations for peripheral venous testing in section 4B. The guideline for documentation of lower extremity venous duplex for reflux states the following (section 4.7.2B):

4.7.2.1B Transverse grayscale images without and with transducer compressions (when anatomically possible or not contraindicated) must be documented as required by the protocol and must include at a minimum: i. common femoral vein;

   ii. saphenofemoral junction;
   iii. mid femoral vein;
   iv. great saphenous vein;
   v. popliteal vein;

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
vi. small saphenous vein.

4.7.2.2B Spectral Doppler waveforms with the extremity(s) in a dependent position, demonstrating baseline flow and response to distal augmentation and if reflux is present, duration of retrograde flow measured with calipers and documented as required by the protocol and must include at a minimum: i. common femoral vein;

ii. saphenofemoral junction;
iii. great saphenous vein;
iv. mid femoral vein;
v. popliteal vein;
vi. small saphenous vein.

4.7.2.3B Transverse grayscale images of diameter measurement must be documented as required by the protocol and must include at a minimum:

i. saphenofemoral junction;
ii. great saphenous vein at proximal thigh;
iii. great saphenous vein at knee;
iv. small saphenous vein (at saphenopopliteal junction).

ENDOVENOUS ABLATION

Society for Vascular Surgery and the American Venous Forum

The 2011 Society for Vascular surgery (SVS) and the American Venous Form (AVF) clinical practice guidelines on varicose veins and chronic venous disease included recommendations for endovenous radiofrequency or laser ablation for the treatment of incompetent long saphenous veins.[66]

- A Grade 1B recommendation was made in favor of endovenous thermal ablation over foam sclerotherapy and high ligation and stripping due to the reduced convalescence, pain, and morbidity. A Grade 1B recommendation was defined as a strong recommendation based on moderate quality evidence.
- A Grade 1B recommendation was made against treatment of incompetent perforator veins with CEAP class C2, but recommend treating these veins if they are located underneath a healed or active ulcer (Grade 2B recommendation defined as a weak recommendation based on moderate quality evidence.)
- The guideline does not make recommendations for saphenous vein diameter.

The 2014 SVS/AVF guidelines for management of venous ulcers included the following recommendations in favor of standard compressive therapy and ablation of incompetent superficial veins that have axial reflux directed to the bed of the ulcer[67]:

- In a patient with a venous leg ulcer and incompetent superficial veins to 1) improve ulcer healing (Grade 2B recommendation defined as a weak recommendation based on moderate quality evidence), and 2) prevent recurrence (Grade 1C recommendation defined as a strong recommendation based on low- to very low-quality evidence)
- To prevent ulceration in a patient with skin changes at risk for venous leg ulcer, and incompetent superficial veins (Grade 2C recommendation defined as a weak recommendation based on low- to very low- quality evidence)
• To aid in ulcer healing and to prevent recurrence in a patient who also has pathological perforating veins located beneath or associated with the ulcer bed (Grade 2C recommendation defined as a weak recommendation based on low- to very low-quality evidence)
• To prevent ulceration or ulcer recurrence in a patient with skin changes at risk for venous leg ulcer or healed venous ulcer and incompetent superficial veins (Grade 2C recommendation defined as a weak recommendation based on low- to very low-quality evidence).
• If a patient is expected to benefit from pathologic perforator vein ablation, percutaneous ablation with ultrasound-guided sclerotherapy or endovenous RFA or EVLA is recommended over open venous perforator surgery (Grade 1C recommendation defined as a strong recommendation based on low- to very low-quality evidence)

American College of Radiology\textsuperscript{[32]}

The 2012 the American College of Radiology (ACR) published appropriateness criteria for the treatment of lower-extremity venous insufficiency considered endovenous radiofrequency or laser ablation at least as effective as surgery. Cryoablation and mechnochemical ablation are not addressed. The criteria do not include patient selection criteria related to vein size.

Society of Interventional Radiography, Cardiovascular Interventional Radiological Society of Europe, American College of Phlebology, Canadian Interventional Radiology Association\textsuperscript{[68]}

The 2010 the Society of Interventional Radiography (SIR), Cardiovascular Interventional Radiological Society of Europe (CIRSE), American College of Phlebology (ACP), Canadian Interventional Radiology Association (CIRA) published a joint consensus statement on endovenous thermal ablation using either laser or radiofrequency devices under imaging guidance and monitoring an effective treatment of extremity venous reflux and varicose veins under the following conditions:

I. The endovenous treatment of varicose veins may be medically necessary when one of the following indications (A–E) is present:

A. Persistent symptoms interfering with activities of daily living in spite of conservative/nonsurgical management. Symptoms include aching, cramping, burning, itching, and/or swelling during activity or after prolonged standing.
B. Significant recurrent attacks of superficial phlebitis
C. Hemorrhage from a ruptured varix
D. Ulceration from venous stasis where incompetent varices are a contributing factor
E. Symptomatic incompetence of the great or small saphenous veins (symptoms as in A above)

II. A trial of conservative, nonoperative treatment has failed. This would include mild exercise, avoidance of prolonged immobility, periodic elevation of legs, and compressive stockings.

III. The patient's anatomy is amenable to endovenous ablation.
SCLEROTHERAPY

Society for Vascular Surgery and the American Venous Forum

The 2011 Society for Vascular Surgery (SVS) and the American Venous Forum (AVF) published practice guidelines[^66] and included the following recommendations concerning sclerotherapy in varicose vein treatment:

- Grade 1B (strong recommendation based on moderate quality evidence) recommendation for the use of sclerotherapy to treat varicose tributaries
- Grade 1B recommendation against selective treatment of perforating vein incompetence in patients with simple varicose veins
- Grade 2B (weak recommendation based on moderate quality evidence) for sclerotherapy to treat pathologic perforating veins (i.e., outward flow of ≥ 500 ms duration and a diameter of ≥ 3.5 mm) located under healed or active ulcers (CEAP class C5-C6)

The 2014 SVS/AVF guidelines[^67] for management of venous ulcers included the following recommendations:

- Grade 1C (Strong recommendation, low quality or very-low quality evidence) For those patients who would benefit from pathologic perforator vein ablation, we recommend treatment by percutaneous techniques that include ultrasound-guided sclerotherapy or endovenous thermal ablation (radiofrequency or laser) over open venous perforator surgery to eliminate the need for incisions in areas of compromise skin.

**SUMMARY**

There is enough research to determine that treatment of certain symptomatic varicose veins using ligation, phlebectomy, endovenous treatment with radiofrequency or laser ablation, and sclerotherapy may improve short-term clinical outcomes (e.g., pain and return to work). Therefore, these procedures may be considered medically necessary in select patients when the policy criteria are met. Procedures not meeting the policy criteria may be considered not medically necessary. In addition, follow-up venous studies performed within six months following the most recent treatment in the absence of complications is considered not medically necessary.

There is not enough research to show improvement in health outcomes for endovenous ablation or sclerotherapy of the investigational indications listed in the medical policy criteria. Further, the current evidence has limitations including no comparator groups, small study population, and short-term follow-up.

There is not enough research to show that mechanochemical ablation of varicose veins improves patient outcomes and is safe. Therefore, the use of mechanochemical ablation of any vein is considered investigational.

There is not enough research to show that endovenous glues/adhesives improve patient outcomes and is safe. Therefore, the use of endovenous glues/adhesives of any vein is considered investigational.

