Health Technology Clinical Committee Findings and Coverage Decision

Topic: Bone Growth Stimulation
Meeting Date: August 28th, 2009
Final Adoption: October 30th, 2009

Number and Coverage Topic

20090828B – Bone Growth Stimulation

HTCC Coverage Determination

Bone Growth Stimulation is a **covered benefit with conditions** consistent with the criteria identified in the reimbursement determination**.**

HTCC Reimbursement Determination

❖ Limitations of Coverage

Bone Growth Stimulation coverage is consistent with Medicare's national coverage decision plus ultrasonic stimulation for treatment of fresh fractures that are at high risk of non-union. For BGS used as an adjunct to another treatment, the primary treatment must also be covered.

Medicare Covered conditions include:

- *Electrical Noninvasive and Invasive Stimulator device is covered only for the following indications: (a)* Nonunion of long bone fractures (3 or more months ceased healing, 2 radiographs minimum 90 days apart); (b) Failed fusion, where a minimum of 9 months has elapsed since the last surgery; or adjunct to fusion for patients with a previously failed fusion and high risk of psuedarthrosis at the same site or for multiple level fusion involving 3 or more vertebrae (e.g.L3-L5, L4-S1); and (c) Congenital psuedarthrosis (noninvasive only).
- *Ultrasonic stimulator: (a)* Nonunion confirmed by 2 radiographs minimum 90 days apart and physician statement of no clinical evidence of fracture healing.

❖ Non-Covered Indicators

- Nonunion of skull, vertebrae or tumor related
- Ultrasonic stimulator – delayed fractures and concurrent use with other noninvasive stimulator.

❖ Agency Contact Information

Agency	Contact Phone Number
Labor and Industries	1-800-547-8367
Public Employees Health Plan	1-800-762-6004
Health and Recovery Services Administration	1-800-562-3022

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Health Technology Background

The Bone Growth Stimulator topic was selected and published in December 2008 to undergo an evidence review process. Bone fractures are a common musculoskeletal injury with 7.9 million occurring in the US annually. Majority of fractures heal without complications following standard nonsurgical or surgical therapy, healing is delayed or impaired in 5% to 10% of cases. Delayed healing is associated with longer recovery, reduction in quality of life and function, and pain. There is no standard definition of nonunion; FDA considers a nonunion to be established "when a minimum of 9 months has elapsed since injury and the fracture site shows no visibly progressive signs of healing for minimum of 3 months." There are variations in the clinical and radiographic findings used to diagnose nonunion. Bone union is also a potential concern in patients who undergo joint fusion surgery and in patients with fresh fractures who are at risk of delayed or nonunion. Lifestyle modification (smoking, obesity, alcoholism) and infection control are important. Clinical Theory: bone healing requires stability and blood supply. Clinical studies demonstrate that bone healing is associated with electrical potentials (appropriate blood flow) at the site.

BGS attempts to harness the electrical-biological link through the use of applied electrical fields to promote healing but link between biophysical stimulation and the cellular responses is not fully understood. BGS uses either electrical stimulation or low intensity pulsed ultrasound to induce bone growth and promote fracture healing. Invasive BGS are surgically implanted; non-invasive or worn externally. BGS are used as an adjunctive treatment with other fracture healing treatments including immobilization; surgical techniques; bone grafts; treatment of infection or other causes of non-union; and orthobiologics.

In July 2009, the HTA posted a draft and then followed with a final report from a contracted research organization that reviewed publicly submitted information; searched, summarized, and evaluated trials, articles, and other evidence about the topic. The comprehensive, public and peer reviewed, Bone Growth Stimulators report is 134 pages, and identified a relatively large amount of literature.

The committee received public comments on the draft findings and decision document from October 12th thru 26th, 2009, and at the August 28th public meeting. The committee has incorporated those public comments in the finalization of this decision.

An independent group of eleven clinicians who practice medicine locally meet in public to decide whether state agencies should pay for the health technology based on whether the evidence report and other presented information shows it is safe, effective and has value. The committee met on August 28th, reviewed the report, including peer and public feedback, and heard public and agency comments. Meeting minutes detailing the discussion are available through the HTA program or online at http://www.hta.hca.wa.gov under the committee section.

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Committee Findings

Having considered the evidence based technology assessment report and the written and oral comments, the committee identified the following key factors and health outcomes, and evidence related to those health outcomes and key factors:

1. Evidence availability and technology features

The committee concludes that the best available evidence on bone growth stimulators has been collected and summarized. The evidence is comprehensive and robust:

- Bone Growth Stimulators. The evidence based technology assessment report identified previously completed Hayes Medical Technology Directory Reports published in 2003 and 2004 and primary studies published more recently if they were not included in the selected systematic reviews and if they met sample size thresholds and/or provided information not available from the systematic reviews.

