Uniform Medical Plan coverage limits

Updates effective 12/1/2019

The benefit coverage limits listed below apply to these UMP plans:

- Uniform Medical Plan (UMP) Classic (PEBB)
- UMP Consumer-Directed Health Plan (UMP CDHP) (PEBB)
- UMP Plus–Puget Sound High Value Network (UMP Plus–PSHVN) (PEBB)
- UMP Plus–UW Medicine Accountable Care Network (UMP Plus–UW Medicine ACN) (PEBB)

- UMP Achieve 1 (SEBB)
- UMP Achieve 2 (SEBB)
- UMP High Deductible Plan (SEBB)
- UMP Plus–Puget Sound High Value Network (UMP Plus–PSHVN) (SEBB)
- UMP Plus–UW Medicine Accountable Care Network (UMP Plus–UW Medicine ACN) (SEBB)

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.**

Uniform Medical Plan Pre-authorization List

The Uniform Medical Plan (UMP) Pre-authorization List includes services and supplies that require pre-authorization or notification for UMP members.

Click to view important upcoming pre-authorization changes

- Pharmacy: Infusion Drug Site of Care – effective January 1, 2020
- Physical Medicine
    - Physical therapy, speech therapy, occupational therapy (PT/OT/ST) – effective March 1, 2020
        - PEBB: UMP Classic, UMP CDHP and UMP Plus – Limit 60 annual visits
        - SEBB: UMP Achieve 1, UMP Achieve 2, UMP High Deductible – Limit 80 annual visits
        - SEBB: UMP Plus – Limit 60 annual visits
    - Pain management – effective January 1, 2020
    - Joint management – effective January 1, 2020
    - Spine – effective January 1, 2020
- Radiology – effective January 1, 2020
- Sleep Medicine – effective January 1, 2020

Radiology

These services or supplies have coverage limits	The rules or policies that define the coverage limits	Limit applies to these codes (chosen by your provider to bill for services)
Cardiac Nuclear Imaging	HTCC decision	• 78451, 78452, 78453, 78454, 78459, 78466, 78468, 78469, 78491, 78492
Coronary Artery Calcium Scoring	HTCC decision	• S8092 Note: CPT 75571 for Cardiac Artery Calcium Scoring is not a covered benefit; reference HTCC decision
Coronary Computed Tomographic Angiography (CTA)	HTCC decision	• 75574
Discography	HTCC decision	• 62290, 62291, 72285, 72295
Dopamine Transporter Single-Photon Emission Computed Tomography (DAT-SPECT)	Regence Medical Policy Rad57	• A9584, 78607
Imaging for Rhinosinusitus	HTCC decision	• 70450, 70460, 70470, 70486, 70487, 70488, S8042 • Please see AIM criteria for pre-authorization requirements for indications other than Rhinosinusitis for codes 70450, 70460, 70470, 70486, 70487, 70488
Single Photon Emission Computed Tomography (SPECT) of the Brain	Regence Medical Policy Rad44	• Requests for SPECT for functional neuroimaging for primary degenerative dementia or mild cognitive impairment is not a covered benefit for 78607

Radiology Quality Initiative

Check for specific HTCC pre-authorization requirements documented under Cardiac Nuclear Imaging and Imaging for Rhinosinusitis.

We partner with AIM to administer our Radiology Quality Initiative (RQI) program.

- Phone 1 (877) 291-0509

Contact AIM to obtain an order number for the following codes:

70336, 70450, 70460, 70470, 70480, 70481, 70482, 70486, 70487, 70488, 70490, 70491, 70492, 70496, 70498, 70540, 70542, 70543, 70544, 70545, 70546, 70547, 70548, 70549, 70551, 70552, 70553, 70554, 70555, 71250, 71260, 71270, 71275, 71550, 71551, 71552, 71555, 72125, 72126, 72127, 72128, 72129, 72130, 72131, 72132, 72133, 72141, 72142, 72146, 72147, 72148, 72149, 72156, 72157, 72158, 72159, 72191, 72192, 72193, 72194, 72195, 72196, 72197, 72198, 73200, 73201, 73202, 73206, 73218, 73219, 73220, 73221, 73222, 73223, 73225, 73700, 73701, 73702, 73706, 73718, 73719, 73720, 73721, 73722, 73723, 73725, 74150, 74160, 74170, 74174, 74175, 74176, 74177, 74178, 74181, 74182, 74183, 74185, 74712, 75557, 75559, 75561, 75563, 75572, 75573, 75574, 75635, 77046, 77047, 77048, 77049, 77078, 77084, 78451, 78452, 78453, 78454, 78459, 78466, 78468, 78469, 78472, 78473, 78481, 78483, 78491, 78492, 78494, 78608, 78609, 78811, 78812, 78813, 78814, 78815, 78816, 93303, 93304, 93306, 93307, 93308, 93312, 93313, 93314, 93315, 93316, 93317, 93350, 93351, G0297, 0501T, 0502T, 0503T, 0504T

*UMP is subject to HTCC decision: 70554, 70555, 78607, 78608. Functional neuroimaging for primary degenerative dementia or mild cognitive impairment is not a covered benefit for 70554, 70555, 78607, 78608, 78609.

Medical Policy Manual Radiology, Policy No. 44

Single Photon Emission Computed Tomography (SPECT) of the Brain

Effective: June 1, 2019

Next Review: March 2020
Last Review: April 2019

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

Single photon emission computed tomography (SPECT) is a nuclear imaging technique that is used to visualize functional information about body organs, including the brain.

MEDICAL POLICY CRITERIA

Notes:

- This policy addresses only single photon emission computed tomography (SPECT) of the brain. This policy does not address the use of SPECT other than SPECT of the brain.
- This policy does not address the use of dopamine transporter (DAT)-SPECT. Please refer to the Cross References below for the health plan commercial policy on DAT-SPECT.

I. Single photon emission computed tomography (SPECT) of the brain for indications other than those listed below may be considered **medically necessary**.

II. SPECT of the brain is considered **investigational** for the following conditions:

A. Attention-deficit/hyperactivity disorder (ADHD)

B. Autism

C. Behavioral health disorders (including, but not limited to bipolar disorder, major depressive disorder, schizophrenia, and personality disorders)

D. Cerebrovascular disease (including stroke, transient ischemic attack, and subarachnoid hemorrhage)

E. Chronic fatigue syndrome

F. Dementias (including Alzheimer's, vascular dementia, frontal temporal dementia, Pick's disease and dementia with Lewy bodies)

G. Encephalopathy (including but not limited to Lyme, Wernicke's, hypoglycemia, and hypoxic-ischemic encephalopathy)

H. Motor neuron disorders [including amyotrophic lateral sclerosis (ALS), progressive bulbar palsy, primary lateral sclerosis, and progressive (spinal) muscular atrophy]

I. Multiple sclerosis

J. Parkinsonian syndromes and essential tremor

K. Substance-related disorders (including alcohol)

L. Traumatic brain injury

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

LIST OF INFORMATION NEEDED FOR REVIEW

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.

- History and physical/chart notes
- Diagnosis and indication for testing

CROSS REFERENCES

1. Dopamine Transporter Single-Photon Emission Computed Tomography (DAT-SPECT), Radiology, Policy No. 57

BACKGROUND

Brain imaging requires the use of radiopharmaceuticals that cross the blood-brain barrier. The radioactive isotope decay results in emission of gamma rays that are detected by a gamma camera which allows reconstruction of cross-sectional slices.

SPECT has been used to determine dopamine and serotonin receptor availability and to study regional cerebral blood flow in the brain. Because cerebral blood flow correlates with brain metabolism, the images provide information regarding which regions of the brain are affected, which in turn aids with differential diagnosis. In addition, SPECT has been proposed as a tool to diagnose and estimate treatment response in attention deficit/hyperactivity disorder (ADHD), Alzheimer's disease /dementias, and other psychiatric conditions, such as major depression.

REGULATORY STATUS

There are a number of radiopharmaceutical agents that have been approved by the U.S. Food Drug Administration (FDA) for use with SPECT for a variety of indications. Some of these include:

- Adreview (iobenguane sulfate I-123)
- Technetium TC-99m (mebrofenin)
- I-123 isopropyliodoamphetamine (IMP, Spectamine)
- Tc-99m HMPAO (hexamethyl propylamine oxime, Ceretec)
- Tc-99m ECD (ethyl cysteinate dimer, Neurolite)
- thallium 201 diethyldithiocarbamate (T1-DDC)

EVIDENCE SUMMARY

The most rigorous evaluation of the impact of a diagnostic test on clinical outcomes is a randomized controlled trial (RCT) that evaluates health outcomes in patients who receive the new diagnostic test compared with patients who are evaluated without the new test and according to standard of care. Evidence from RCTs are necessary in order to establish how SPECT may be used in the clinical setting to either diagnose or direct treatment

A significant number of published studies have focused on investigating pathologic differences in regional cerebral perfusion, for the purpose of diagnosis of disease, in response to drug therapy or for the evaluation of brain function for a number of neurological, psychiatric, and neurodegenerative conditions. The majority of these studies are case reports or small case series/cohort studies that may limit the conclusions that can be drawn about the clinical utility of SPECT.[1-41] Furthermore, evidence regarding the use of SPECT to evaluate brain function for a number of clinical indications listed above is limited to case series and studies that utilize SPECT as a component of the study design, but do not evaluate the clinical utility of this imaging technique compared to other standard modalities.

There have been comparative studies performed for a number of indications including autism, chronic fatigue syndrome, dementia, essential tremor, and stroke that were published more than ten years ago. However, these older studies are not described here.[3,42-54]

The evidence summarized below is focused on systematic reviews, randomized controlled trials, and comparative studies that investigate the utility of SPECT compared to other imaging modalities and/or standard clinical diagnostic criteria. In addition, the evidence summary only addresses the investigational indications listed in the policy criteria.

CEREBROVASCULAR DISEASE

Nonrandomized Studies

Mutoh (2018) performed a cohort study to analyze the ability of SPECT to predict prognosis in 29 patients following aneurysmal subarachnoid hemorrhage (SAH).[55] Patients who had undergone surgery for ruptured anterior communicating artery aneurysms underwent routine measurements using technetium-99 m hexamethyl propyleneamine oxine SPECT on days four and 14 after SAH. SPECT results were analyzed by three-dimensional stereotactic surface projection (3D-SPP) and an age-matched normal database (NDB) was used as a reference. The analysis showed that cortical hypoperfusion around the surgical site in bilateral frontal lobes was evident on day four ($p<0.05$ vs NDB), and was improved significantly on day 14. The recovery was significantly less complete in patients with poor clinical grades ($p<0.05$) and patients presenting symptoms attributable to delayed cerebral ischemia ($p<0.05$). SPECT results indicating mild to moderate recovery were independently associated with poor functional outcome at three months in a multivariate analysis ($p=0.014$; odds ratio [OR], 2.5; 95% confidence interval [CI], 1.93-3.31)

Kincaid (2009) performed a retrospective analysis on 152 patients with subarachnoid hemorrhage to assess the accuracy of the routine clinical use of transcranial Doppler (TCD) ultrasonography and SPECT in predicting angiographically demonstrated cerebral vasospasm.[56] TCD was able to predict vasospasm with an OR of 27 (95% CI 3-243) in the anterior cerebral arteries (ACA), 17 (95% CI 5.4-55) in the middle cerebral arteries (MCA) and 4.4 (95% CI 0.72-27) in the basilar cerebral arteries (BA). Conversely, SPECT was able only to predict vasospasm with an OR of 0.97 (95% CI 0.36-2.6) in the ACA, 2.0 (95% CI 0.71-5.5) in the MCA, and 5.6 (95% CI 0.89-36), in the BA. Overall, the investigators concluded that the standard transcranial Doppler appeared to be more predictive of cerebral vasospasms in multiple areas of the brain compared to SPECT.