[^66]: Reference to practice guidelines
[^67]: Reference to 2014 guidelines

October 1, 2017

*These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.*
## Appendix 1: CEAP Classification

<table>
<thead>
<tr>
<th>Clinical classification (C)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C0: no visible or palpable signs of venous disease</td>
<td></td>
</tr>
<tr>
<td>C1: telangiectasias or reticular veins</td>
<td></td>
</tr>
<tr>
<td>C2: varicose veins (&gt;3 mm diameter)</td>
<td></td>
</tr>
<tr>
<td>C3: edema</td>
<td></td>
</tr>
<tr>
<td>C4: skin and subcutaneous tissue changes</td>
<td></td>
</tr>
<tr>
<td>C4a: pigmentation or eczema</td>
<td></td>
</tr>
<tr>
<td>C4b: lipodermatosclerosis or atrophie blanche</td>
<td></td>
</tr>
<tr>
<td>C5: healed venous ulcer</td>
<td></td>
</tr>
<tr>
<td>C6: active venous ulcer</td>
<td></td>
</tr>
</tbody>
</table>

Each clinical class is further characterized by a subscript for symptomatic (S) or asymptomatic (A), for example, C2A or C5S.

<table>
<thead>
<tr>
<th>Etiologic classification (E)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ec: congenital</td>
<td></td>
</tr>
<tr>
<td>Ep: primary</td>
<td></td>
</tr>
<tr>
<td>Es: secondary (postthrombotic)</td>
<td></td>
</tr>
<tr>
<td>En: no venous cause identified</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Anatomic classification (A)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>As: superficial veins</td>
<td></td>
</tr>
<tr>
<td>Ap: perforator veins</td>
<td></td>
</tr>
<tr>
<td>Ad: deep veins</td>
<td></td>
</tr>
<tr>
<td>An: no venous location identified</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pathophysiologic classification</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basic CEAP</td>
<td></td>
</tr>
<tr>
<td>Pr: reflux</td>
<td></td>
</tr>
<tr>
<td>Po: obstruction</td>
<td></td>
</tr>
<tr>
<td>Pr,o: reflux and obstruction</td>
<td></td>
</tr>
<tr>
<td>Pn: no venous pathophysiology identifiable</td>
<td></td>
</tr>
</tbody>
</table>

Advanced CEAP includes the addition of any of following 18 venous segments as locators:

### Superficial veins
- Telangiectasias or reticular veins
- Great saphenous vein above knee
- Great saphenous vein below knee
- Small saphenous vein
- Nonsaphenous veins

### Deep veins
- Inferior vena cava
- Common iliac vein
- Internal iliac vein
- External iliac vein
- Pelvic: gonadal, broad ligament veins, other
- Common femoral vein
- Deep femoral vein
- Femoral vein
- Popliteal vein
- Crural: anterior tibial, posterior tibial, peroneal veins (all paired)
- Muscular: gastrocnemial, soleal veins, other

### Perforating veins
- Thigh
- Calf

## REFERENCES

17. van der Velden, SK, Biemans, AA, De Maeseneer, MG, et al. Five-year results of a randomized clinical trial of conventional surgery, endovenous laser ablation and


31. Rautio, T, Ohinmaa, A, Perala, J, et al. Endovenous obliteration versus conventional stripping operation in the treatment of primary varicose veins: a randomized controlled...


review for medical and pharmacological sciences. 2012 Jul;16(7):873-7. PMID: 22953634


49. Todd, KL, 3rd, Wright, D. The VANISH-2 study: a randomized, blinded, multicenter study to evaluate the efficacy and safety of polidocanol endovenous microfoam 0.5% and 1.0% compared with placebo for the treatment of saphenofemoral junction incompetence. *Phlebology*. 2014. PMID: 23864535

50. U.S. Food and Drug Administration Center for Drug Evaluation and Research. Varithena Summary Review. 2013. [cited 03/22/17]; Available from: [http://www.accessdata.fda.gov/drugsatfda_docs/nda/2013/205098Orig1s000SumR.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/nda/2013/205098Orig1s000SumR.pdf)


October 1, 2017

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.


**CODES**

- There is no specific CPT code for mechanochemical treatment devices (e.g., the ClariVein® device) which should be reported with an unlisted procedure code such as 37799. Per CPT definitions, it is inappropriate to use codes 37241-37244 or 37475-37479 to report this procedure.
- Varithena is not separately reimbursable using any CPT or HCPCS Code.
- There is no specific CPT code for transilluminated powered phlebectomy. Providers might elect to use CPT codes describing stab phlebectomy (37765 or 37766), excision of varicose vein cluster(s) (37785), or unlisted vascular surgery procedure (37799).
- There is no specific CPT for microfoam sclerotherapy. Providers might elect to use CPT codes describing sclerotherapy (36468-36471) or the unlisted vascular surgery procedure code 37799. Use of codes 36475-36476 would be inappropriate as the procedure is not ablation therapy.
<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>36468</td>
<td>Single or multiple injections of sclerosing solutions, spider veins (telangiectasia); limb or trunk</td>
</tr>
<tr>
<td></td>
<td>36470</td>
<td>Injection of sclerosing solution; single vein</td>
</tr>
<tr>
<td></td>
<td>36471</td>
<td>Injection of sclerosing solution; multiple veins, same leg</td>
</tr>
<tr>
<td></td>
<td>36473</td>
<td>Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, mechanochemical; first vein treated</td>
</tr>
<tr>
<td></td>
<td>36474</td>
<td>; subsequent vein(s) treated in a single extremity, each through separate access sites (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td></td>
<td>36475</td>
<td>Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, radiofrequency; first vein treated</td>
</tr>
<tr>
<td></td>
<td>36476</td>
<td>; subsequent vein(s) treated in a single extremity, each through separate access sites (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td></td>
<td>36478</td>
<td>Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, laser; first vein treated</td>
</tr>
<tr>
<td></td>
<td>36479</td>
<td>; subsequent vein(s) treated in a single extremity, each through separate access sites (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td></td>
<td>37700</td>
<td>Ligation and division of long saphenous vein at saphenofemoral junction, or distal interruptions</td>
</tr>
<tr>
<td></td>
<td>37718</td>
<td>Ligation, division, and stripping, short saphenous vein (for bilateral procedure, use modifier 50)</td>
</tr>
<tr>
<td></td>
<td>37722</td>
<td>Ligation, division, and stripping, long (greater) saphenous veins from saphenofemoral junction to knee or below</td>
</tr>
<tr>
<td></td>
<td>37735</td>
<td>Ligation and division and complete stripping of long or short saphenous veins with radical excision of ulcer and skin graft and/or interruption of communicating veins of lower leg, with excision of deep fascia</td>
</tr>
<tr>
<td></td>
<td>37760</td>
<td>Ligation of perforators veins, subfascial, radical (Linton type) including skin graft, when performed, open, 1 leg</td>
</tr>
<tr>
<td></td>
<td>37761</td>
<td>Ligation of perforator vein(s), subfascial, open, including ultrasound guidance, when performed, 1 leg</td>
</tr>
<tr>
<td></td>
<td>37765</td>
<td>Stab phlebectomy of varicose veins, one extremity; 10-20 stab incisions</td>
</tr>
<tr>
<td></td>
<td>37766</td>
<td>Stab phlebectomy of varicose veins, one extremity; more than 20 incisions</td>
</tr>
<tr>
<td></td>
<td>37780</td>
<td>Ligation and division of short saphenous vein at saphenopopliteal junction (separate procedure)</td>
</tr>
<tr>
<td></td>
<td>37785</td>
<td>Ligation, division, and/or excision of varicose vein cluster(s), one leg</td>
</tr>
<tr>
<td></td>
<td>37799</td>
<td>Unlisted procedure, vascular surgery</td>
</tr>
<tr>
<td></td>
<td>93970</td>
<td>Duplex scan of extremity veins including responses to compression and other maneuvers; complete bilateral study</td>
</tr>
<tr>
<td></td>
<td>93971</td>
<td>Duplex scan of extremity veins including responses to compression and other maneuvers; unilateral or limited studies</td>
</tr>
<tr>
<td>HCPCS</td>
<td>J3490</td>
<td>Unclassified drugs</td>
</tr>
<tr>
<td></td>
<td>S2202</td>
<td>Echosclerotherapy</td>
</tr>
</tbody>
</table>
Date of Origin: October 1999

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Medical and surgical treatments of gender dysphoria in transgender individuals involves psychotherapy, hormonal therapy and, in some cases, gender affirmation surgery.