- Key data limitations included the overall available body of evidence was limited to small sample sizes, few studies per indication, no RCT's for some indications, substantial loss to follow up, difficulty separating treatment effect of stimulation from placebo effect or other effects where multiple interventions used, and no assessment of pain or functional outcomes in most studies. Studies of application to fresh fractures were further weakened by the use of radiographic fusion as the only measure of healing. The appropriate clinical and patient oriented endpoints are not clearly identified or agreed upon; the number of surgical interventions avoided is a central concern but not adequately reported.

- Ultrasonic stimulators: had two systematic reviews, a Hayes Medical Technology Directory Report (2003), and a systematic review and meta-analysis from the peer-reviewed literature. The Hayes report included three RCTs and two retrospective case series studies published in October 2003 or earlier. Five primary studies -- these five studies consisted of three prospective, uncontrolled studies; one randomized, placebo-controlled study that provided long-term (18 month) follow-up data; and one retrospective study with multiple regression analysis to evaluate prognostic factors.

- Electrical Stimulation, Invasive and semi-invasive -- A Hayes Medical Technology Directory Report (2004a) was the only systematic review. This report included two RCTs, eight nonrandomized comparative studies, and five case series studies published in February 2004 or earlier and three primary studies. A total of 3,683 patients were involved across all studies, with sample sizes ranging from 28 to 1,686.

- Electrical Stimulation, Noninvasive -- A Hayes Medical Technology Directory Report (2004b) and a systematic review from the peer-reviewed literature. The report reviewed 15 studies, including 10 RCTs and five primary studies. A total of 2,130 patients were involved across all studies, with sample sizes ranging from 16 to 201 in most studies, with one study having a sample size of 1,098. Eight of the 15 studies investigated pulsed electromagnetic field (PEMF) stimulation, 5 investigated capacitive coupling, and 2 investigated combined magnetic field (CMF) stimulation. The review by Mollon and colleagues included 11 RCTs. Four selected trails, which were published in 1996 or earlier, were not reviewed in the Hayes report. The

Hayes report included some observational studies that were excluded by Mollon, as well as three RCTs that were not included by Mollon.

2. Is the technology safe?

The committee discussed multiple key factors and health outcomes that were important for consideration in their overall decision on whether the technology is safe. Summary of committee considerations follows.

- Mortality: Device related complications from DCES (implanted) were not found, though general and surgical complications do occur, the relationship to the device is unknown, as well as an long term implications for elderly or adolescents. Serious device related complications were not reported by any of the large number of studies in non-invasive technology and though quantity of long term date is modest, the literature does not suggest suspicion of long term adverse effects.
- Morbidity: For external devices, evidence does not demonstrate serious complications; implanted devices addressed above.
- Overall: the committee agreed that no evidence of mortality or serious adverse effects risk for external BGS exist; however, for implanted BGS devices an increased risk of infection, by virtue of additional devices is likely, though additional harm risk is limited. No data separately reported on stimulator related infection.
- Special populations: no children or safety data was presented and committee was concerned that the generalizability of safety data would not extend to patients that are not yet skeletally mature.

3. Is the technology effective?

The committee discussed multiple key factors and health outcomes that were important for consideration in their overall decision on whether the technology is effective. Summary of committee considerations follows.

Lumbar Spinal Fusion –

- The committee concluded that of the four studies on lumbar fusion, none of them selected high risk patients. All four reported high results. Sample sizes ranged from 179 to 201 patients; fusion success in the controlled group; 13% to 30% absolute difference in healing; follow-up ranging from 9 months to 1 year; and included all initial fusion, including smokers and non-smokers. In controlled group, healing rates occurred in the range of 43% to 86% (successfully fused). In the stimulated group, healing rates occurred in the range of 64% to 91%. Below is a breakdown of all the systematic studies from the technology evidence report the committee reviewed and discussed:
  - Mooney, 1990 – in a moderate size, multicenter, randomized trial, consistent users of pulsed electromagnetic field (≥8 hrs / day, later set to 2 hrs / day) had significantly higher success rate of interbody spinal fusion than patients in placebo group (92% and 67%, respectively). Inconsistent pulsed electromagnetic field users achieved success rate similar to patients in placebo group.
  - Jenis, 2000 – a small, randomized trial compared the effect of adjunctive noninvasive pulsed electromagnetic field and invasive direct current stimulation on augmentation of instrumented lumbar spinal fusion. Neither