DEMENTIAS

Systematic Reviews

Archer (2015) performed a Cochrane systematic review in 2015 to assess the diagnostic accuracy of cerebral blood flow (rCBF) SPECT for diagnosing frontal temporal dementia (FTD) in populations with suspected dementia settings and the ability of SPECT to differentiate between FTD from other dementia subtypes.[57] Five cohort studies (two retrospective cohort studies and three prospective) were included to assess the diagnostic capabilities of SPECT in patients with suspected dementia.[58,59] Six case-control studies were included that assessed the ability of SPECT to differentiate between different types of dementias in participants who had a clinical diagnosis of FTD or other dementia subtype using standard clinical diagnostic criteria.[60] The review found that study design and methods varied widely between included studies, participant selection was not well described, and that the studies had either high or unclear risk of bias. The reviewers also reported that in most studies the threshold used to define a positive SPECT result was not predefined. Sensitivities and specificities for differentiating FTD from non-FTD ranged from 0.73 to 1.00 and from 0.80 to 1.00, respectively, for the three multiple-headed camera studies. However, sensitivities were significantly lower for the two single-headed camera studies; reporting sensitivities from 0.36 to 0.40. The reviewers recommended against the use of SPECT in these patients due to insufficient evidence.

In 2015, the Washington State Health Care Authority published a health technology assessment on “Functional Neuroimaging for Primary Degenerative Dementia or Mild Cognitive Impairment”.[61] This study assessed a number of neuroimaging techniques including

FDG-PET, C-DTBZ-PET, SPECT and fMRI for the diagnosis of primary degenerative dementia or mild cognitive impairment. The authority concluded that there was sufficient evidence not to cover SPECT for these indications. The reliability of HMPAO-SPECT in providing a differential diagnosis of either AD or FTD in patients with an uncertain diagnosis was determined by the inclusion of two studies. [60,62] The diagnostic accuracy of HMPAO-SPECT was determined by one study by Bonte, which found that SPECT had a sensitivity of 93% and a specificity of 85% in in differentiating between AD and non-AD dementia in post-mortem samples.[63]

Davison and O'Brien (2014) performed a systematic review in 2014 comparing FDG-PET and rCBF SPECT in the diagnosis of neurodegenerative dementias, including nine studies that directly compared the two imaging modalities (N=117 subjects with AD, 46 subjects with other dementias and 100 controls).[64] Eight of these studies involved patients with AD, four of which included vascular dementia, frontal temporal dementia, or Pick's disease. One study examined patients with Dementia with Lewy Bodies.[45,65] Published studies of SPECT sensitivities ranged from 65-85% for diagnosing Alzheimer's disease (AD) and specificities (for other neurodegenerative dementias) of 72-87%. PET sensitivities and specificities were slightly higher than SPECT, ranging from 75-99% and 71-93%, respectively. Both of these modalities are therefore just as sensitive at predicting and diagnosing AD as the current standard for clinical diagnosis, NINCDS-ADRDA, which has sensitivity ranging from 65-96%. Limitations of the included studies listed were small sample size, poorly matched control groups, and heterogeneity in study design.

Yeo (2013) performed systematic review of the diagnostic utility of HMPAO SPECT in neurodegenerative dementia, and pooled studies with a clinical diagnosis and those using 99mTc-HMPAO SPECT in a meta-analysis.[66] Forty-nine studies were included in the review; AD versus FTD (n = 13), AD versus VD (n = 18), AD versus DLB (n = 5), and AD versus NC (n = 18). However, the majority of these included studies had small sample sizes, with only five studies having more than 100 subjects. The reviewer reported sensitivity and specificity of 99mTc-HMPAO-SPECT in distinguishing clinically diagnosed AD from FTD are 79.7 and 79.9%, respectively, AD from VD are 74.5 and 72.4%, AD from DLB are 70.2 and 76.2%, and AD from NC are 76.1 and 85.4%. Limitations of this analysis include small numbers of studies for each diagnostic comparison group and high methodological heterogeneity between studies. The reviewers concluded that SPECT is valuable in differentiating Alzheimer's disease from frontotemporal dementia and normal controls, but should only be used in with clinical information and other test results.

Nonrandomized Studies

In a 2017 retrospective study, Höller compared SPECT with EEG and with a combination of SPECT and EEG in patients with diagnosed dementias.[67] Standard clinical electroencephalography (EEG) and 99mTc-hexamethyl-propylene-aminoxime (HMPAO)-SPECT were used to assess 39 patients with Alzheimer's dementia (AD), 69 patients with depressive cognitive impairment (DCI), 71 patients with amnestic mild cognitive impairment (aMCI), and 41 patients with amnestic subjective cognitive complaints (aSCC). Patient groups were classified pairwise (using a linear support vector machine) separately for each biomarker and then again for each EEG biomarker combined with SPECT. HMPAO-SPECT alone was not able to reliably identify the individual disorders, but a combination of HMPAO-SPECT with EEG outperformed EEG alone and was able to classify aSCC verus AD, aMCI versus AD, and AD versus DCI.

Brayet (2017) analyzed the ability of SPECT scans to differentiate between AD patients and healthy controls.[68] Eight aMCI subjects and 16 age-matched controls underwent SPECT scans during wakefulness and during REM sleep. A significant decrease in perfusion in the anterior cingulate cortex was reported in aMCI cases during wakefulness ($p<0.024$), and a larger decrease was reported during REM sleep ($p<0.001$).

Chiba (2016) evaluated the early differential diagnosis between Alzheimer's disease and dementia with Lewy bodies which compared (18)F-FDG PET and (123)I-IMP SPECT.[69] The study was small, with only nine patients, limiting the conclusions that can be drawn. However, the authors concluded that for the occipital regions, there was significant accuracy in a differential diagnosis for both FDG PET and IMP SPECT. FDG PET was more useful than IMP SPECT for the differential diagnosis of mild cognitive impairment Alzheimer's disease versus dementia with Lewy bodies.

O'Brien (2014) compared the diagnostic ability of perfusion SPECT with FDG-PET to differentiate between Alzheimer and Lewy body dementias.[70] Subjects clinically diagnosed with Alzheimer disease (AD; n = 38) and dementia with Lewy bodies (DLB; n = 30), and controls (n = 30) underwent FDG-PET and SPECT; and area under the curve (AUC) of receiver-operating-characteristic analysis was reported. Investigators reported that diagnosis, as determined by two clinicians, indicated that FDG-PET was superior to SPECT for both dementia vs. no-dementia (AUC = 0.93 vs. 0.72, $p=0.001$) and AD vs. DLB (AUC = 0.80 vs. 0.58, $p=0.005$). The investigators concluded that perfusion SPECT is of limited diagnostic utility for differentiating DLB from AD.

Takahashi (2014) compared the ability of perfusion SPECT with 3D arterial spin-labeled brain perfusion imaging to diagnose AD.[71] This study included 68 patients with clinically suspected AD who underwent both 3D arterial spin-labeling and SPECT. Images were assessed by two clinicians and the area under the ROC curve distinguishing AD from non-AD was 0.80-0.82 for SPECT alone and 0.69 for 3D ASL images alone. Statistical parametric mapping showed that the perisylvian and medial parieto-occipital perfusion in the arterial spin-labeled images was significantly higher than that in the SPECT images. The investigators concluded that diagnostic performance of 3D arterial spin-labeling and SPECT for Alzheimer disease was almost equivalent.

Ito (2013) performed a multicenter prospective cohort study to examine the ability of ^{123}I-N-isopropyl-4-iodoamphetamine cerebral blood flow (IMP-CBF) SPECT to diagnose AD in patients with mild cognitive impairment (MCI).[72] One hundred and thirteen patients with amnestic MCI underwent clinical and neuropsychological examinations and ^{123}I-IMP-CBF SPECT at baseline and were followed for three years and evaluated for progression to dementia. SPECT images were classified as AD/DLB (dementia with Lewy bodies) pattern and non-AD/DLB pattern by image interpretation. Ninety-nine of the 113 patients converted to AD within the observation period. Image interpretation predicted conversion to AD with 56% diagnostic accuracy (sensitivity, 76%; specificity, 39%). Multivariate logistic regression analysis identified SPECT as a predictor, which distinguished AD converters from non-converters. The ability of a positive SPECT to predict conversion to AD on its own was low (OR 2.5, but if used in combination with gender and mini-mental state examination there was an improved diagnostic accuracy (OR 20.08). Therefore, SPECT on its own was concluded to be sensitive but relatively nonspecific for prediction of clinical outcome during the 3-year follow-up.

MULTIPLE SCLEROSIS

Nonrandomized Studies

Assadi (2010) performed a small study of 16 patients with confirmed multiple sclerosis (MS) to evaluate with ability of SPECT with Tc-99m MIBI or Tc-99m ECD (ethyl cysteinate dimer) to detect brain abnormalities compared to MRI.[73] MRI was performed on 16 patients (13 women and three men, aged 16-38 years) and an average of 1-10 lesions in a number of different areas of the brain, including periventricular white matter, juxtacortical white matter, corpus callosum, cerebellar peduncles, and brainstem. Of the 16 patients, eight had SPECT with Tc-99m MIBI, and the other eight had SPECT with Tc-99m ECD. Neither type of SPECT was able to detect any abnormality, indicating that the use of SPECT is insufficient to evaluate brain lesions in multiple sclerosis.

PARKINSONIAN SYNDROMES AND ESSENTIAL TREMOR

Systematic Reviews

Sharifi (2014) performed a systematic review of the role of neuroimaging techniques in the diagnosis and evaluation of essential tremor.[74] The reviewers included two small studies using SPECT to determine rCBF at rest.[75,76] One confirmed increased bilateral cerebellar activity, whereas the other did not find any significant differences between essential tremor patients and healthy controls. One study focused on cognitive functioning and related the rCBF with cognitive performances in patients and healthy controls, and determined differences in test performances, but showed no difference in rCBF values.[76]

In a 2007 systematic review of the literature on diagnostic accuracy of SPECT in parkinsonian syndromes, Vlaar included 15 small case series that used SPECT with post-synaptic tracers, which measure dopamine receptor density.[42] When SPECT was used to differentiate between PD and essential tremor (ET), two studies were included and the pooled OR with 95% CI was 2 (0.4–5). Five studies were included in a pooled analysis to determine if SPECT could reasonably differentiate between PD and atypical parkinsonian syndromes, with a pooled OR with 95% CI of 2.0 (0.8 – 6). The reviewers concluded that the accuracy of SPECT with post-synaptic tracers to differentiate between PD and atypical parkinsonian syndrome is relatively low.

PRACTICE GUIDELINE SUMMARY

AMERICAN PSYCHIATRIC ASSOCIATION (APA)

An APA 2012 consensus report from the APA work group on neuroimaging markers of psychiatric disorders,[77] recommends the following steps for biomarker validation in psychiatric disorders:

1. There should be at least two independent studies that specify the biomarker's sensitivity, specificity, and positive and negative predictive values;
2. Sensitivity and specificity should be no less than 80%; positive predictive value should approach 90%;
3. The studies should be well powered, conducted by investigators with expertise to conduct such studies, and the results published in peer-reviewed journals;
4. The studies should specify type of control subjects, including normal subjects and those with a dementing illness but not AD; and

5. Once a marker is accepted, follow-up data should be collected and disseminated to monitor its accuracy and diagnostic value.

According to this standard, the report concludes, "...the psychiatric imaging literature currently does not support the application of a diagnostic biomarker to positively establish the presence of any primary psychiatric disorder."