Background

This policy supports applicable professional association statements,[1-5] and is also intended to support the Affordable Care Act (ACA) Section 1557 final implementing regulations published on May 18, 2016, and applicable state requirements[6].

Medical and Surgical Treatment of Gender Dysphoria

A clinical diagnosis of gender dysphoria is required prior to treatment of the disorder. Treatments typically include psychotherapy, hormone therapy and in some cases surgical gender affirmation procedures. Psychotherapy followed by hormone therapy is often the first medical treatment sought, although not all transgender individuals on hormone therapy choose to undergo gender-affirming surgery.[2]

Psychotherapy
Psychotherapy provided by a mental health professional typically includes an initial assessment of gender identity and dysphoria, the historical development of gender dysphoric feelings, and severity of resulting stress caused by the condition. The goal of therapy is to assess, diagnose, and discuss treatment options, if needed, and is typically required prior to hormone therapy and/or surgical treatment.

**Hormone Therapy**

Hormone therapy is undertaken in order to feminize or masculinize individuals’ bodies to conform to their desired gender identities. For transgender individuals, hormone replacement therapy (HRT) causes the development of many of the secondary sexual characteristics of their gender identity. Prescribed hormones differ depending upon the natal gender of the individual. For MTF individuals, hormone treatment may include estradiol, finasteride, and spironolactone. For FTM individuals, hormone treatment may include androgenic hormones such as testosterone.

**Surgical Treatment**

Surgical treatment for gender dysphoria differs depending upon the natal gender of the individual. For MTF individuals, surgery may involve removal of the testicles and penis and the creation of a pseudo vagina, clitoris, and labia. Complications of MTF genital surgery may include necrosis of the vagina and labia, neovaginal prolapse, fistulas from the bladder or bowel into the vagina, stenosis of the urethra, and small or short vaginas.

For FTM individuals, surgery may involve removal of the uterus, ovaries, and vagina, and creation of a neophallus and scrotum with scrotal and/or penile prostheses. The creation of a neophallus for FTM patients is a multistage reconstructive procedure. Currently, techniques for penile reconstruction procedures vary and complications may include frequent urinary tract stenoses and fistulas, donor site scarring and necrosis of the neophallus. In addition, breast size does not significantly decrease with hormonal therapy and as a result, FTM patients may choose to undergo mastectomy to remove breast tissue. For many patients this may be the only surgery undertaken. Mastectomy may involve a complete resection of all breast tissue; however, the nipple/areola sparing technique is typically performed to preserve the nipple/areola.

There are various additional aesthetic surgical procedures which may be sought in order to complete the physical gender transformation and align an individual to their gender identity. However, conflicting opinions exist regarding whether these procedures are essential in treating gender dysphoria.

The WPATH recommends that patients, “engage in 12 continuous months of living in a gender role that is congruent with their gender identity…” prior to gender reassignment surgery so that patients may socially adjust to their desired gender role. WPATH notes that changing a gender role may have personal and social consequences which should be adequately explored prior to undergoing an irreversible surgery.

---

### MEDICAL POLICY CRITERIA

**Note:** Member contracts for covered services vary. Member contract language takes precedent over medical policy.
I. Medical Treatments of Gender Dysphoria

A. Psychotherapy may be considered medically necessary as a treatment of gender dysphoria

B. Continuous hormone therapy may be considered medically necessary as a treatment of gender dysphoria when all of the following criteria are met:

1. Clinical records document that the patient has the capacity to make fully informed decisions and consent for treatment; and

2. A licensed mental health professional has diagnosed gender dysphoria as defined by the DSM-5 criteria (see Appendix 1); and

3. At least one of the following criteria must be met for a period of 3 or more months prior to the initiation of hormone therapy:
   a. Documentation of living as the desired gender; and/or
   b. Psychotherapy with a licensed mental health professional.

II. Surgical Treatments of Gender Dysphoria may be considered medically necessary when either A. or B. are met:

A. Gender affirmation surgery (see Policy Guidelines) may be considered medically necessary in the treatment of gender dysphoria when all of the following criteria are met:

1. Age at least 18 years (Note: age requirement will not be applied to mastectomy in Female-to-Male patients with documented provider determination of medical necessity of earlier intervention); and

2. Clinical records document that the patient has the capacity to make fully informed decisions and consent for treatment, and that any other mental health condition, if present, is adequately controlled; and

3. At least 2 licensed mental health professionals have diagnosed gender dysphoria as defined by the DSM-5 criteria (see Appendix 1), and recommend surgical treatment (Note: only 1 mental health professional referral is required for mastectomy in Female-To-Male patients); and

4. Documentation of continuous hormonal therapy for at least 12 months, unless there is a documented contraindication to hormonal therapy (Note: hormonal therapy is not required prior to mastectomy in Female-To-Male patients); and

5. Twelve months of living in a gender role that is congruent with the patient’s gender identity.

B. When the criteria in II.A. above are met or have been met, the following procedures may be considered medically necessary when clinical information is submitted expressly

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
documenting that the particular requested procedure would improve otherwise
documented significant gender dysphoria:

1. Breast augmentation
2. Hair removal
3. Hair transplantation
4. Nipple/areola reconstruction in the absence of concurrent or prior subcutaneous or
   simple/total mastectomy
5. Mastopexy

III. Other than gender affirmation surgeries listed in the Policy Guidelines, and/or surgeries in
criteria II above, additional treatments to change specific appearance characteristics are
considered not medically necessary as treatments of gender dysphoria including, but not
limited to the following:

A. Abdominoplasty
B. Blepharoplasty
C. Brow lift
D. Calf implants
E. Cheek/malar implants
F. Chin/nose implants
G. Collagen injections
H. Face-lift
I. Facial bone reduction
J. Forehead lift
K. Lip reduction
L. Liposuction
M. Neck tightening
N. Pectoral implants
O. Reduction thyroid chondroplasty
P. Rhinoplasty
Q. Suction-assisted lipoplasty of the waist
R. Voice modification surgery
S. Voice therapy/lessons

IV. Reversal of gender affirmation surgery is considered **not medically necessary** as a treatment of gender dysphoria.

**POLICY GUIDELINES**

**Gender Affirmation Surgery**

Surgical treatment for gender dysphoria differs depending upon the birth gender of the individual. The World Professional Association for Transgender Health (WPATH) indicated that, “(p)hysicians who perform surgical treatments for gender dysphoria should be urologists, gynecologists, plastic surgeons, or general surgeons, and board-certified as such by the relevant national and/or regional association. Surgeons should have specialized competence in genital reconstructive techniques as indicated by documented supervised training with a more experienced surgeon.”[4]

**Female-To-Male (FTM)**

For females transitioning to males, the following procedures may be included as part of gender affirmation surgery:[4,8]

- Hysterectomy
- Mastectomy (subcutaneous mastectomy or simple/total mastectomy, which may include related nipple/areola reconstruction)
- Metoidioplasty
- Nipple/areola reconstruction related to subcutaneous or simple/total mastectomy with nipple/areola excision or repositioning
- Penile prostheses implantation
- Phallic reconstruction/Phalloplasty
- Salpingo-oophorectomy
- Scrotoplasty
- Testicular prostheses implantation
- Urethroplasty
- Vaginectomy

*Definitions:*

Subcutaneous mastectomy: skin-sparing mastectomy which removes tissue through an incision under the breast, leaving the skin, areola, and nipple intact.