form of electrical stimulation resulted in improved fusion rates or clinical outcome (pain, function) in instrumented lumbar arthrodesis. However, there was an insignificant trend toward increased fusion mass bone mineral density in both electrical stimulation groups relative to surgery-only group.
    - Goodwin, 1999 – in 1 moderate-size RCT, capacitive coupling was used adjunctively to primary lumbar spine fusion. The overall success rate (both clinical and radiographic) was 85% for the active group compared with 65% for the placebo group, a statistically significant difference. When clinical outcomes were assessed separately, between group difference favored stimulation.
    - Linovitz, 2002 – in 1 RCT with 201 patients with noninstrumented posterolateral fusions, adjunctive use of combined electromagnetic field electrical stimulation significantly increased the 9-month radiographic fusion success rates in the overall (64% vs 43%). In addition, there was an acceleration of the healing process.
- Invasive stimulation (referenced as Table 3 & 4 in the report) – 2 RCTs reported conflicting results. Other studies had historical or conflicting controls. High risk patients. 81% in the stimulated and 54% in the un-stimulated – 63 patients total in this trial. The committee concluded that mostly positive large evidence exists for non-invasive stimulation; however, conflicting data and lack of evidence exists for invasive stimulation. Below is the study the committee reviewed and discussed from the technology evidence report:
    - Kane, 1988 – 1 RCT reported successful spinal fusion in 81% of high-risk patients who had direct current electrical stimulation as adjunct to noninstrumented spinal fusion, compared with only 54% of high-risk patients who underwent surgery alone (63 patients met inclusion criteria, 59 available for follow-up [9.4%]).
- The committee discussed and read the 2005 CMS coverage decision. The committee concluded that the CMS coverage decision included spinal fusion and revision surgery (external or adjunct); although, in sufficient data was presented on revision surgery.
- The committee concluded that some RCT data exists for lumbar fusion; however no data exists on revision surgery (or failed surgery). Effectiveness level of evidence is moderate, at best.

Fractures –

- Non-union fractures versus delayed union – committee agreed that overall low quality evidence was presented (referenced as Table 5 and 6 in the report) – consistent results from RCTs in benefits. Below the studies the committee reviewed and discussed from the technology evidence report are expressed below:
    - Sharrard study, 1990 – 1 small RCT; nonunion or delayed union fractures (tibial fractures); 45 strictly selected patients total; actively stimulated group; radiographic assessment found significant differences in healing in favor of pulsed electromagnetic field group (50% of patients with some radiographic evidence of healing, pulsed electromagnetic field; 8% control); double-blinded; no significant differences between groups on clinician assessment of pain or movement.
    - Simonis study, 2003 – in 1 RCT of pulsed electromagnetic field stimulation for established tibial nonunions, radiographic and clinical evaluation showed

that 89% of the pulsed electromagnetic field group fractures united versus only 50% of placebo group. Pulsed electromagnetic field stimulation was associated with significant increase in rate of union, but only before adjustment for smoking.
    - Scott and King study, 1994 – in a small RCT of 21 patients with established non-unions of the tibia, ulnar, or femur, 60% of actively managed patients and no controls achieved union by radiographic and clinical criteria, a statistically significant difference.
    - Molan, 2008 – meta-analysis did not find any statistically significant treatment (or therapy) effect of electromagnetic stimulation for improving radiographic outcomes for nonunion or delayed union fractures, fresh fractures, or tibial osteotomy. Electromagnetic stimulation treatment (or therapy) generally did not improve clinical outcomes, although 1 of 4 studies noted reduction of pain in a subgroup of patients. Evidence regarding the effect of electromagnetic stimulation on bone densitometry measures varied both across and within studies.
    - Punt, 2008 – retrospective, before-and-after, blinded analysis of pulsed electromagnetic field for salvage treatment (or therapy) of nonunion of traumatic fractures. Compared with clinical conditions at the time of initiation of bone growth stimulation, patients with a diagnosis of nonunion experienced substantial clinical improvement and radiographic evidence of healing. Overall clinical and radiographic success was similar for long bone-fracture and nonlong bone fracture.
- Committee agreed that efficacy evidence identified in the technology assessment report was of overall low quality and insufficient.