AMERICAN COLLEGE OF RADIOLOGY (ACR)

The 2015 ACR Appropriateness Criteria® for evaluating head trauma[78] indicated that SPECT is usually not appropriate (rating: 1) in the following situations:

- Initial evaluation of minor, mild, moderate or severe acute closed head injury
- Short-term follow-up imaging of acute traumatic brain injury with or without neurologic deterioration, delayed recovery, or persistent unexplained deficits
- Subacute or chronic traumatic brain injury with new cognitive and/or neurologic deficit(s)
- Suspected intracranial arterial injury
- Suspected intracranial venous injury

The 2014 Appropriateness Criteria® for evaluating seizures and epilepsy[79] indicated that SPECT with perfusion agents may be appropriate (rating: 5) to provide confirmatory localization information in patients with medically refractory epilepsy. However, the ACR guidelines conclude, "Only electroencephalogram (EEG) (using either scalp electrodes or intracranial electrodes [iEEG]) and magnetoencephalography (MEG) directly measure the brain's electrical activity. As such, they could or should be the gold standard for seizure localization." In addition, the ACR guidelines state that the utility of SPECT with regards to clinical diagnosis, management, or outcomes of new-onset seizure patients has not been scientifically established.

The 2015 ACR Appropriateness Criteria® for dementia and movement disorders[80] provides guidance on the use of SPECT. A rating of 2 or 3 ("usually not appropriate") was assigned to the following conditions:

- Dementia and movement disorders (consider for problem solving)
- Probable or possible Alzheimer's disease
- Suspected frontotemporal dementia
- Suspected vascular dementia
- Suspected normal pressure hydrocephalus
- Suspected Huntington disease
- Clinical features suggestive of neurodegeneration with brain iron accumulation
- Motor neuron disease (consider for problem solving)
- Parkinson disease with typical clinical features and responsive to levodopa
- Parkinsonian syndrome with atypical clinical features not responsive to levodopa.

A rating of 4 or 5 ("may be appropriate") was assigned to the following conditions:

- Suspected prion disease (Creutzfeldt-Jakob, iatrogenic, or variant)
- Suspected dementia with Lewy bodies

- Parkinson disease with typical clinical features and responsive to levodopa.

The 2016 ACR-Society for Pediatric Radiology (SPR)[81] developed a practice parameter that states SPECT brain perfusion is clinically indicated for the following:

- Evaluating patients with suspected dementia
- Localizing epileptic foci preoperatively
- Diagnosing encephalitis
- Monitoring and assessing vascular spasm following subarachnoid hemorrhage
- Mapping of brain perfusion during interventions
- Detecting and evaluating cerebrovascular disease
- Predicting the prognosis of patients with cerebrovascular accidents
- Corroborating the clinical impression of brain death

In addition, for other indications, such as neuropsychiatric disorders and chronic fatigue syndrome, the findings of SPECT brain perfusion imaging have not been fully characterized. In human immunodeficiency virus (HIV) encephalopathy, SPECT brain perfusion imaging can detect altered brain perfusion.

SUMMARY

For some indications, there is enough research to show that single photon emission computed tomography (SPECT) of the brain improves health outcomes. Therefore, SPECT for the brain may be considered medically necessary when criteria are met.

There is not enough research to show that single photon emission computed tomography (SPECT) of the brain in the evaluation, diagnosis or treatment for a variety of indications improves health outcomes. Additional research is needed to know how SPECT may be used to guide patient management compared to other imaging techniques and standard clinical diagnostic criteria. Therefore, SPECT of the brain is considered investigational for the neurologic, psychiatric, psychological, as well as other nononcologic indications as specified in the policy criteria.

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CODES

Codes	Number	Description
CPT	78607	Brain imaging, tomographic (SPECT)
HCPCS	None	

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Medical Policy Manual Radiology, Policy No. 57

Dopamine Transporter Single-Photon Emission Computed Tomography (DAT-SPECT)

Effective: January 1, 2019

Next Review: January 2020
Last Review: December 2018

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

Dopamine transporter single-photon emission computed tomography (DAT-SPECT) detects presynaptic dopaminergic deficit by measuring DAT binding. In general, striatal DAT binding is reduced in certain neurological conditions, while striatal DAT binding is in the normal range in others. Therefore, use of DAT-SPECT is being proposed to improve differential diagnosis between certain types of neurological conditions.

MEDICAL POLICY CRITERIA

Note: This policy only addresses SPECT when used with dopamine transporter ligands for diagnosing specific neurological disorders. Use of SPECT that does not incorporate these ligands is currently addressed in another commercial policy (please see Cross References below).

I. Dopamine transporter single-photon emission computed tomography (DAT-SPECT) may be considered **medically necessary** for any of the following:
   A. Suspected diagnosis of Parkinson disease when unable to be confirmed clinically; or

B. Suspected diagnosis of dementia with Lewy bodies when unable to be confirmed clinically.

II. Dopamine transporter single-photon emission computed tomography (DAT-SPECT) is considered **investigational** for all other indications.

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

POLICY GUIDELINES

SUBMISSION OF DOCUMENTATION

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

- History and physical/chart notes
- Diagnosis and indication for testing

CROSS REFERENCES

1. Biochemical Markers of Alzheimer's Disease, Laboratory, Policy No. 22
2. Transcranial Magnetic Stimulation as a Treatment of Depression and Other Disorders, Medicine, Policy No. 148
3. Magnetic Resonance Spectroscopy, Radiology, Policy No. 27
4. Single Photon Emission Computed Tomography (SPECT) for the Diagnosis of ADHD, Dementias and Other Psychiatric Conditions, Radiology, Policy No. 44
5. Deep Brain Stimulation, Surgery, Policy No. 84

BACKGROUND

Parkinsonian syndromes (PS) are a group of diseases that share similar cardinal signs, characterized by bradykinesia, rigidity, resting tremor, and gait disturbance. Parkinson disease (PD) is the most common cause of parkinsonism; however, diagnosing PD in the early stage of the disease can be difficult. In addition, other etiologies such as essential tremor (ET), corticobasal degeneration, multisystem atrophy, progressive supranuclear palsy, vascular parkinsonism, and drug-induced parkinsonism can lead to a similar set of symptoms. Even in specialized movement disorders centers, up to 25% of patients may be misclassified, and some patients, such as those with ET who have been diagnosed with PD, may be erroneously treated.[1] This has led to the development of additional tests to improve the accuracy of clinical diagnosis of PD and other PSs. One recent approach is to evaluate the integrity of dopaminergic pathways in the brain using dopamine transporter single-photon emission computed tomography (DAT-SPECT).

DAT-SPECT detects presynaptic dopaminergic deficit by measuring DAT binding. In general, striatal DAT binding is reduced in PD, genetic parkinsonism, dementia with Lewy bodies (DLB), corticobasal degeneration, progressive supranuclear palsy, and multiple system atrophy, while striatal DAT binding is in the normal range in AD, ET, dystonic tremor, orthostatic tremor, drug-induced parkinsonism, psychogenic parkinsonism, and vascular parkinsonism.[2] It is proposed that an abnormal DAT-SPECT supports the diagnosis of PD or other neurodegenerative PS (multisystem atrophy, progressive supranuclear palsy), while a normal DAT-SPECT in a symptomatic patient increases the likelihood of a disease not affecting the nigrostriatal dopaminergic pathway. There is, however, a significant percentage of

patients with clinically diagnosed PD who do not show reduced DAT-SPECT binding. These are commonly referred to as scans without evidence of dopaminergic deficit. Additional research may shed light on these cases.[3]

Due to the degeneration of nigrostriatal neurons in DLB, DAT-SPECT is also proposed to differentiate DLB from AD. Some note a severe sensitivity to neuroleptics (potentially life-threatening) in patients with DLB. However, newer agents are usually well-tolerated, and patients with DLB may also respond to the cholinesterase inhibitors that are more commonly used to treat AD.

Analysis of DAT-SPECT images can be visual, semiquantitative, or quantitative. Because patients typically do not become symptomatic before a substantial number of striatal synapses have degenerated, visual interpretation of the scan is thought to be sufficient for clinical evaluation. A variety of methods are being tested to improve the validity and reliability of ratings, including commercially available software to define the region of interest (ROI) for analysis and the development of an atlas for visual interpretation. Quantitative interpretation may aid visual interpretation and, if performed rigorously, may increase diagnostic accuracy; however, interobserver variability tends to be high with manual ROI-based semiquantification.[4] Semiquantitative analysis also requires normal control values and varies across imaging systems.

Dopamine transporter ligands include ^{123}I-β-CIT, ^{123}I-FP-CIT, and 99mTc-TRODAT-1.2 ^{123}I-β-CIT requires a delay between injection and scan of about 24 hours. ^{123}I-FP-CIT (DaTscan™) is a fluoropropyl derivate of β-CIT that can be injected three to six hours before the scan.

REGULATORY STATUS

DaTscan™ (GE Healthcare) has been in use in Europe since 2000 with a diagnostic indication for use in parkinsonian patients and with expanded use since 2006 in patients suspected of DLB. DaTscan was approved by the U.S. Food Drug Administration (FDA) in 2011 as a new molecular entity (NME) and is “indicated for striatal dopamine transporter visualization using single-photon emission computed tomography (SPECT) brain imaging to assist in the evaluation of adult patients with suspected parkinsonian syndromes (PS). In these patients, DaTscan may be used to help differentiate essential tremor from tremor due to PS (idiopathic Parkinson's disease, multiple system atrophy and progressive supranuclear palsy). DaTscan is an adjunct to other diagnostic evaluations.”

EVIDENCE SUMMARY

Assessment of a diagnostic technology typically focuses on the following three categories of evidence:

1. Analytic validity (technical feasibility) is demonstrated, including reproducibility and precision. For comparison among studies, a common standardized protocol for the new diagnostic technology is established.
2. Clinical validity (diagnostic accuracy) - sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) compared to standards are established in relevant populations of patients, such as those with suspected early Parkinson disease (PD) or inconclusive diagnosis.
3. Clinical utility of a diagnostic technique, i.e., how the results of the study can be used to benefit patient management, is established. The clinical utility of both positive and

negative tests must be established. The effect on patient outcomes (demonstration that the diagnostic information can be used to improve patient outcomes through a randomized controlled trial [RCT] or demonstration of a tightly linked chain of evidence from diagnostic accuracy to outcomes).

The criterion standard for the diagnosis of parkinsonian syndromes (PS) and dementia is postmortem neuropathologic examination. In the absence of comparisons with the criterion standard, long-term clinical follow-up may be used as a surrogate standard to evaluate the ability of dopamine transporter (DAT) imaging with single-photon emission computed tomography (DAT-SPECT) to discriminate degenerative PS from normality or from nondegenerative disorders that present with similar symptoms, and to discriminate dementia with Lewy bodies (DLB) from Alzheimer disease (AD).

The analytic validity of DAT-SPECT is the same, regardless of the indication it is used for, therefore in the evidence summary below, only clinical validity and utility are addressed separately for each indication.

ANALYTIC VALIDITY

DAT-SPECT is based on the selective affinity of ligands for the DAT and the exclusive location of the DAT in dopamine synthesizing neurons.[2] ^{123}I-β-CIT is a cocaine analog that has a high affinity to the DAT and serotonin transporters. ^{123}I-FP-CIT (DaTscan™) is a fluoropropyl derivate of β-CIT that is selective for brain striatal DAT, but it can also bind to the serotonin transporter. Although antiparkinsonian drugs do not interfere with DAT binding, it is unknown if dopamine agonists and levodopa affect DAT expression, which could influence the ability of DAT-SPECT to monitor progression of disease.