Simple/total mastectomy: removal of the entire breast and commonly any excess skin, including the areola and nipple.
Male-To-Female (MTF)

For males transitioning to females, the following procedures may be included as part of gender affirmation surgery:\[4\]

- Clitoroplasty
- Labiaplasty
- Orchiectomy
- Penectomy
- Vaginoplasty

**SCIENTIFIC EVIDENCE**

Evidence regarding the treatment of gender dysphoria in transgender individuals primarily consists of two systematic reviews consisting of small cohort studies. Randomized clinical trials (RCTs) comparing gender dysphoria treatments with the non-treatment are ideal, however, there are challenges in conducting RCTs to evaluate treatments of gender dysphoria due to several factors, such as small patient populations and ethical concerns regarding the high morbidity and mortality rates associated with non-treatment. Therefore, large RCTs are not anticipated. This policy relies on the following systematic reviews and non-randomized studies, as well as professional association recommendations to support applicable federal and state requirements.

**Literature Appraisal**

**Systematic Reviews**

Only one of two systematic reviews is considered good quality\[9\] (Murad et al.) and reported on the resolution of gender dysphoria psychiatric comorbidities, quality of life, and sexual satisfaction outcomes for individuals treated with both hormonal and surgical treatments for gender identity disorder (GID).

In 2009, Murad and colleagues assessed quality of life and other psychosocial outcomes of transgendered individuals with GID, receiving hormonal therapy as part of gender affirmation surgery.\[9\] Twenty-eight cohort studies were included in the review which included pooled data from 1,833 patients with GID (1,093 MTF and 801 FTM). Significant improvements were reported after gender affirmation compared to pre-treatment status: 80% of patients reported improvement in gender dysphoria (95% CI = 68-89%; 8 studies) 78% reported significant improvement in psychological symptoms (95% CI = 56-94%; 7 studies) 80% reported significant improvement in quality of life (95% CI = 72-88%; 16 studies); and 72% reported significant improvement in sexual function (95% CI = 60-81%; 15 studies). Significant study heterogeneity was reported for all outcomes. Although the authors acknowledge the low quality of evidence used in the analysis, gender affirmation that included hormonal interventions in patient with GID was thought to likely improve symptoms of gender dysphoria and overall quality of life.

In 2009, Elamin and colleagues evaluated the use of sex steroids on cardiovascular risk in transgender individuals.\[10\] A total of 16 studies were included in the review with a total of 1,471 male-to-female (MTF) patients and 651 female-to-male (FTM) patients. Steroid use was associated with increased serum triglycerides in both MTF and FTM patients and a nonsignificant effect on HDL-cholesterol and...
systolic blood pressure in FTM patients. Authors noted that the quality of evidence was low due to methodological limitations of included studies, including but not limited to, heterogeneity of patient population and variable follow-up periods and uncontrolled study design.

**Nonrandomized Studies**

Primary evidence is limited to cohort studies with a variety of methodological limitations, including but not limited to small sample size, short-term follow-up, lack of comparison group, and varied treatment methods. Despite these limitations, significant improvements in quality of life, psychological comorbidities, and sexual functioning were consistently reported in patients who received gender-confirming medical treatments.[11]

Imbimbo et al., evaluated the clinical and psychosocial profile of male-to-female transgendered individuals who had undergone reconstructive surgery.[12] The average age of patients was 31 years old, 72% had high educational levels, half of patients’ contemplated suicide at some point prior to surgery and 4% had attempted suicide. Improved sex life satisfaction was reported in 75% of patients, with almost all patients’ reporting satisfaction with their new sexual status. Additional studies sought to evaluate the sociodemographic profile of transgender individuals with GID in an effort to better characterize and provide treatment for this population.[13]

Heylens and colleagues assessed comorbidities and psychosocial factors at various phases of the gender affirmation process in 57 patients with GID.[14] The Symptom Checklist-90 (SCL-90) was administered at three time points: baseline, after the start of hormone therapy, and after sex reassignment surgery (SRS) (also known as [aka] gender affirmation surgery). Psychopathological parameters include overall psychoneurotic distress, anxiety, agoraphobia, depression, somatization, paranoid ideation/psychoticism, interpersonal sensitivity, hostility, and sleeping problems and the psychosocial parameters consist of relationship, living situation, employment, sexual contacts, social contacts, substance abuse, and suicide attempt. The greatest improvement in psychoneurotic distress was observed after the initiation of hormone therapy (p<0.001). In addition, significant decreases in anxiety, depression, interpersonal sensitivity and hostility were reported after hormone therapy. No significant differences were observed in pre- and postoperative assessments.

Fisher et al. described clinical and sociodemographic features of 140 transmen (n=48) and transwomen (n=92) with GID and without affirmation surgery.[15] The following assessment tests were administered: the Body Uneasiness Test (a self-rating scale exploring different areas of body-related psychopathology), Symptom Checklist-90 Revised (a self-rating scale to measure psychological state), and the Bem Sex Role Inventory (a self-rating scale to evaluate gender role). Authors reported that transmen displayed significantly better social functioning than transwoman.

Gorin-Lazard et al. reported a case series which assessed a variety of gender dysphoria symptoms with hormonal treatment preceding gender affirmation surgery. Pre- and post- hormone treatment self-esteem (Social Self-Esteem Inventory), mood (Beck Depression Inventory), QoL (Subjective Quality of Life Analysis), and global functioning (Global Assessment of Functioning) scores were compared in 49 patients.[16] Hormone therapy was reported to be an independent factor in greater self-esteem, a reduction in depression, and improved QoL scores.

Gomez-Gil and colleagues evaluated symptoms of social distress, anxiety and depression in 187 transgendered individuals.[17] Of those included in the study, 120 had undergone hormonal sex-reassignment (SR) (aka gender affirmation) treatment and 67 had not. Social anxiety was assessed with
the Social Anxiety and Distress Scale (SADS) and depression and anxiety were assessed with the Hospital Anxiety and Depression Scale (HADS). The non-hormone group was reported to be significantly younger than the treatment group (mean age 25.9 vs. 33.6 years, \( p=0.001 \)) and was less likely to have undergone surgical interventions (\( p<0.001 \)). After adjusting for confounding factors, the authors reported that patients who were receiving hormone treatment had significantly lower prevalence of depression, anxiety, and social anxiety than those not receiving hormones.