Ultrasound –

- Committee reviewed and discussed two low-intensity pulsed ultrasonography RCT systematic reviews that assessed ultrasound bone growth stimulators. Systematic reviews assessed the effectiveness and safety of ultrasound bone growth stimulators used alone or in combination with another treatment (or therapy) for fresh, delayed union, and nonunion fractures. Below is a description of both of the RCTs reviewed and discussed by the committee from the technology evidence report:
    - Heckman, 1994 & Kristiansen, 1997 – Data from 2 RCTs, 96 patients (Heckman) and 83 patients (Kristiansen), indicate that low-intensity ultrasound accelerates healing of fresh tibial shaft and distal radius fractures and decreases incidence of nonunion in tibial fractures in selected patients.
    - Non-operative versus operative: Busse, 2009 – 6 reviewed studies with measures of radiographic healing; low-intensity pulsed ultrasonography appears to accelerate healing time by 33.6%. Meta-analysis by type of fracture indicated a significant reduction in healing time with low-intensity pulsed ultrasonography treatment (or therapy) for non-operative management fresh fractures and bone grafting for nonunions, but not for operative management fresh fractures. However, meta-analysis did not find a significant effect of low-intensity pulsed ultrasonography treatment (or therapy) on functional recovery for any type of fracture, including non-operative management fresh fractures, non-operative management stress fractures, or operative management fresh fractures.

- Committee agreed that efficacy evidence identified in the technology assessment report for ultrasound was also of overall low quality, though it included the highest level of evidence of the different stimulator types.

4. Is the technology cost-effective?

The committee discussed multiple key factors that were important for consideration in their overall decision on whether the technology has value and is cost-effective. Summary of committee considerations follows.

- The committee discussed the evidence report cost information. Articles on cost were available for ultrasound bone growth stimulation for fresh fractures. No economic evaluations for electrical stimulation for the treatment of bone fractures were identified in the literature search. One limitation to the economic articles is that there is low quality effectiveness information.
- The Hayes (2003) review included a 2001 systematic review that evaluated the cost-effectiveness of low-intensity ultrasound (LIPUS) to treat fresh tibia, radius, and scaphoid fractures. The analysis indicated that the total cost of treatment per patient, incorporating both direct and indirect costs, was higher for ultrasound treatment than for standard non-operative treatment for all three fracture types. Treating fresh fractures with ultrasound was far less cost effective than interventions for other common health problems. At the time of the review, there was insufficient evidence regarding the effectiveness of ultrasound treatment for delayed and nonunion fractures to permit a cost-effectiveness analysis for these indications.
- In 2005, Busse, et al. conducted a burden of illness (BOI) study from the perspective of both local government (the Ontario Ministry of Health and Long-Term Care) and society, and concluded that reamed intramedullary nailing was most cost effective. Ultrasound with casting was judged possibly economical, but additional clinical effectiveness and actual cost information was needed.
- Washington agency cost data ranged from $2,800 for ultrasound to $3,700 for electrical non-invasive.

5. <u>Medicare Decision and Expert Treatment Guidelines</u>

Committee reviewed and discussed the Medicare coverage decision and expert guidelines as identified and reported in the technology assessment report.

- Centers for Medicare and Medicaid Services (2005) –
  - *Electrical Noninvasive and Invasive Stimulator device is covered only for the following indications:*
    a. Nonunion of long bone fractures (3 or more months ceased healing, 2 radiographs minimum 90 days apart);
    b. Failed fusion, where a minimum of 9 months has elapsed since the last surgery; or adjunct to fusion for patients with a previously failed fusion and high risk of psuedarthrosis at the same site or for multiple level fusion involving 3 or more vertebrae (e.g., L3-L5, L4-S1); and
    c. Congenital psuedarthrosis (noninvasive only).
  - *Ultrasonic stimulator:*
    a. Nonunion confirmed by 2 radiographs minimum 90 days apart and physician statement of no clinical evidence of fracture healing.

- *Non Covered Indications:*
  a. Nonunion of skull, vertebrae or tumor related;
  b. Ultrasonic stimulator – fresh, delayed fractures and concurrent use with other noninvasive stimulator.

- Guidelines – two guidelines were stated in the technology assessment evidence report, those included:
  - American Association of Neurological Surgeons / Congress of Neurological Surgeons (AANS / CNS), 2009, guideline regarding BGS and lumbar fusion – Treatment standard: Insufficient evidence. Treatment guideline: electrical stimulation recommended as an adjunct to spinal fusion for patients at high risk for arthrodesis; PMEF stimulation recommended as adjunct to increase fusion rates in similar patients treated with lumbar interbody fusion procedures.
  - Agency for Healthcare Research and Quality (AHRQ), 2005, evidence review for CMS – Overall evidence quality low; treatment effect of device could not be distinguished from possible therapeutic effects of concurrent treatments.