In 2014, Seibyl reported intra- and interrater agreement for DAT-SPECT images with data from five multicenter trials (818 patients).[5] DAT binding was classified as “normal” or “abnormal.” Within-reader agreement was assessed in one study, and showed complete (100%) agreement when image evaluation was blinded. In all trials, between-reader agreement was high (κ>0.8) for PD, but decreased when comparing blinded image evaluation and on-site readers for DLB.

In a 2012 study, Papathanasiou evaluated interobserver variability in the visual interpretation of DAT-SPECT.[6] Eighty-nine previously obtained DAT-SPECT scans were blindly reviewed by three independent observers with different levels of experience (consultant, resident doctor, radiographer), classified as “normal” or “abnormal,” and assigned visual DAT-SPECT uptake scores (2 = normal, 1 = reduced, 0 = no uptake). Results were compared with the diagnosis at last visit to the clinician, divided into PS or no PS. There was good interobserver agreement in 85 of 89 studies for classifying scans as “normal” or “abnormal” (κ range, 0.89-0.93) and moderate agreement in assignment of uptake scores (κ range, 0.71-0.80 for putamina; 0.50-0.79 for caudate nuclei). All three observers achieved a sensitivity of 100%, with specificities of 89-96%.

Section Summary

Preclinical studies to determine the analytical validity of DAT-SPECT report specificity of ligand binding for the striatal DAT. There is limited evidence on the effects of medications on DAT expression. Studies report a high level of interobserver agreement on visual interpretation of images for PD, suggesting that reliability of visual interpretation for this disorder is high. There

was less interobserver agreement on visual interpretation of images for DLB. The analytic validity of DAT-SPECT is the same, regardless of the indication it is used for, therefore in the evidence summary below, only clinical validity and utility are addressed in the following evidence sections.

PARKINSONIAN SYNDROMES

Clinical Validity

The most informative evaluation of clinical validity requires prospective, independent, and blinded assessment of test results compared with a criterion standard in an appropriate population.

In 2015, Jakobson reported a prospective study on the diagnostic accuracy of visual assessment of DAT-SPECT in individuals with early-stage parkinsonian diseases.[7] Strengths of this study include an independent clinical diagnosis made at baseline and follow-up, and blinded reading of the DAT scans. Patients (N=171) were identified incidentally from an ongoing longitudinal population-based research project on parkinsonian disorders. All met criteria for stage one disease on the U.K. Parkinson's Disease Society Brain Bank clinical criteria for PD. Patients with a Mini-Mental State Examination scores less than 24 or evidence of ET or secondary parkinsonism were excluded. The results of DAT-SPECT were compared with criteria-based clinical diagnoses at a mean follow-up of 4.6 years. The clinical diagnoses at baseline and follow-up were performed independently of DAT-SPECT findings. Image analysis was performed by two nuclear medicine specialists who were blinded to the clinical diagnosis. The study also included 37 age-matched healthy controls who underwent DAT-SPECT imaging for evaluation of specificity. There was a discrepancy between the reviewers in 10 cases (9.3%); these were reevaluated to reach a consensus. Visual assessment in this enriched population was found to have a sensitivity of 94% and specificity of 92%, with 3 of 37 controls considered false positives and 10 of 171 patients considered false negatives at baseline. However, at this time, it is not known if the SWEDDs are true false negatives or were misdiagnosed as having a PS.

In 2009 Marshall, reported a prospective, investigator-initiated industry-funded, 36-month European multicenter study with repeat DAT-SPECT and criterion standard clinical diagnosis (video at 36 months by two movement disorders specialists) in 99 diagnostically uncertain cases of PD or essential tremor (ET).[8] Patients with other potential causes of parkinsonism/tremor and patients with major comorbid illness were excluded; three healthy volunteers were included. For analysis, the clinical diagnosis was considered as either PD (including atypical PD) or non-PD (including ET, dystonic tremor, vascular parkinsonism). There was 50% loss to follow-up over the three years of the study (199 enrolled), although patients with PD were not more likely to drop out than patients without PD. DAT-SPECT scans were evaluated by three blinded nuclear physicians using visual criteria, and the inter-reader agreement for rating scans as normal or abnormal was high for scans at baseline, 18 months, and 36 months (κ range, 0.94-0.97).

At 36 months criterion standard diagnosis was degenerative parkinsonism in 71 cases and non-PD in 28 cases. The initial clinical diagnosis had sensitivity of 93% and specificity of 46% compared with diagnosis at follow-up, indicating overdiagnosis of PD. DAT-SPECT at baseline had a sensitivity of 78% and specificity of 97%, with a PPV of 98.2% and an NPV of 66.2%. DAT-SPECT scans were considered normal in 21% of the cases with a criterion standard diagnosis of PD and did not change over the three years of the study. These cases are

referred to as SWEDDS (Subjects with Scans Without Evidence of Dopamine Deficiency). DAT-SPECT did not improve diagnostic accuracy in the SWEDDS patients at the 36-month clinical assessment. Although this study indicates that an abnormal DAT-SPECT scan may help to confirm a clinical diagnosis of PD in the majority of patients, the low NPV suggests that a normal DAT-SPECT scan cannot be used to rule out disease and thus may not be helpful in preventing the potential clinical overdiagnosis of PD.

A number of published studies and meta-analyses have not included an independent reference standard of either blinded clinical diagnosis at follow-up or post mortem analysis of substantia nigra neuron degeneration. When a reference standard is not independent of the diagnostic test, it can result in an apparent increase in the sensitivity and specificity of the test. Therefore, the diagnostic accuracy reported in these studies must be interpreted with caution. These studies are described below.

In 2014 Brigo reported a meta-analysis of DAT-SPECT to differentiate between PD and vascular or drug-induced parkinsonisms.[9] The meta-analysis included five studies that had diagnosis confirmed by imaging. There were a number of study limitations, most notably, in three studies, it was not clear if the diagnosis at follow-up (criterion standard) was made blinded to the results of DAT-SPECT and could thus be considered an independent reference standard. Two studies published in 2014 analyzed data from Kupsch (2012)[10] The studies included 92 patients with clinically uncertain parkinsonian syndromes (CUPS) at baseline who had confirmed clinical diagnosis at one year. Bajaj (2014)assessed the effect of age, disease stage, and other clinical and neurocognitive measures on the diagnostic performance of DAT-SPECT.[11] Hauser (2014) reported that the diagnostic accuracy of DAT-SPECT was higher than clinical diagnosis at baseline.[12] Both studies are limited because clinical diagnosis atone year was influenced by the imaging results and cannot be considered an independent reference standard.

Other studies provide limited information on diagnostic accuracy because they were not conducted in an appropriate population that included patients with clinically uncertain PD or ET. These studies are described below.

In 2014, O'Brien published an industry-funded pooled analysis of four clinical studies that were submitted in support of the new drug application to the U.S. Food and Drug Administration (FDA).[13] All studies assessed the sensitivity and specificity of DAT-SPECT to detect nigrostriatal cell loss in patients with signs and symptoms of movement disorders and/or dementia. The clinical diagnosis, determined at baseline or at 12, 24, or 36 months after imaging, was performed independently of DAT-SPECT results in three of the four studies. The study populations ranged from patients with uncertain clinical diagnosis to patients with established clinical diagnosis. Pooled analysis showed sensitivity of 93.1% (range, 75.0%-96.5%) and specificity of 91.1% (range, 83%-100%) in the intention-to-treat population of 726 patients. Interpretation of this study is limited by heterogeneity in the included studies. Only two studies included a population of patients with an uncertain diagnosis, one of which was an open-label phase VI study where the clinical diagnosis was not independent of DAT-SPECT. Individual studies are described in greater detail in the Clinical Utility section.

Vlaar reported a retrospective study of the diagnostic value of DAT and postsynaptic dopamine receptor binding in 248 patients with unclassified PS in 2008.[14] Two investigators established a clinical diagnosis according to generally accepted clinical criteria and were certain enough to make a final diagnosis from the clinical records or after follow-up in all but 25 of the cases. Of

the 248 patients, 80 underwent DAT-SPECT alone, 38 underwent dopamine receptor SPECT, and 130 underwent both scans. Scans were analyzed by a nuclear medicine specialist blinded to the clinical diagnosis, with ligand binding of two standard deviations above or below healthy controls considered abnormal. Using clinical diagnosis as the comparator, DAT-SPECT was able to distinguish between PD and ET (odds ratio [OR] = 82); between PD and vascular parkinsonism (OR=61); between PD and drug-induced parkinsonism (OR=36); and between PD and atypical PS (OR=1).

In 2000, Benamer conducted a multicenter study that included 158 patients with an established clinical diagnosis of parkinsonism, 27 cases of definite ET, and 35 healthy volunteers.[15] Striatal uptake of the ligand was graded visually as normal or abnormal by an institutional reader who was blinded to the clinical data and a blinded consensus panel of five readers. The institutional reader scored 154 of 158 cases of parkinsonism as abnormal, all 27 cases of ET as normal, and 34 of 35 healthy volunteers as normal, resulting in sensitivity of 97% and specificity (for ET) of 100%. For the consensus blinded read, sensitivity and specificity were 95% and 93%, respectively. A limitation of this study is the population, which was not comprised of patients with atypical or clinically uncertain parkinsonism or ET.

Diagnostic accuracy of DAT-SPECT can be compared with the diagnostic accuracy of clinical diagnosis.

A longitudinal study by Adler (2014) found that, compared with neuropathologic findings of PD as the criterion standard, clinical diagnosis by a movement disorder specialist of possible PD (n=34) had only 26% accuracy.[16] Clinical diagnosis by a movement disorder specialist of probable PD (n=97) on the first visit had 53% PPV in cases with a disease duration less than five years and 88% PPV in patients with disease duration of five years or more.

Joutsa (2014) reported a retrospective study of the diagnostic accuracy of PD by general neurologists.[17] Of 1362 individuals who had been examined post mortem, 122 cases were identified with a clinical and/or neuropathologic diagnosis of PD. The sensitivity of clinical diagnosis of PD was 89.2% and the specificity was 57.8% compared with post mortem neuropathologic diagnosis, indicating that 25% of diagnoses by general neurologists were incorrect.

One study addressed the use of DAT-SPECT in asymptomatic LRRK2 G2019S carriers for predicting conversion to PD.[18] In this prospective study by Sierra (2017), 32 asymptomatic carriers of LRRK2 G2019S were evaluated at baseline and four years later, including clinical examination and DAT-SPECT. Three carriers had converted to PD at the second evaluation, and these participants had a statistically significantly lower striatal DAT binding at baseline than those that did not convert. There was no significant difference between the slope of DAT binding decline between the two scans.

Section Summary

The literature on the clinical validity of DAT-SPECT to diagnose and distinguish Parkinsonian syndromes includes meta-analyses of a number of small studies along with a large and well-conducted industry-sponsored study on the diagnostic accuracy of DAT-SPECT. In general, this evidence supports moderately high sensitivity and high specificity for the test. However, most studies had methodologic limitations, primarily the lack of a true criterion standard for the diagnosis of PS. In the highest quality study, in which the criterion standard was 36-month clinical diagnosis by a panel of independent experts, the sensitivity and specificity of testing

was 78% and 97%, respectively. The PPV was 98.2% and the NPV was 66.2% in a population of patients with a prevalence of underlying PD of approximately 70%. This indicates that, in a population of patients with a high pretest likelihood of PD, a positive test may be useful in confirming PD, while a negative test is less useful in ruling out the disorder.

Clinical Utility

The most rigorous evaluation of the impact of a diagnostic test on clinical outcomes is an RCT that evaluates health outcomes in patients who received the new diagnostic test compared with patients who are evaluated without the new test according to the standard of care.