Johansson et al., reported long-term (5-year) outcomes of transgendered individuals (n=42) with GID who had completely transitioned (n=32), were in progress (n=5) or who were on hormone therapy (n=5).\[18\] Authors reported that no patient regretted affirmation and clinicians rated the global outcome as favorable in 62% of the cases, compared to 95% according to the patients themselves, with no differences between the subgroups. At follow-up, more than 90% of patients reported stable or improved work situations, partner relations and sex-life. However 5-15% of patients reported dissatisfaction with hormonal treatment, results of surgery, total gender affirmation procedure, or their present general health.

Asscheman and colleagues evaluated the long-term (1-year) effects of cross-sex hormones in 966 male-to-female (MTF) and 365 female-to-male (FTM) transgendered individuals.\[19\] MTF patients received different doses of estrogen and cyproterone acetate and FTM patients received parenteral/oral testosterone esters or testosterone gel. Hormone treatment levels varied at pre- and post-surgical affirmation time points. High mortality rates were reported in the MTF group when compared to the general population (51%); however, this increased rate was due to non-hormone-related causes such as suicide, acquired immunodeficiency syndrome (AIDS), cardiovascular disease, drug abuse and other unknown causes. No significant increase in mortality was observed in FTM patients compared to the general population.

Clinical Practice Guidelines

World Professional Association for Transgender Health

The World Professional Association for Transgender Health (WPATH) is a multidisciplinary professional society representing the specialties of medicine, psychology, social sciences and law that has published clinical guidelines regarding health services for patients with gender disorders. In 2012, WPATH updated their evidence and consensus-based guideline regarding, the Standards of Care (SOC) for the Health of Transsexual, Transgender, and Gender Nonconforming Peoples.\[4\] WPATH listed the following options for individuals seeking treatment for gender dysphoria:

- Changes in gender expression and role (which may involve living part time or full time in another gender role, consistent with one’s gender identity);
- Hormone therapy to feminize or masculinize the body;
- Surgery to change primary and/or secondary sex characteristics;
- Psychotherapy (individual, couple, family, or group) for purposes such as exploring gender identity, role, and expression; addressing the negative impact of gender dysphoria and stigma on mental health; alleviating internalized transphobia; enhancing social and peer support; improving body image; or promoting resilience.

WPATH guidelines describe surgical procedures as “irreversible changes to the body.” Therefore, WPATH guidelines recommend the appropriate care should be taken to ensure patients have sufficient time (at least 24 hours) to consider all the information and can provide informed consent. WPATH
notes, “(t)hese surgeries may be performed once there is written documentation that this assessment has occurred and that the person has met the criteria for a specific surgical treatment. By following this procedure, mental health professionals, surgeons, and patients share responsibility for the decision to make irreversible changes to the body.”

Physical Interventions for Adolescents

WPATH guidelines state that physical interventions for adolescents fall into three categories or stages:

1. Fully reversible interventions. These involve the use of GnRH analogues to suppress estrogen or testosterone production and consequently delay the physical changes of puberty. Alternative treatment options include progestins (most commonly medroxyprogesterone) or other medications (such as spironolactone) that decrease the effects of androgens secreted by the testicles of adolescents who are not receiving GnRH analogues. Continuous oral contraceptives (or depot medroxyprogesterone) may be used to suppress menses.

2. Partially reversible interventions. These include hormone therapy to masculinize or feminize the body. Some hormone-induced changes may need reconstructive surgery to reverse the effect (e.g., gynaecomastia caused by estrogens), while other changes are not reversible (e.g., deepening of the voice caused by testosterone).

3. Irreversible interventions. Reversible and irreversible interventions are outlined in the standards of care, specifying intervention sequencing in adolescents. It is also stated that “[t]wo goals justify intervention with puberty suppressing hormones: (i) their use gives adolescents more time to explore their gender nonconformity and other developmental issues; and (ii) their use may facilitate transition by preventing the development of sex characteristics that are difficult or impossible to reverse if adolescents continue on to pursue sex reassignment.”

Referral for Surgery

WPATH guidelines indicate that surgical treatments can be initiated by a referral from a qualified mental health professional. One or two referrals may be required depending upon the type of surgery requested. “The mental health professional provides documentation—in the chart and/or referral letter—of the patient’s personal and treatment history, progress, and eligibility.” WPATH guidelines specifically recommend the following:

- One referral from a qualified mental health professional is needed for breast/chest surgery (e.g., mastectomy, chest reconstruction, or augmentation mammoplasty).
- Two referrals—from qualified mental health professionals who have independently assessed the patient—are needed for genital surgery (i.e., hysterectomy/salpingo-oophorectomy, orchiectomy, genital reconstructive surgeries).

Criteria for Breast/Chest Surgery (One Referral)

WPATH lists the following criteria for mastectomy and creation of a male chest in FTM patients:

1. Persistent, well-documented gender dysphoria;
2. Capacity to make a fully informed decision and to consent for treatment;
3. Age of majority in a given country;
4. If significant medical or mental health concerns are present, they must be reasonably well controlled.

Hormone therapy is not a prerequisite.

Criteria for Genital Surgery (Two Referrals)

WPATH lists the following criteria for genital surgery:

1. Persistent, well-documented gender dysphoria;
2. Capacity to make a fully informed decision and to consent for treatment;
3. Age of majority in a given country;
4. If significant medical or mental health concerns are present, they must be reasonably well controlled.
5. 12 continuous months of hormone therapy as appropriate to the patient’s gender goals (unless hormones are not clinically indicated for the individual).

In addition, WPATH made specific recommendations regarding breast augmentation procedures:

Breast Augmentation

The WPATH guideline recommends MTF patients undergo feminizing hormone therapy for a minimum of 12 months prior to augmentation surgery and lists specific criteria for breast augmentation (implants/lipofilling).

The Endocrine Society

In 2009, the Endocrine Society in conjunction with European Society of Endocrinology, European Society for Pediatric Endocrinology, Lawson Wilkins Pediatric Endocrine Society, and World Professional Association, published the only evidence-based guidelines regarding the treatment of transsexual persons. The guideline employed transparent methods for evidence review and for rating the quality of evidence. All recommendations were based upon evidence which was rated to be low quality. The consortium made the following recommendations:

Diagnostic Procedure

1. We recommend that the diagnosis of gender identity disorder (GID) be made by a mental health professional (MHP). For children and adolescents, the MHP should also have training in child and adolescent developmental psychopathology.
2. Given the high rate of remission of GID after the onset of puberty, we recommend against a complete social role change and hormone treatment in prepubertal children with GID.
3. We recommend that physicians evaluate and ensure that applicants understand the reversible and irreversible effects of hormone suppression (e.g. GnRH analog treatment) and cross-sex hormone treatment before they start hormone treatment.
4. We recommend that all transsexual individuals be informed and counseled regarding options for fertility prior to initiation of puberty suppression in adolescents and prior to treatment with sex hormones of the desired sex in both adolescents and adults.

Treatment of Adolescents

These criteria do not imply or guarantee approval. Please check with your plan to ensure coverage. Preauthorization requirements are only valid for the month published. They may have changed from previous months and may change in future months.
1. We recommend that adolescents who fulfill eligibility and readiness criteria for gender reassignment initially undergo treatment to suppress pubertal development.

2. We recommend that suppression of pubertal hormones start when girls and boys first exhibit physical changes of puberty (confirmed by pubertal levels of estradiol and testosterone, respectively), but no earlier than Tanner stages 2–3.

3. We recommend that GnRH analogs be used to achieve suppression of pubertal hormones.

4. We suggest that pubertal development of the desired opposite sex be initiated at about the age of 16 year, using a gradually increasing dose schedule of cross-sex steroids.