Committee Decision

Based on the deliberations of key health outcomes, the committee decided that it had the most complete information: a comprehensive and current evidence report, public comments, input from a clinical expert, and agency and state utilization information. The committee considered all the evidence and gave greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable.

The committee concluded unanimously that the current evidence on Bone Growth Stimulators demonstrates that there is sufficient evidence to indicate that the bone growth stimulators are equally safe as alternatives. A majority found that the evidence on Bone Growth Stimulators for all stimulator types and all bone types is unproven as to clinical effectiveness and cost effectiveness based on overall low quality evidence for each indication and stimulator type, though ultrasound for fresh fractures did have the strongest low level of supporting evidence. Key data limitations included the overall available body of evidence was limited to small sample sizes, few studies per indication, no RCT's for some indications, substantial loss to follow up, difficulty separating treatment effect of stimulation from placebo effect or other effects where multiple interventions used, and no assessment of pain or functional outcomes in most studies. Studies of application to fresh fractures were further weakened by the use of radiographic fusion as the only measure of healing. The appropriate clinical and patient oriented endpoints are not clearly identified or agreed upon and the number of surgical interventions avoided is a central question, but not adequately reported.

However, a National Medicare Coverage Decision exists that is based on CMS' evidence review from 2005 and the committee acknowledged its responsibility to be consistent with Medicare, unless based on its review of the systematic assessment, substantial evidence exists about safety, efficacy, or cost-effectiveness to support a contrary determination. The committee found that it did not have significant evidence to support a contrary determination because evidence about the effectiveness and cost-effectiveness are

unproven and thus may support CMS' decision, or ultimately when additional evidence is available, may not.

Given equipoise, a finding of equivalent safety, and a recent and evidence based Medicare national decision, the committee voted to cover Bone Growth Stimulators with conditions equivalent to the national Medicare coverage decision, with one exception. Ultrasonic stimulation for fresh fractures is specifically non-covered in Medicare's policy, however the committee found that the technology assessment report identified the highest level of evidence (though still unproven overall) for this indication and stimulation type, and therefore there is sufficient evidence to include this indication in the covered conditions.

Based on these findings, the committee unanimously voted 9 to 0 to cover Bone Growth Stimulators, with conditions: conditions for BGS treatment are limited to those in the Medicare National Coverage Decision as of August 2009, with the addition of ultrasonic stimulation for fresh fractures at high risk of non-union.
Medicare National Coverage is summarized below:

- *Electrical Noninvasive and Invasive Stimulator device is covered only for the following indications:*
  - Nonunion of long bone fractures (3 or more months ceased healing, minimum of 2 radiographs separated by minimum 90 days prior to start of treatment);
  - Failed fusion, where a minimum of 9 months has elapsed since the last surgery; or adjunct to fusion for patients with a previously failed fusion and high risk of psuedarthrosis at the same site or for multiple level fusion involving 3 or more vertebrae (e.g., L3-L5, L4-S1); and
  - Congenital psuedarthrosis (noninvasive only).
- *Ultrasonic stimulator:*
  - Nonunion fractures confirmed by 2 sets of radiographs minimum 90 days apart prior to start of treatment with written physician interpretation of no clinically significant evidence of fracture healing.
- Non Covered Indications:
  - Nonunion of skull, vertebrae or tumor related;
  - Ultrasonic stimulators may not be used concurrently with other non-invasive osteogenic devices
  - Ultrasonic stimulators for delayed fractures

Note: The committee voted 7-2 regarding the specific coverage conditions including the Medicare National Coverage guidelines plus ultrasound for fresh fractures.

Health Technology Clinical Committee Authority

Washington State's legislature believes it is important to use a scientific based, clinician centered approach for difficult and important health care benefit decisions. Pursuant to chapter 70.14 RCW, the legislature has directed the Washington State Health Care Authority, through its Health Technology Assessment program to engage in a process for evaluation process that gathers and assesses the quality of the latest medical evidence using a scientific research company and takes public input at all stages. Pursuant to RCW 70.14.110 a Health Technology Clinical Committee (HTCC) composed of eleven independent health care professionals reviews all the information and renders a decision at an open public meeting. The Washington State Health Technology Clinical Committee

(HTCC), determines how selected health technologies are covered by several state agencies. RCW 70.14.080-140. These technologies may include medical or surgical devices and procedures, medical equipment, and diagnostic tests. HTCC bases their decisions on evidence of the technology's safety, efficacy, and cost effectiveness. Participating state agencies are required to comply with the decisions of the HTCC. HTCC decisions may be re-reviewed at the determination of the HCA Administrator.