Bhattacharjee (2017) retrospectively assessed the impact of DAT-SPECT performed for diagnosis and clinical management.[19] Of a total of 48 scans reported, 24 were to confirm early Parkinson's disease, five were to exclude drug-induced parkinsonism, eight were to distinguish essential tremor from parkinsonism, two were to distinguish Lewy body diseases from Alzheimer's dementia, and four were for other indications. There were 26 abnormal scans and 21 scans confirmed a diagnosis of degenerative parkinsonism. In 23% of patients, the scan results altered diagnosis and management.

Oravivattanakul (2015) reported on the concordance between pre-scan diagnosis and scan results in 175 CUPS patients who were seen by movement disorders neurologists.[20] When essential/dystonic tremor was suspected, the scan was normal in 79%. DaTscan influenced medical treatment more when scans were abnormal than when normal. Only 4% of patients with abnormal scans remained off medications, while 24% of patients with normal scans remained on medication.

Sadasivan and Friedman (2015) also reported on the clinical outcome of the change in management.[21] Sixty-five CUPS patients were referred for DAT-SPECT over a 17-month period. Scans were abnormal in 22 patients, leading to a final diagnosis of PD in 22 patients and a change in management in 41 patients (63%). Of the 41 patients with a change in management, 30 (73%) were clinically stable or improved at follow-up. This included 10 patients who were found to have drug-induced PD without any striatal neurodegeneration, leading to discontinuation or reduction in dose of the drug.

In a retrospective study from a hospital imaging facility in Europe, Thiriez (2015) evaluated whether routine clinical requests for DAT-SPECT were considered appropriate or inappropriate and whether the results led to a change in management.[22] Appropriateness was determined by consensus of two movement disorders specialists, and a request was considered inappropriate if DAT-SPECT was unable to answer the question or if DAT-SPECT results would not change patient care. For example, a differential diagnosis between parkinsonian tremor and ET was considered appropriate, while evaluation of the severity of dopaminergic cell loss in already diagnosed PD was always considered to be inappropriate. Of 516 consecutive requests over an 8-year period, 37% were considered inappropriate. They included requests to assess the degree of dopaminergic denervation in already diagnosed patients (n=40) and confirmation of a clinically evident diagnosis (n=64). Scan requests by movement disorder specialists were considered appropriate more frequently than requests from other physicians (79% vs 57%, $p<0.01$). A change in management was identified in 13% of patients with an inappropriate scan compared with 92% of the patients with an appropriate scan, and a change in management was more frequently observed if the scan was requested by movement disorders specialists than by other physicians (71% vs 56%, $p=0.01$).

Bega (2015) reported a study from a tertiary care center that evaluated 83 scans ordered over a two-year period with specific features that led the physician to question the diagnosis.[23] The greatest impact was to differentiate ET from PD, with a change in diagnosis, management, or both in 72.2% of these patients.

In a retrospective review of the effect of DAT-SPECT on diagnosis by referring physicians, Siefert and Weiner (2013) found that confidence in a diagnosis of PD or non-PD was significantly increased with abnormal scans, but not with normal scans.[24] For many patients, the scan confirmed the diagnosis of PD, despite a poor response to medication and resulted in a change in medication.

In 2012-2013, Kupsch reported an industry-sponsored, open-label, multicenter randomized trial from 19 university hospital centers in Europe and the United State that assessed the impact of DAT-SPECT on diagnosis, confidence of diagnosis, clinical management, health resource use, and safety in 273 patients with CUPS.[10,25] Criteria of uncertainty included at least one of the following: only one of the three cardinal signs of parkinsonism; two signs without bradykinesia; atypical signs; signs of mild intensity; poor response to L-dopa; and lack of disease progression. After the baseline visit and establishment of a clinical management plan, patients were randomized to DAT-SPECT or no imaging controls; the DAT-SPECT scans were visually classified as normal or abnormal by a nuclear medicine physician at each center who was blinded to clinical signs and/or symptoms. Patients were then followed for one year (visits at four weeks, 12 weeks, one year) by neurologists with (n=12) or without (n=7) movement disorder specialization.

The primary outcome was the proportion of patients in the efficacy population (baseline and 12-week visits) who had one or more changes in clinical management. Significantly more patients in the DAT-SPECT group had at least one change in their clinical management plan by 12 weeks than the control group (50% vs 31%, p=0.002). This was due to a greater change in management by movement disorder specialists (51% DAT-SPECT vs 28% controls, p<0.001). Medications were initiated in 29% of patients and withdrawn in 18% of patients after DAT-SPECT (patients could be counted in both categories). Changes included initiation of dopaminergic therapy or more aggressive dopaminergic therapy in patients with an abnormal scan, discontinuation of dopaminergic therapy, or initiation of tremor control drugs in patients with a normal scan, and unplanned diagnostic tests. For the general neurologists, clinical management was not affected by the DAT-SPECT results, with a change in management in 48% of DAT-SPECT patients versus 43% of controls. Changes in diagnosis occurred in 45%, 46%, and 54% of DAT-SPECT patients by four weeks, 12 weeks, and one year, respectively (per protocol population), compared with a change in diagnosis in 9%, 12%, and 23% of control patients at the same time points (p<0.001 for all comparisons). The changes were in the direction of better agreement between the clinical diagnosis and imaging results. Clinicians had increased confidence in diagnosis at four weeks, 12 weeks, and one year in the DAT-SPECT group; the greatest change in confidence in diagnosis was for patients with an initial inconclusive diagnosis (62% vs 22% controls, p<0.001). There were no significant differences in quality of life or health resource utilization during the one-year follow-up period. No serious adverse events occurred during the study.

Bairactaris evaluated the impact of DAT-SPECT on diagnoses of patients with PS in a 2009 report.[26] Sixty-one consecutive patients with an initial diagnosis of parkinsonism (n=40) or uncertain tremor disorder (n=21) by their treating community neurologist were reexamined by two neurologists who were blinded to the original diagnosis (overall agreement between the

two, 75.7%; κ=0.461). Patients then underwent DAT-SPECT imaging, which was evaluated by two masked independent and experienced nuclear medicine physicians using a semiquantitative approach and classified as normal or abnormal (κ=0.855). Based on DAT-SPECT imaging, the initial diagnosis was altered for 21 patients (34.4%) relative to the initial classification from the community neurologist and for six patients (9.8%) diagnosed at their center. All patients were reexamined by two neurologists at the center at one-year follow-up and classified as having neurodegenerative or non-neurodegenerative disorders. With the final diagnosis as the reference standard, DAT-SPECT had a sensitivity of 95%, specificity of 82%, and PPVs and NPVs of 90%. Although this study appears to have been well-conducted, evaluation of DAT-SPECT scans by two experienced nuclear medicine physicians using a semiquantitative approach may not be representative of results obtained outside of the investigational setting. As noted by the authors, DAT-SPECT studies did not appear to add a great deal to the diagnosis made by an expert in movement disorders.

In 2004, Catafau and Tolosa reported a prospective multicenter trial of the impact of DAT-SPECT on diagnosis and clinical management of 118 patients with CUPS, with two-year follow-up reported in 2007.[27,28] Criteria of uncertainty were assessed by referring neurologists and included at least one of the following: only one of the three cardinal signs of parkinsonism, with or without asymmetry; two signs without bradykinesia; atypical signs; signs of mild intensity; poor response to L-dopa; and lack of disease progression. Excluded were patients with an established clinical diagnosis and patients where the uncertainty was between PD, multisystem atrophy, and progressive supranuclear palsy. Following clinical diagnosis into categories (presynaptic or nonpresynaptic PS, or inconclusive diagnosis), all patients underwent DAT-SPECT with visual assessment of images by a trained nuclear medicine physician. After reviewing the DAT-SPECT results, the neurologists again provided a diagnosis and recorded proposed changes in the planned management. At baseline, 67 patients were classified as suspected presynaptic PS, 26 as suspected nonpresynaptic PS, and 25 as inconclusive. DAT-SPECT results were not consistent with the initial diagnosis in 36% of patients with suspected presynaptic PS (normal image) and 54% of patients with nonpresynaptic PS (abnormal image). After imaging, 19 (76%) inconclusive patients were reclassified and 16 of 118 patients (14%) were reclassified as inconclusive. Overall, imaging resulted in a change in the diagnosis in 52% of patients and in a change in management in 72% of cases. All patients with a final diagnosis of presynaptic PS had an abnormal image, whereas 94% of patients with nonpresynaptic PS had a normal scan.

At two years, 85 patients (72%) were available for follow-up.[28] In eight patients (9.4%), the neurologist was unable to provide a definite diagnosis, and in 69 of the remaining 77 patients (90%), the initial DAT-SPECT results agreed with the clinical diagnosis at follow-up. The rate of agreement was higher when the final diagnosis was presynaptic PS (97%) than when it was nonpresynaptic PS (77%). The rate of agreement between clinical diagnosis at baseline (before DAT-SPECT) and follow-up was 56%. This increased to 81% when the diagnosis after DAT-SPECT was compared with the diagnosis at follow-up. If clinical diagnosis at follow-up differed from that suggested by the initial scan (6/8 agreed to a second scan) or was inconclusive (n=8), a second DAT-SPECT scan was performed. There were discrepancies between the first and second scans in 6 of the 14 patients, and in five of these six, the initial scan was considered abnormal. The second DAT-SPECT results helped to establish a diagnosis in seven of eight patients (87.5%) with a previously inconclusive diagnosis.

Additional retrospective studies support a change in diagnosis and increase in confidence in diagnosis following DAT-SPECT. Several tertiary referral centers have reported a change in diagnosis and management for a majority of patients with CUPS.[20,21,23,29]

Other literature indicates that the level of DAT-SPECT binding does not predict disease severity or have prognostic value for the progression of motor symptoms in PD.[30,31]

Section Summary

Evidence on clinical utility of DAT-SPECT includes one well-conducted RCT, a prospective multicenter trial, and several retrospective studies that have evaluated the effect of DAT-SPECT on diagnosis of CUPS and subsequent changes in treatment. These studies report that the use of this technology can result in changes in diagnosis in a minority of patients, greater confidence in the diagnosis by the treating clinician, and changes in treatment (e.g., medication management). However, there is only one retrospective series to indicate that these changes result in improvements in health outcomes. A limitation of this evidence is the lack of a criterion standard diagnosis to evaluate whether the changes were in the direction of more accurate diagnosis and more appropriate management. For example, the RCT showed that more patients evaluated with DAT-SPECT have changes in diagnosis and management than controls without imaging; however, no improvement in quality of life was observed by the one-year follow-up. The evidence is insufficient to determine the effects of the technology on health outcomes.

DEMENTIA WITH LEWY BODIES

Clinical Validity

In a 2017 study by Shimizu, DAT-SPECT was performed in 95 AD patients and 133 DLB patients and the relationship between symptoms and DAT uptake was examined.[32] Patients with parkinsonism had significantly lower DAT uptake than AD patients in the entire striatum, entire putamen, and anterior putamen but there were no differences in any subregion of the striatum. There was a small but statistically significant correlation between severity of parkinsonism and DAT uptake in the entire striatum in patients with DBL. Other symptoms examined did not correlate with DAT uptake in any region of the striatum.

A 2015 meta-analysis by Brigo evaluated the diagnostic accuracy of DAT-SPECT to distinguish between DLB and other dementias.[33] Eight studies were included, of which three studies used histopathology as the reference standard. Studies that used clinical diagnosis as the reference standard showed diagnostic accuracy between 84-86% (ten studies) when using visual or semiquantitative analysis. The two studies using a histopathologic reference standard and visual analysis showed similar sensitivity (87%) and slightly higher specificity (92%) compared with studies that used clinical diagnosis as the reference standard. The single study that used semiquantitative analysis with histopathology as a reference standard correctly identified the 15 patients with DLB (100% sensitivity) and had 90% specificity in the identification of the eight patients with non-DLB dementia. Because only 23 patients enrolled in this study, additional research is needed to corroborate these results.