5. We recommend referring hormone-treated adolescents for surgery when:
   a. the real-life experience (RLE) has resulted in a satisfactory social role change;
   b. the individual is satisfied about the hormonal effects; and
   c. the individual desires definitive surgical changes.

6. We suggest deferring surgery until the individual is at least 18 year old.

Hormonal Therapy for Transsexual Adults

1. We recommend that treating endocrinologists confirm the diagnostic criteria of GID or transsexualism and the eligibility and readiness criteria for the endocrine phase of gender transition.

2. We recommend that medical conditions that can be exacerbated by hormone depletion and cross-sex hormone treatment be evaluated and addressed prior to initiation of treatment.

3. We suggest that cross-sex hormone levels be maintained in the normal physiological range for the desired gender.

4. We suggest that endocrinologists review the onset and time course of physical changes induced by cross-sex hormone treatment.

Adverse Outcome Prevention and Long-term Care

1. We suggest regular clinical and laboratory monitoring every 3 months during the first year and then once or twice yearly.

2. We suggest monitoring prolactin levels in male-to-female (MTF) transsexual persons treated with estrogens.

3. We suggest that transsexual persons treated with hormones be evaluated for cardiovascular risk factors.

4. We suggest that bone mineral density (BMD) measurements be obtained if risk factors for osteoporosis exist, specifically in those who stop hormone therapy after gonadectomy.

5. We suggest that MTF transsexual persons who have no known increased risk of breast cancer follow breast screening guidelines recommended for biological women.

6. We suggest that MTF transsexual persons treated with estrogens follow screening guidelines for prostatic disease and prostate cancer recommended for biological men.

7. We suggest that female-to-male (FTM) transsexual persons evaluate the risks and benefits of including total hysterectomy and oophorectomy as part of sex reassignment surgery.

Surgery for Sex Reassignment

1. We recommend that transsexual persons consider genital sex reassignment surgery only after both the physician responsible for endocrine transition therapy and the MHP find surgery advisable.
2. We recommend that genital sex reassignment surgery be recommended only after completion of at least 1 year of consistent and compliant hormone treatment.
3. We recommend that the physician responsible for endocrine treatment medically clear transsexual individuals for sex reassignment surgery and collaborate with the surgeon regarding hormone use during and after surgery.

**American College of Obstetricians and Gynecology**

In 2011, American College of Obstetricians and Gynecology (ACOG) published a committee opinion regarding health care services for transgendered individuals. Although this guideline is not based in evidence, ACOG does make the following recommendations, “Obstetrician–gynecologists should be prepared to assist or refer transgender individuals for routine treatment and screening as well as hormonal and surgical therapies. Hormonal and surgical therapies for transgender patients may be requested, but should be managed in consultation with health care providers with expertise in specialized care and treatment of transgender patients.”

In addition, ACOG guidelines made specific recommendations regarding hormone therapy, surgery and screening for both female-to-male and male-to-female patients:

**Female-to-Male Transgender Individuals**

**Hormones**

Methyltestosterone injections every 2 weeks are usually sufficient to suppress menses and induce masculine secondary sex characteristics. Before receiving androgen therapy, patients should be screened for medical contraindications and have periodic laboratory testing, including hemoglobin and hematocrit to evaluate for polycythemia, liver function tests, and serum testosterone level assessments (goal is a mid-normal male range of 500 microgram/dL), while receiving the treatment.

**Surgery**

Hysterectomy, with or without salpingo-oophorectomy, is commonly part of the surgical process. An obstetrician–gynecologist who has no specialized expertise in transgender care may be asked to perform this surgery, and also may be consulted for routine reasons such as dysfunctional bleeding or pelvic pain. Reconstructive surgery should be performed by a urologist, gynecologist, plastic surgeon, or general surgeon who has specialized competence and training in this field.

**Screening**

Age-appropriate screening for breast cancer and cervical cancer should be continued unless mastectomy or removal of the cervix has occurred. For patients using androgen therapy who have not had a complete hysterectomy, there may be an increased risk of endometrial cancer and ovarian cancer.

**Male-to-Female Transgender Individuals**

**Hormones**

Estrogen therapy results in gynecomastia, reduced hair growth, redistribution of fat, and reduced testicular volume. All patients considering therapy should be screened for medical contraindications.
After surgery, doses of estradiol, 2–4 mg/d, or conjugated equine estrogen, 2.5 mg/d, are often sufficient to keep total testosterone levels to normal female levels of less than 25 ng/dL. Nonoral therapy also can be offered. It is recommended that male-to-female transgender patients receiving estrogen therapy have an annual prolactin level assessment and visual field examination to screen for prolactinoma.

**Surgery**

Surgery usually involves penile and testicular excision and the creation of a neovagina. Reported complications of surgery include vaginal and urethral stenosis, fistula formation, problems with remnants of erectile tissue, and pain. Vaginal dilation of the neovagina is required to maintain patency. Other surgical procedures that may be performed include breast implants and nongenital surgery, such as facial feminization surgery.

**Screening**

Age-appropriate screening for breast and prostate cancer is appropriate for male-to-female transgender patients. Opinion varies regarding the need for Pap testing in this population. In patients who have a neocervix created from the glans penis, routine cytologic examination of the neocervix may be indicated. The glands are more prone to cancerous changes than the skin of the penile shaft, and intraepithelial neoplasia of the glans is more likely to progress to invasive carcinoma than is intraepithelial neoplasia of the neocervix.

**Summary**

The research lacks well-designed studies comparing the safety and effectiveness of non-treatment for gender dysphoria with treatments such as hormone therapy and gender affirmation surgery. However, there are challenges in conducting large studies to evaluate existing treatments, and such studies are not expected in the near future. Although additional research is needed, the research has consistently suggested significant improvement in symptoms and overall quality of life in those who have received treatment for gender dysphoria. Therefore, treatment of gender dysphoria in transgender individuals may be considered medically necessary when specified policy criteria are met.

The World Professional Association for Transgender Health (WPATH) Standards of Care (SOC) for the Health of Transsexual, Transgender, and Gender Nonconforming Peoples describe reversible and irreversible interventions, and the ideal order and timing of these approaches. Surgery as an intervention is considered irreversible by WPATH. Therefore, reversal of gender affirmation surgery is considered not medically necessary as a treatment of gender dysphoria.

**REFERENCES**


5. Delegates, AMAHo. Resolution #114. American Medical Association House of Delegates. “Removing Barriers to Care for Transgender Patients” [cited; Available from:


**CROSS REFERENCES**

- *Endometrial Ablation*, Surgery, Policy No. 01
- *Cosmetic and Reconstructive Surgery*, Surgery, Policy No. 12
- *Reconstructive Breast Surgery/Mastopexy, and Management of Breast Implants*, Surgery, Policy No. 40
- *Reduction Mammoplasty*, Surgery, Policy No. 60
- *Autologous Fat Grafting to the Breast and Adipose-derived Stem Cells*, Surgery, Policy No. 182
- *AndroGel®, AndroGel Pump® topical testosterone gel 1% and 1.62%*, Medication Policy Manual, Policy No. dru360
- *finasteride 1 mg (generic, Propecia®)*, Medication Policy Manual, Policy No. dru474