Papathanasiou reported a meta-analysis of the diagnostic accuracy of DAT-SPECT in DLB in 2012.[34] Four studies with a total of 419 patients were included in the meta-analysis (including the study by McKeith previously described). The studies included both patients with an uncertain diagnosis and patients with a certain diagnosis. Three studies used clinical diagnosis

as the reference standard while one used post mortem histopathology. The estimated pooled sensitivity of DAT-SPECT to differentiate DLB from no DLB was 86.5%, the specificity was 93.6%, and the diagnostic OR was 48.95. Funnel plot analysis showed no significant publication bias. These results might differ if the reference standard (clinical diagnosis) is flawed. The sole study to assess diagnostic accuracy in histologically verified cases (n=23) reported no false negatives and sensitivity of 100%.

The largest study to evaluate the diagnostic accuracy of DAT-SPECT for DLB is a 2007 prospective, investigator-initiated, industry-sponsored, multicenter study by McKeith, who assessed 326 patients with clinical diagnosis of probable (n=94) or possible (n=57) DLB or non-DLB (n=147).[35] In 28 patients, no diagnosis was made. The diagnoses were established by a consensus panel of three clinicians who did not have access to DAT-SPECT results, and DAT-SPECT scans were assessed visually by three nuclear medicine physicians with expertise in DAT-SPECT imaging who were unaware of the clinical diagnosis. DAT-SPECT had a mean sensitivity of 77.7% for detecting clinical probable DLB, a specificity of 90.4% for excluding non-DLB dementia, a PPV of 82.4%, and an NPV of 87.5%. This study did not use long-term clinical follow-up as the standard.

Several studies have followed patients with inconsistent results from DAT-SPECT and clinical diagnosis.

Van der Zande (2016) reported on seven (10.4%) of 67 patients who were clinically diagnosed with DLB but had normal scans.[36] In five of the seven, second DAT-SPECT scans (average 1.5 years later) were abnormal. There were no differences in baseline clinical characteristics, but patients with initially normal scans were less severely affected after one year. This study evaluated small numbers of subjects and lacked autopsy findings to confirm the diagnosis.

In 2013, Siepel reported a longitudinal study of patients who had inconsistent clinical criteria for DLB and DAT-SPECT results at baseline.[37] Fifty patients were evaluated with clinical criteria and DAT-SPECT results and followed for two to five years. Twenty-eight patients met clinical criteria for DLB or non-DLB; the remaining patients were clinically inconclusive and not included in the analysis. For 18 patients the DAT-SPECT scan and clinical criteria were concordant. Blinded analysis showed seven patients who had an abnormal scan but did not initially meet the clinical criteria for DLB developed typical clinical features over follow-up. Three patients who met clinical criteria for DLB but had a normal DAT-SPECT at baseline continued to meet clinical criteria for DLB over follow-up, indicating a false-negative scan (SWEDD) in 6% of patients. The study is limited by the small number of subjects and the lack of autopsy findings to confirm the diagnosis.

Clinical Utility

In 2015, Walker reported an industry-funded RCT to determine whether DAT-SPECT would lead to a change in diagnosis and more confidence in diagnosis in patients with probable DLB or non-DLB dementia.[38] Patients were included in the study if they were diagnosed as possible DLB by local physicians (neurologists or geriatric psychiatrists). Patients were included if they had dementia and either one core feature or one or more suggestive features of DLB. Excluded from the study were patients with: an established clinical diagnosis of probable DLB or non-DLB dementia; Parkinson features for more than one year; significant vascular pathology; severe mental or physical illness that could account for dementia; or a medication known to influence DAT-SPECT binding (including amphetamine, benatropine, bupropion, cocaine, mazindol, methylphenidate, phentermine, and sertraline). A total of 187

patients were randomized in a 2:1 ratio to have DAT-SPECT scans or clinical diagnosis alone. Onsite clinicians recorded DLB features and rated their confidence in diagnosis using a visual analog scale (VAS, 0-100). The readers, who had variable expertise, rated 57% of scans as normal and 43% as abnormal. At both 8- and 24-week follow-ups, the onsite clinicians were more likely to change the diagnosis in patients who had imaging compared with control patients (e.g., 71% revised vs 16%, $p<0.001$) and were more confident in their diagnosis ($p<0.001$). Clinicians were also more likely to change the diagnosis if the scan was abnormal than if it was normal (82% vs 46%).

Kemp (2011) conducted a retrospective study of the impact of DAT-SPECT on the clinical diagnosis and subsequent management of 80 consecutive patients with possible DLB.[39] The patients had been referred for imaging with suspected DLB by 33 specialists in older-age psychiatry working at 11 memory clinics in the U.K. All DAT-SPECT scans were interpreted visually by a single observer in conjunction with the clinical referral details and any other relevant imaging. DAT-SPECT imaging results were found to be abnormal (indicating DLB) in 20 (25%) and normal in 60 (75%) patients. Of the 20 patients with an abnormal scan, 18 had a postscan working clinical diagnosis of DLB (90%), one had a diagnosis of vascular dementia (5%), and one had no recorded outcome (5%). Fifty-eight of the 60 patients with a normal DAT-SPECT scan had an alternative clinical diagnosis (95%). Subsequent to DAT-SPECT, scan findings and diagnoses were discussed with patients and/or their caregivers in 94% of cases. Pharmacologic management affecting antipsychotic, dopaminergic, or cholinergic medication was changed in about half of the patients after the scan, although many (irrespective of the imaging results) were in the earliest phase of their disease process and did not require immediate treatment for symptoms. In addition, the small numbers did not allow substantive conclusions about changes in specific therapies.

Section Summary

Evidence of clinical utility includes one RCT that evaluated changes in diagnosis and confidence in diagnosis following DAT-SPECT imaging. This study indicates that DAT-SPECT can influence diagnosis of DLB, particularly when the scan is abnormal. It cannot be determined from this study whether the revised diagnosis was more accurate or resulted in a beneficial change in patient management. Longer follow-up of patients in this study may lead to greater certainty regarding the effect of this technology on health outcomes.

PRACTICE GUIDELINE SUMMARY

AMERICAN COLLEGE OF RADIOLOGY

The American College of Radiology (ACR) published appropriateness criteria for dementia and movement disorders in 2015.[40] ACR states that the diagnosis of idiopathic PD is usually based on patient history and physical examination alone and that, when clinical signs and symptoms and response to medication are typical of PD, neuroimaging is not required. In patients with unusual clinical features, incomplete or uncertain medication responsiveness, or clinical diagnostic uncertainty, imaging to exclude alternative pathologies may be indicated. ACR states that positron emission tomography and SPECT tracer studies exploring the presynaptic nigrostriatal terminal function and the postsynaptic dopamine receptors have been unable to reliably classify the various PSs and may not reliably measure disease progression. Use of DAT-SPECT was rated as “may be appropriate” to evaluate suspected DLB or PD with either typical or atypical clinical features.

AMERICAN ACADEMY OF NEUROLOGY

The 2006 practice parameters (reaffirmed in July 2013) from the American Academy of Neurology state that β-CIT and IBZM (iodobenzamide) SPECT are possibly useful in distinguishing PD from essential tremor (ET; five class III studies).[41] There was insufficient evidence to determine if these modalities are useful in distinguishing PD from other forms of Parkinsonism.

MOVEMENT DISORDERS SOCIETY

The Movement Disorder Society's (MDS) diagnostic criteria for PD from 2015 are intended for use in clinical research but may be used to guide clinical diagnosis.[42] MDS considers clinical expert opinion to be the criterion standard to diagnose PD and that diagnoses are usually made clinically without need for ancillary diagnostic testing. Methods that may become available as knowledge advances are diagnostic biochemical markers, anatomical neuroimaging, and methods to detect alpha-synuclein deposition. MDS noted that, although dopaminergic neuroimaging can help to distinguish parkinsonism from PD mimics like ET, "it does not qualify as a criterion for the differentiation of PD from other parkinsonian conditions like atypical parkinsonian syndromes." Normal functional neuroimaging of the presynaptic dopaminergic system is also listed as criteria for exclusion from diagnosis of PD in patients with early/de novo PD.[43]

SOCIETY OF NUCLEAR MEDICINE AND MOLECULAR IMAGING

The Society of Nuclear Medicine and Molecular Imaging (previously known as the International Society of Nuclear Medicine), provided a practice guideline for DAT imaging with SPECT in 2011.[4] The guideline states that the main indication for DAT-SPECT is striatal DAT visualization in the evaluation of adult patients with suspected PS to help differentiate ET from tremor due to presynaptic PS (PD, multiple-system atrophy, progressive supranuclear palsy). However, the pattern of ^{123}I-ioflupane uptake cannot discriminate between the latter disorders with any high degree of accuracy.

Other indications are the early diagnosis of presynaptic PS, differentiation of presynaptic PS from parkinsonism without presynaptic dopaminergic loss (e.g., drug-induced parkinsonism, psychogenic parkinsonism), and differentiation of DLB from AD. The guidance states that visual interpretation of the scan is usually sufficient for clinical evaluation, where the striatal shape, extent, symmetry, and intensity differentiate normal from abnormal. For semiquantitative analysis, each site should establish its own reference range by scanning a population of healthy controls or by calibrating its procedure with another center that has a reference database.

SUMMARY

It appears that dopamine transporter single-photon emission computed tomography (DAT-SPECT) may improve health outcomes for people with a suspected diagnosis of Parkinson disease or dementia with Lewy bodies. Clinical guidelines based on research recommend DAT-SPECT for certain indications. Therefore, DAT-SPECT may be considered medically necessary for a suspected diagnosis of Parkinson disease or dementia with Lewy bodies when policy criteria are met.

In all other situations, there is not enough research to show that dopamine transporter single-photon emission computed tomography (DAT-SPECT) improves health outcomes. Therefore, DAT-SPECT is considered investigational for all other indications.

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44. BlueCross BlueShield Association Medical Policy Reference Manual "Dopamine Transporter Imaging With Single-Photon Emission Computed Tomography." Policy No. 6.01.54

CODES

Codes	Number	Description
CPT	78607	Brain imaging, tomographic (SPECT)
HCPCS	A9584	Iodine I-123 ioflupane, diagnostic, per study dose, up to 5 millicuries

Date of Origin: *January 2016*

Important upcoming pre-authorization changes

- Pharmacy: Infusion Drug Site of Care - effective January 1, 2020
- Physical Medicine
    - Physical therapy, speech therapy, occupational therapy (PT/OT/ST) - effective March 1, 2020
        - PEBB: UMP Classic, UMP CDHP and UMP Plus - Limit 60 annual visits
        - SEBB: UMP Achieve 1, UMP Achieve 2, UMP High Deductible - Limit 80 annual visits
        - SEBB: UMP Plus - Limit 60 annual visits
    - Pain management - effective January 1, 2020
    - Joint management - effective January 1, 2020
    - Spine - effective January 1, 2020
- Radiology - effective January 1, 2020
- Sleep Medicine - effective January 1, 2020

Pharmacy

UMP has a separate vendor – Washington State Rx Services – for their prescription drug benefit. Pre-authorization is necessary for certain injectable drugs that are not normally approved for self-administration when obtained through a retail pharmacy, a network mail-order pharmacy, or a network specialty pharmacy. These drugs are indicated on the UMP Preferred Drug List.

Drugs usually payable under the member's medical benefit and pre-authorized will continue with the same Regence process.

Infusion Drug Site of Care

Effective January 1, 2020: Certain provider administered infusion medications covered on the medical benefit are subject to the Site of Care Program (dru408) medication policy (PDF). This policy does not apply to members covered under UMP Plus plans.

Physical Medicine

We partner with eviCore healthcare to administer our Physical Medicine program.

Providers obtain or verify an authorization with eviCore:

1. Sign in to eviCore's portal
2. Phone (855) 252-1115
3. Fax (855) 774-1319

If HTCC criteria is used for authorization – see below for links to that criteria

Effective March 1, 2020: Physical therapy, speech therapy, occupational therapy (PT/ST/OT)

- Members aged 17 and younger: Select pediatric diagnosis codes are excluded from the program (PDF).
- **We require authorization from eviCore for these codes: 92507, 92508, 92521, 92522, 92523, 92524, 92526, 92597, 92607, 92608, 92609, 92610, 92626, 92627, 92630, 92633, 95831, 95832, 95833, 95834, 95851, 95852, 96105, 97012, 97014, 97016, 97018, 97022, 97024, 97026, 97028, 97032, 97033, 97034, 97035, 97036, 97039, 97110, 97112, 97113, 97116, 97127, 97139, 97150, 97161, 97162, 97163, 97164, 97165, 97166, 97167, 97168, 97530, 97533, 97542, 97750, 97755, 97760, 97761, 97763, 97799, G0151, G0152, G0157, G0158, G0159, G0160, G0283, G0515, S8950, S9128, S9129, S9131, S9152**

Effective March 1, 2020: HTCC decisions administered by eviCore related to physical therapy, speech therapy, occupational therapy

- **Treatment of chronic migraine and chronic tension-type headache**
    - **UMP is subject to HTCC Decision (PDF): 97140**

Effective January 1, 2020: Pain management

- **We require authorization from eviCore for these codes: 00640, 27096, 61790, 61791, 62320, 62321, 62322, 62323, 62324, 62325, 62326, 62327, 62350, 62351, 62360, 62361, 62362, 64405, 64510, 64520, 72275, G0259, G0260**

Effective January 1, 2020: HTCC decisions administered by eviCore related to pain management

- **Discography**
  - **UMP is subject to HTCC Decision (PDF): 62290, 62291, 72285, 72295**
- **Facet Neurotomy**
  - **UMP is subject to HTCC Decision (PDF): 64633, 64634, 64635, 64636**
- **Spinal Injections**
  - **UMP is subject to HTCC Decision (PDF): 62320, 62321, 62322, 62323, 64479, 64480, 64483, 64484, 64490, 64491, 64492, 64493, 64494, 64495**
  - **This coverage policy does not apply to those with systemic inflammatory disease such as ankylosing spondylitis, psoriatic arthritis or enteropathic arthritis**

Effective January 1, 2020: Joint management

- **We require authorization from eviCore for these codes: 23470, 23472, 23473, 23474, 27125, 27130, 27132, 27134, 27137, 27138, 27442, 27443, 27486, 27487, 27488, 27580, 29805, 29806, 29807, 29819, 29820, 29821, 29822, 29823, 29824, 29825, 29826, 29827, 29828, 29860, 29861, 29862, 29863, 29868, 29870, 29871, 29873, 29875, 29876, 29879, 29880, 29881, 29882, 29883, 29884, 29885, 29886, 29887, 29888, 29889, 29891, 29892, 29893, 29894, 29895, 29897, 29898, 29899, 29904, 29905, 29906, 29907**

Effective January 1, 2020: HTCC decisions administered by eviCore related to joint management

- **Hip Surgery for Femoroacetabular Impingement Syndrome (FAI)**
  - **UMP is subject to HTCC Decision (PDF): 29914, 29915, 29916**
- **Knee Arthroscopy for Osteoarthritis of the Knee**
  - **UMP is subject to HTCC Decision (PDF): 29874, 29877**
- **Total Knee Arthroplasty**
  - **UMP is subject to HTCC Decision (PDF): 27437, 27438, 27440, 27441, 27445, 27446, 27447**

Effective January 1, 2020: Spine

- **We require authorization from eviCore for these codes: 20931, 20937, 20938, 22100, 22101, 22102, 22103, 22110, 22112, 22114, 22116,**

22206, 22207, 22208, 22210, 22212, 22214, 22216, 22220, 22222, 22224, 22226, 22325, 22326, 22327, 22328, 22532, 22534, 22548, 22556, 22585, 22590, 22595, 22600, 22610, 22614, 22632, , 22634, 22800, 22802, 22804, 22808, 22810, 22812, 22818, 22819, 22830, 22840, 22842, 22843, 22844, 22845, 22846, 22847, 22848, 22849, 22850, 22852, 22855, 62380, 63001, 63003, 63005, 63011, 63012, 63015, 63016, 63017, 63020, 63040, 63043, 63045, 63046, 63050, 63051, 63055, 63064, 63066, 63075, 63076, 63077, 63078, 63081, 63082, 63085, 63086, 63087, 63088, 63101, 63102, 63103, 63170, 63172, 63173, 63180, 63182, 63185, 63190, 63191, 63194, 63195, 63196, 63197, 63198, 63199, 63200, 63250, 63251, 63252, 63265, 63266, 63267, 63268, 63270, 63271, 63272, 63273, 63275, 63276, 63277, 63278, 63280, 63281, 63282, 63283, 63285, 63286, 63287, 63290, 63295, 63300, 63301, 63302, 63303, 63304, 63305, 63306, 63307, 63308, S2350, S2351

Effective January 1, 2020: HTCC decisions administered by eviCore related to spine

- **Cervical Fusion for Degenerative Disc Disease**
  - **UMP is subject to HTCC Decision (PDF): 22551, 22552, 22554, 22853, 22854, 22859, 22600**
- **Lumbar Fusion for Degenerative Disc Disease**
  - **UMP is subject to HTCC Decision (PDF): 22533, 22558, 22612, 22630, 22633, 22853, 22854, 22859**
  - **Lumbar Fusion for degenerative disc disease uncomplicated by comorbidities is not a covered benefit per HTCC Decision**
  - **Note: This decision does not apply to patients with the following conditions: radiculopathy, spondylolisthesis (>grade 1), severe spinal stenosis, acute trauma or systemic disease affecting spine, e.g., malignancy**
  - **UMP is subject to HTCC Decision (PDF) for Bone Morphogenic Protein: 22533, 22558, 22612, 22630, 22633**
  - **Bone morphogenetic protein-7 (rhBMP-7) is not a covered benefit**
  - **HTCC for bone morphogenetic protein does not apply to those under age 18**
- **Surgery for Lumbar Radiculopathy**
  - **UMP is subject to HTCC Decision (PDF): 62380, 63030, 63035, 63042, 63044, 63047, 63048, 63056, 63057, 63090, 63091**

Radiology

AIM Specialty Health

We partner with AIM to administer our Advanced Imaging Authorization radiology program. Providers:

- Login to AIM's ProviderPortal
- Phone 1 (877) 291-0509

NOTE: If HTCC criteria is used for pre-authorization, see below for links to that criteria. If there are no HTCC criteria, AIM criteria will apply.

Effective January 1, 2020: Contact AIM to obtain an order number for the following codes: 70336, 70480, 70481, 70482, 70490, 70491, 70492, 70496, 70498, 70544, 70545, 70546, 70547, 70548, 70549, 70551, 70552, 70553, 71250, 71260, 71270, 71275, 71550, 71551, 71552, 71555, 72125, 72126, 72127, 72128, 72129, 72130, 72131, 72132, 72133, 72141, 72142, 72146, 72147, 72148, 72149, 72156, 72157, 72158, 72159, 72191, 72192, 72193, 72194, 72195, 72196, 72197, 72198, 73200, 73201, 73202, 73206, 73218, 73219, 73220, 73221, 73222, 73223, 73225, 73700, 73701, 73702, 73706, 73718, 73719, 73720, 73721, 73722, 73723, 73725, 74150, 74160, 74170, 74174, 74175, 74176, 74177, 74178, 74181, 74182, 74183, 74185, 74712, 75557, 75559, 75561, 75563, 75572, 75573, 75635, 77078, 77084, 78472, 78473, 78481, 78483, 78494, 93303, 93304, 93306, 93307, 93308, 93312, 93313, 93314, 93315, 93316, 93317, 93350, 93351, G0297, 0501T, 0502T, 0503T, 0504T

Effective January 1, 2020: HTCC decisions administered by AIM

- **Breast MRI**
  - **UMP is subject to HTCC Decision (PDF): 77046, 77047, 77048, 77049**
  - **HTCC criteria applies to all member requests regardless of gender**
- **Cardiac Nuclear Imagining**
  - **UMP is subject to HTCC Decision (PDF): 78451, 78452, 78453, 78454, 78459, 78466, 78468, 78469, 78491, 78492**
- **Coronary Computed Tomographic Angiography (CTA)**
  - **UMP is subject to HTCC Decision (PDF): 75574**
- **Functional Neuroimaging for Primary Degenerative Dementia or Mild Cognitive Impairment**
  - **UMP is subject to HTCC Decision (PDF): 70554, 70555, 78608, 78609**

    - **Please see AIM criteria for pre-authorization requirements for indications other than primary degenerative dementia or mild cognitive impairment**
- **Imaging for Rhinosinusitis**
    - **UMP is subject to HTCC Decision (PDF): 70450, 70460, 70470, 70486, 70487, 70488, 70540, 70542, 70543**
    - **Please see AIM criteria for pre-authorization requirements for indications other than Rhinosinusitis**
- **Positron Emission Tomography (PET) Scans for Lymphoma**
    - **UMP is subject to HTCC Decision (PDF): 78811, 78812, 78813, 78814, 78815, 78816**

Sleep Medicine

We partner with AIM to administer our Sleep Medicine program. Providers:

- Login to AIM's ProviderPortal
- Phone 1 (877) 291-0509

Effective January 1, 2020: contact AIM to obtain an order number for the following codes: 95782, 95783, 95805, E0470, E0471

AIM uses HTCC to pre-authorize sleep medicine diagnosis and equipment. Also refer to the Surgery section for additional information about Sleep Apnea Diagnosis and Treatment.

Effective January 1, 2020: HTCC decisions administered by AIM:

- **Sleep Apnea – Diagnosis and Equipment**
    - **UMP is subject to HTCC Decisions (PDF): 95800, 95801, 95806, 95807, 95808, 95810, 95811, E0561, E0562, E0601, G0398, G0399, G0400**
    - Please see AIM criteria for indications other than Sleep Apnea

Regence Oregon and Utah

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Medication Policy Manual

Policy No: dru408

Topic: Site of Care Review

Date of Origin: July 10, 2015

Committee Approval Date: July 24, 2019

Next Review Date: July 2020

Effective Date: October 1, 2019

Description

This policy is to review the requested site of care (SOC) for provider-administered medications. Many medications historically infused in hospital-based infusion centers have been evaluated and determined to be safe for infusion outside of hospital-based settings. Use of non-hospital-based infusion centers and home infusion services is an accepted standard medical practice and sometimes referred to as an "alternate site of care." These settings offer high-quality services for patients and reduce the overall cost of care, as compared to costly hospital-based infusion centers.

This policy applies to fully-insured commercial plans, exchange plans, and select self-insured groups [a.k.a. administrative-services only (ASO)] based in Washington, Oregon, Idaho, and Utah. This policy does **not** apply to Medicare plans.

IMPORTANT REMINDER

This Medication Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

Description

The purpose of medication policy is to provide a guide to coverage. Medication Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Policy/Criteria

I. Under most contracts, medications included in the infusion drug site of care program (see *Appendix 1*) may be considered medically necessary when individual medication policy criteria are met **AND** one of the following criteria (A. or B.) below are met**:**

A. The medication is administered in an approved site of care. (No formal "Site of Care" review is required)

OR

B. The medication is administered in an unapproved site of care (see Appendix 2), such as an unapproved hospital-based infusion center, when at least one of the criteria below (1. or 2.) are met:

NOTE: Site of care review criteria will be waived for payment of the first dose of a medication, to allow for adequate transition time to an approved site of care for subsequent infusions.