<table>
<thead>
<tr>
<th>CODES</th>
<th>NUMBER</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>11970</td>
<td>Replacement of tissue expander with permanent prosthesis</td>
</tr>
<tr>
<td></td>
<td>11971</td>
<td>Removal of tissue expander(s) without insertion of prosthesis</td>
</tr>
<tr>
<td></td>
<td>15775</td>
<td>Punch graft for hair transplant; 1 to 15 punch grafts</td>
</tr>
<tr>
<td></td>
<td>15776</td>
<td>Punch graft for hair transplant; more than 15 punch grafts</td>
</tr>
<tr>
<td></td>
<td>17380</td>
<td>Electrolysis epilation, each 30 minutes</td>
</tr>
<tr>
<td>CODES</td>
<td>NUMBER</td>
<td>DESCRIPTION</td>
</tr>
<tr>
<td>-------</td>
<td>--------</td>
<td>-------------</td>
</tr>
<tr>
<td></td>
<td>19303</td>
<td>Mastectomy, simple, complete</td>
</tr>
<tr>
<td></td>
<td>19304</td>
<td>Mastectomy, subcutaneous</td>
</tr>
<tr>
<td></td>
<td>19316</td>
<td>Mastopexy</td>
</tr>
<tr>
<td></td>
<td>19318</td>
<td>Reduction mammaplasty</td>
</tr>
<tr>
<td></td>
<td>19324</td>
<td>Mammaplasty, augmentation; without prosthetic implant</td>
</tr>
<tr>
<td></td>
<td>19325</td>
<td>Mammaplasty, augmentation; with prosthetic implant</td>
</tr>
<tr>
<td></td>
<td>19350</td>
<td>Nipple/areola reconstruction</td>
</tr>
<tr>
<td></td>
<td>53400</td>
<td>Urethroplasty; first stage, for fistula, diverticulum, or stricture (eg, Johannsen type)</td>
</tr>
<tr>
<td></td>
<td>53405</td>
<td>Urethroplasty; second stage (formation of urethra), including urinary diversion</td>
</tr>
<tr>
<td></td>
<td>53410</td>
<td>Urethroplasty, 1-stage reconstruction of male anterior urethra</td>
</tr>
<tr>
<td></td>
<td>53415</td>
<td>Urethroplasty, transpubic or perineal, 1-stage, for reconstruction or repair of prostatic or membranous urethra</td>
</tr>
<tr>
<td></td>
<td>53420</td>
<td>Urethroplasty, 2-stage reconstruction or repair of prostatic or membranous urethra; first stage</td>
</tr>
<tr>
<td></td>
<td>53425</td>
<td>Urethroplasty, 2-stage reconstruction or repair of prostatic or membranous urethra; second stage</td>
</tr>
<tr>
<td></td>
<td>53430</td>
<td>Urethroplasty, reconstruction of female urethra</td>
</tr>
<tr>
<td></td>
<td>54125</td>
<td>Amputation of penis; complete (Penectomy)</td>
</tr>
<tr>
<td></td>
<td>54520</td>
<td>Orchiectomy, simple (including subcapsular), with or without testicular prosthesis, scrotal or inguinal approach</td>
</tr>
<tr>
<td></td>
<td>54660</td>
<td>Insertion of testicular prosthesis</td>
</tr>
<tr>
<td></td>
<td>54690</td>
<td>Laparoscopy, surgical; orchiectomy</td>
</tr>
<tr>
<td></td>
<td>55175</td>
<td>Scrotoplasty; simple</td>
</tr>
<tr>
<td></td>
<td>55180</td>
<td>Scrotoplasty; complicated</td>
</tr>
<tr>
<td></td>
<td>55899</td>
<td>Phallic reconstruction/Phalloplasty (Unlisted procedure, male genital system)</td>
</tr>
<tr>
<td></td>
<td>55970</td>
<td>intersex surgery; male to female</td>
</tr>
<tr>
<td>CODES</td>
<td>NUMBER</td>
<td>DESCRIPTION</td>
</tr>
<tr>
<td>-------</td>
<td>--------</td>
<td>-------------</td>
</tr>
<tr>
<td>55980</td>
<td>Plastic repair of introitus</td>
<td></td>
</tr>
<tr>
<td>56800</td>
<td>Clitoroplasty for intersex state</td>
<td></td>
</tr>
<tr>
<td>56805</td>
<td>Vaginectomy, partial removal of vaginal wall</td>
<td></td>
</tr>
<tr>
<td>57106</td>
<td>Vaginectomy, complete removal of vaginal wall;</td>
<td></td>
</tr>
<tr>
<td>57291</td>
<td>Construction of artificial vagina; without graft</td>
<td></td>
</tr>
<tr>
<td>57292</td>
<td>Construction of artificial vagina; with graft</td>
<td></td>
</tr>
<tr>
<td>57295</td>
<td>Revision (including removal) of prosthetic vaginal graft; vaginal approach</td>
<td></td>
</tr>
<tr>
<td>57296</td>
<td>Revision (including removal) of prosthetic vaginal graft; open abdominal approach</td>
<td></td>
</tr>
<tr>
<td>57335</td>
<td>Vaginoplasty for intersex state - the physician uses various plastic surgery techniques to correct a small, underdeveloped vagina due to the overproduction of male hormones</td>
<td></td>
</tr>
<tr>
<td>57426</td>
<td>Revision (including removal) of prosthetic vaginal graft, laparoscopic approach</td>
<td></td>
</tr>
<tr>
<td>58150</td>
<td>Total abdominal hysterectomy (corpus and cervix), with or without removal of tube(s), with or without removal of ovary(s)</td>
<td></td>
</tr>
<tr>
<td>58180</td>
<td>Supracervical abdominal hysterectomy (subtotal hysterectomy), with or without removal of tube(s), with or without removal of ovary(s)</td>
<td></td>
</tr>
<tr>
<td>58260</td>
<td>Vaginal hysterectomy, for uterus 250 g or less</td>
<td></td>
</tr>
<tr>
<td>58262</td>
<td>Vaginal hysterectomy, for uterus 250 g or less; with removal of tube(s), and/or ovary(s)</td>
<td></td>
</tr>
<tr>
<td>58275</td>
<td>Vaginal hysterectomy, with total or partial vaginectomy;</td>
<td></td>
</tr>
<tr>
<td>58290</td>
<td>Vaginal hysterectomy, for uterus greater than 250 g</td>
<td></td>
</tr>
<tr>
<td>58291</td>
<td>Vaginal hysterectomy, for uterus greater than 250 g; with removal of tube(s) and/or ovary(s)</td>
<td></td>
</tr>
<tr>
<td>58541</td>
<td>Laparoscopy, surgical, supracervical hysterectomy, for uterus 250 g or less</td>
<td></td>
</tr>
<tr>
<td>58542</td>
<td>Laparoscopy, surgical, supracervical hysterectomy, for uterus 250 g or less; with removal of tube(s) and/or ovary(s)</td>
<td></td>
</tr>
<tr>
<td>CODES</td>
<td>NUMBER</td>
<td>DESCRIPTION</td>
</tr>
<tr>
<td>-------</td>
<td>--------</td>
<td>-------------</td>
</tr>
<tr>
<td>57295</td>
<td></td>
<td>Revision (including removal) of prosthetic vaginal graft; vaginal approach</td>
</tr>
<tr>
<td>58543</td>
<td></td>
<td>Laparoscopy, surgical, supracervical hysterectomy, for uterus greater than 250 g</td>
</tr>
<tr>
<td>58544</td>
<td></td>
<td>Laparoscopy, surgical, supracervical hysterectomy, for uterus greater than 250 g; with removal of tube(s) and/or ovary(s)</td>
</tr>
<tr>
<td>58550</td>
<td></td>
<td>Laparoscopy, surgical, with vaginal hysterectomy, for uterus 250 g or less</td>
</tr>
<tr>
<td>58552</td>
<td></td>
<td>Laparoscopy, surgical, with vaginal hysterectomy, for uterus 250 g or less; with removal of tube(s) and/or ovary(s)</td>
</tr>
<tr>
<td>58553</td>
<td></td>
<td>Laparoscopy, surgical, with vaginal hysterectomy, for uterus greater than 250 g</td>
</tr>
<tr>
<td>58554</td>
<td></td>
<td>Laparoscopy, surgical, with vaginal hysterectomy, for uterus greater than 250 g; with removal of tube(s) and/or ovary(s)</td>
</tr>
<tr>
<td>58570</td>
<td></td>
<td>Laparoscopy, surgical, with total hysterectomy, for uterus 250 g or less</td>
</tr>
<tr>
<td>58571</td>
<td></td>
<td>Laparoscopy, surgical, with total hysterectomy, for uterus 250 g or less; with removal of tube(s) and/or ovary(s)</td>
</tr>
<tr>
<td>58572</td>
<td></td>
<td>Laparoscopy, surgical, with total hysterectomy, for uterus greater than 250 g</td>
</tr>
<tr>
<td>58573</td>
<td></td>
<td>Laparoscopy, surgical, with total hysterectomy, for uterus greater than 250 g; with removal of tube(s) and/or ovary(s)</td>
</tr>
<tr>
<td>58720</td>
<td></td>
<td>Salpingo-oophorectomy, complete or partial, unilateral or bilateral (separate procedure)</td>
</tr>
</tbody>
</table>

HCPCS

<table>
<thead>
<tr>
<th>CODES</th>
<th>NUMBER</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1813</td>
<td></td>
<td>Prosthesis, penile, inflatable</td>
</tr>
<tr>
<td>L8039</td>
<td></td>
<td>Breast prosthesis, not otherwise specified</td>
</tr>
<tr>
<td>L8600</td>
<td></td>
<td>Implantable breast prosthesis, silicone or equal</td>
</tr>
</tbody>
</table>

APPENDIX 1

**Gender Dysphoria**[23]

Gender dysphoria is defined by the Diagnostic and Statistical Manual of Mental Disorders DSM-5V as:

*Gender Dysphoria in Children:*
A. A marked incongruence between one's experienced/expressed gender and assigned gender, of at least 6 months duration, as manifested by at least six of the following (one of which must be Criterion A1):

1. A strong desire to be of the other gender or an insistence that one is the other gender (or some alternative gender, different from one's assigned gender)
2. In boys (assigned gender), a strong preference for cross dressing or simulating female attire; or in girls (assigned gender), a strong preference for wearing only typical masculine clothing and a strong resistance to wearing of typical feminine clothing.
3. A strong preference for cross-gender roles in make-believe play of fantasy play.
4. A strong preference for toys, games, or activities stereotypically used or engaged in by the other gender.
5. A strong preference for playmates of the other gender.
6. In boys (assigned gender), a strong rejection of typically masculine toys, games and activities and a strong avoidance of rough and tumble play; or in girls (assigned gender), a strong rejection of typically feminine toys, games and activities.
7. A strong dislike of one's sexual anatomy.
8. A strong desire for the primary and/or secondary sex characteristics that match one's experienced gender.

B. The condition is associated with clinically significant distress or impairment in social, school, or other important areas of functioning.

Specify if:

With a disorder of sex development (e.g., a congenital adrenogenital disorder such as 2.55.2 [E25.0] congenital adrenal hyperplasia or 259.0 [E34.50] androgen insensitivity syndrome)

Coding note: Code the disorder of sex development as well as gender dysphoria.

Gender Dysphoria in Adolescents and Adults:

A. A marked incongruence between one's experienced/expressed gender and assigned gender, of at least 6 months duration, as manifested by at least two of the following:

1. A marked incongruence between one's experienced/expressed gender and primary and/or secondary sex characteristics (on in young adolescents, the anticipated secondary sex characteristics).
2. A strong desire to be rid of one's primary and/or secondary sex characteristics because of a marked incongruence with one's experienced/expressed gender (on in young adolescents, a desire to prevent the development of the anticipated secondary sex characteristics.)
3. A strong desire for the primary and/or secondary sex characteristics of the other gender.
4. A strong desire to be of the other gender) or some alternative gender different from one's assigned gender).
5. A strong desire to be treated as the other gender (or some alternative gender different from one's assigned gender).
6. A strong conviction that one has the typical feelings and reactions of the other gender (or some alternative gender different from one's assigned gender).
APPENDIX 1

B. The condition is associated with clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Specify if:

With a disorder of sex development (e.g., a congenital adrenogenital disorder such as 2.55.2 [E25.0] congenital adrenal hyperplasia or 259.0 [E34.50] androgen insensitivity syndrome)

Coding note: Code the disorder of sex development as well as gender dysphoria.

Specify if:

Post transition: The individual has transitioned to full-time living in the desired gender (with or without legalization of gender change) and has undergone (or is preparing to have) at least one cross-sex medical procedure or treatment regimen- namely regular cross-sex treatment or gender reassignment surgery confirming the desired gender (e.g., appendectomy, vaginoplasty in the natal male; mastectomy or phalloplasty in the natal female).”
SPINAL INJECTION ADDITIONAL INFORMATION FORM

Note: This form must be completed and submitted at the time of claims submission to ensure timely and accurate claims processing. If this information is not submitted with the claim(s), services will be denied until the information is received.

Fax completed form to: 1 (877) 357-3418 Questions or Assistance: 1 (888) 849-3681

<table>
<thead>
<tr>
<th>Patient Information:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Last Name</td>
</tr>
<tr>
<td>UMP Identification Number</td>
</tr>
<tr>
<td>Date(s) of Service</td>
</tr>
<tr>
<td>Procedure Codes</td>
</tr>
</tbody>
</table>

Therapeutic Cervical, Thoracic and Lumbar Epidural Injections and Sacroiliac Joint Injections are a covered benefit for the treatment of chronic pain. Go to www.hta.hca.wa.gov to view the entire Health Technology Assessment.

Limitations of Coverage:
Therapeutic Epidural Injections in the lumbar or cervical-thoracic spine for chronic pain are a covered benefit when all of the following conditions are met:
- For treatment of radicular pain
- Performed with fluoroscopic or CT guidance
- After failure of conservative therapy
- No more than two without clinically meaningful improvement in pain and function, and
- Maximum of 3 in 6 months

Therapeutic Sacroiliac Joint Injections for chronic pain is a covered benefit when all of the following conditions are met:
- Performed with fluoroscopic or CT guidance
- After failure of conservative therapy, and
- No more than one without clinically meaningful improvement in pain and function, subject to plan review

Non-Covered Indications:
Therapeutic Medial Branch Nerve injections, Intradiscal injections and Intraarticular Facet injections are not a covered benefit.

The following services are not addressed by HTA coverage policy: diagnostic spinal injections and radiofrequency nerve ablations. Regence reserves the right to audit these claims and request medical records.

I certify that these services, for the above UMP patient, do not violate the guidelines set forth in the Health Technology Assessment for Spinal Injections and that diagnostic injections are not related to and/or used as a means to subsequently perform non-covered therapeutic injections inclusive of Therapeutic Medial Branch Nerve injections, Intradiscal injections and Intraarticular Facet injections.

Provider Signature __________________________ Date __________________________

Provider Name (please print) __________________________ Office Phone Number __________________________