1. There is no nearby approved site of care **AND** home infusion is not an option, as documented by criteria a. **AND** b. being met:

a. All approved sites of care are greater than 10 miles further from the member's home than from the unapproved site of care, such as an unapproved hospital-based infusion center (example: the member's house is 41 miles from an approved site of care, but 30 miles to the unapproved site of care).

AND

b. The member's home is not eligible for home infusion services for reasons including, but not limited to: the home is not within the service area of the home infusion provider or is deemed unsuitable for care by the home infusion provider, unless the medication is not eligible for home infusion services (see *Appendix 1*)

OR

2. Clinical documentation of at least one medical reason why an approved site of care is not an option, including, but not limited to:

i. The member is 13 years of age or younger.

ii. Significant behavioral issues and/or cognitive impairment including, but not limited to, those associated with developmental delay, down syndrome, dementia, or excessive anxiety such as severe needle phobia.

iii. Prior severe infusion reactions, despite standard pre-medications.

iv. Presence of circulating antibodies which may increase risk of infusion reactions.

v. Treatment within 100 days after hematopoietic stem cell transplantation (HSCT, a.k.a. bone marrow transplant).

vi. Concurrent treatment with medications that require a higher level of monitoring (such as CAR T-cell therapy, intravenous cytotoxic chemotherapy, or blood products).
vii. Treatment of antibody-mediated rejection (a.k.a. vascular rejection, acute humoral rejection) following a solid organ transplant.
viii. Treatment of Kawasaki disease.

II. Limitations and Authorization Period – Authorization **shall** be reviewed at least annually to confirm that current medical necessity criteria are met, including that an approved site of care is still not a treatment option.

III. The medications in the infusion drug site of care program are considered not medically necessary if administered in an unapproved site of care, such as an unapproved hospital-based infusion center, when an approved site of care is a treatment option.

Position Statement

- New technologies and pharmaceuticals allow therapeutic services, such as infusion therapy, to be administered safely, effectively, and much less costly outside of hospital-based infusion centers (a.k.a. hospital outpatient settings). Sites of care such as doctor's offices, infusion centers, home infusion, and approved hospital-based infusion centers are well-established, accepted by physicians, and provide the best value to patients to reduce the overall cost of care.

Site of Care Review:

- Use of non-hospital-based infusion centers and home infusion services is an accepted standard medical practice. These sites offer high-quality services for patients and reduce the overall cost of care, as compared to costly hospital-based infusion centers. [1-8]
- All medications infused outside of a hospital setting have undergone an evaluation for safe infusion and development of infusion standards, including adverse drug reaction management and reporting algorithms.
- At all sites of care, every patient undergoes an assessment during the intake process by the infusion provider, which includes evaluation of individual clinical assessment parameters. These parameters may include, but are not limited to, previous tolerance of products (such as IVIG), assessment of kidney function, risk factors for developing thromboembolic events, and venous access. [9-10]
- For use of home infusion services, an assessment is conducted to determine if the home is a safe, appropriate site of care, with adequate support for infusion in the home.
- Because providers need time to arrange for assessment and coordination of care, the first dose of provider-administered medications may be covered in a hospital-based infusion center, if needed, to allow adequate time for a seamless transition of care. This may include arranging for delivery of medications and/or patient education, such as for self-administration of medications such as subcutaneous immune globulin (SCIG).

- Claims submitted for infusion services performed at an unapproved site of care, such as an unapproved hospital-based infusion center (such as on campus or off campus hospital outpatient settings, denoted by place of service codes 22 or 19; see *Appendix 3*), are considered not medically necessary when an approved site of care is a treatment option.
- Pediatric patients often differ from adult patients in physiology, development, and cognitive and emotional function. They may also require doses, infusion rates, and equipment that vary and differ compared to adult patients. Special infusion training and expertise is needed. Therefore, this policy allows for patients aged 13 years and younger to obtain infusion services in approved sites of care or unapproved sites of care, such as unapproved hospital-based infusion centers.

Appendix 1: Medications Included in the Infusion Drug Site of Care Program

Medication [a]	Effective Date	Policy Number	Home infusion eligible [b]	HCPCS Code
Actemra, tocilizumab [a]	3/1/2015	dru444	Yes	J3262
Adagen, pegademase bovine	4/1/2016	dru426	Yes	J2504
Aldurazyme, laronidase	4/1/2016	dru426	Yes	J1931
Benlysta, belimumab	9/1/2015	dru248	Yes	J0490
Cerezyme, imiglucerase	4/1/2017	dru002	Yes	J1786
Cimzia, certolizumab pegol [a]	3/1/2018	dru444	Yes	J0717
Crysvita, burosumab	11/1/2019	dru547	Yes	J0584
Elaprase, idursulfase	4/1/2017	dru426	Yes	J1743
Elelyso, taliglucerase alfa	9/1/2018	dru002	Yes	J3060
Entyvio, vedolizumab	3/1/2015	dru444	Yes	J3380
Evenity, romosozumab	10/1/2019	dru594	Yes	J3590
Fabrazyme, agalsidase beta	7/1/2015	dru575	Yes	J0180
Inflectra, infliximab-dyyb	1/1/2017	dru444	Yes	Q5103
Immune globulin	3/1/2015	dru020	Yes	J1459, J1555, J1556, J1557, J1559, J1561, J1566, J1568, J1569, J1572, J1575, J1599
Ixifi, infliximab-qbtx	10/1/2018	dru444	Yes	Q5109
Kanuma, sebelipase alfa	6/10/2016	dru426	Yes	J2840
Lumizyme, alglucosidase alfa	7/1/2015	dru426	Yes	J0221
Myozyme, alglucosidase alfa	7/1/2015	dru426	Yes	J0220
Naglazyme, galsulfase	4/1/2016	dru426	Yes	J1458
Ocrevus, ocrelizumab	9/1/2018	dru479	Yes	J2350
Onpattro, patisiran	4/1/2019	dru577	Yes	C9036
Orencia, abatacept [a]	3/1/2015	dru444	Yes	J0129
Prolia, denosumab	7/1/2015	dru223	Yes	J0897
Radicava, edaravone	8/11/2017	dru510	Yes	J1301
Remicade, infliximab	3/1/2015	dru444	Yes	J1745
Renflexis, infliximab-abda	8/11/2017	dru444	Yes	Q5104
Revcovi, elapegademase	4/1/2019	dru426	Yes	J3590
Simponi Aria, golimumab [a]	3/1/2015	dru444	Yes	J1602
Soliris, eculizumab	5/1/2015	dru385	Yes	J1300
Trogarzo, ibalizumab-uiyk	6/1/2018	dru542	Yes	J1746

Medication [a]	Effective Date	Policy Number	Home infusion eligible [b]	HCPCS Code
Tysabri, natalizumab	5/1/2015	dru111	No	J2323
Ultomiris, ravulizumab	7/1/2019	dru385	Yes	J3590
Vimizim, elosulfase alfa	4/1/2016	dru426	Yes	J1322
VPRIV, velaglucerase alfa	4/1/2017	dru002	Yes	J3385

[a] This policy only applies to the formulations of these medications covered under the medical benefit. Formulations for self-administration may be available through the pharmacy benefit for most members.

[b] As of the date of the policy publication

Appendix 2: Glossary	
Term	**Description**
Approved site of care	Location where medications are safely and effectively administered by a health care professional. Approved sites of care include: • Doctor's offices • Standalone ambulatory infusion centers • Home infusion • Approved hospital-based infusion centers
Unapproved site of care	Location where medications are administered by a professional and the facility is reimbursed for the medication and services at a much higher rate than approved sites of care. Unapproved sites of care include: • Unapproved hospital-based infusion centers

Appendix 3: Place of Service Codes and Descriptions [11]		
Place of Service Code	**Place of Service Name**	**Description**
11	Office	Location, other than a hospital, skilled nursing facility (SNF), military treatment facility, community health center, State or local public health clinic, or intermediate care facility (ICF), where the health professional routinely provides health examinations, diagnosis, and treatment of illness or injury on an ambulatory basis.
12	Home	Location, other than a hospital or other facility, where the patient receives care in a private residence.
19	Off Campus-Outpatient Hospital	A portion of an off-campus hospital provider based department which provides diagnostic, therapeutic (both surgical and nonsurgical), and rehabilitation services to sick or injured persons who do not require hospitalization or institutionalization.
22	On Campus-Outpatient Hospital	A portion of a hospital's main campus which provides diagnostic, therapeutic (both surgical and nonsurgical), and rehabilitation services to sick or injured persons who do not require hospitalization or institutionalization.

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Revision History

Revision Date	Revision Summary
7/24/2019	• Added Crysvita (burosumab) and Evenity (romosozumab) to the policy.
4/25/2019	• Added Revcovi (elapegademase) and Ultomiris (ravulizumab) to the policy.
1/31/2019	• Added Onpattro (patisiran) to the policy, effective 4/1/2019. • Updated Appendix 1 HCPCS codes.
8/17/2018	• No criteria changes on this annual review.
6/15/2018	• Clarify home infusion criteria I.B.1.b only applies to medications eligible for home infusion. • Updated Appendix 1, to include home infusion eligibility.
5/18/2018	• No change to intent of coverage criteria. Clarification of description, policy language, and addition of applicable J-codes. Defined approved and unapproved sites of care. • Added the following medications to the policy: o Effective 6/1/2018: Trogarzo (ibalizumab-uiyk) o Effective 9/1/2018: Elelyso (taliglucerase alfa), Ocrevus (ocrelizumab) o Effective 10/1/2018: Ixifi (infliximab-qbtx) • Clarified medical exception criteria for concurrent cancer immunotherapy, including CAR T-cell therapy, and age less than 13 years old.
8/11/2017	Updated Appendix 1.
1/17/2017	Removed Lemtrada and Exondys from site of care program
12/16/2016	Updated Appendix 1.
11/11/2016	Updated Appendix 1.
9/23/2016	Updated Appendix 1.
9/9/2016	Select Utah plans are now included in the site of care review.
7/15/2016	Updated formatting of policy, added additional medical rationale for potential waivers to policy, noted distinction between approved and unapproved hospital outpatient settings, clarified affected members, and updated references.

Drug names identified in this policy are the trademarks of their respective owners.

Code	Description	Code	Description
E75.24	Niemann-Pick disease	G82.51	Quadriplegia, C1-C4 complete
E75.240	Niemann-Pick disease type A	G91.0	Communicating hydrocephalus
E75.241	Niemann-Pick disease type B	G91.1	Obstructive hydrocephalus
E75.242	Niemann-Pick disease type C	G91.3	Post-traumatic hydrocephalus, unspecified
E75.243	Niemann-Pick disease type D	G91.4	Hydrocephalus in diseases classified elsewhere
E75.248	Other Niemann-Pick disease	G91.8	Other hydrocephalus
E75.249	Niemann-Pick disease, unspecified	G91.9	Hydrocephalus, unspecified
E75.3	Sphingolipidosis, unspecified	G93.1	Anoxic brain damage, not elsewhere classified
E75.5	Other lipid storage disorders	G93.40	Encephalopathy, unspecified
E75.6	Lipid storage disorder, unspecified	G93.5	Compression of brain
E76	Disorders of glycosaminoglycan metabolism	G93.6	Cerebral edema
E76.0	Mucopolysaccharidosis, Type I	G93.7	Reye's syndrome
E76.01	Hurler's syndrome	G93.89	Other specified disorders of brain
E76.02	Hurler-Scheie syndrome	G93.9	Disorder of brain, unspecified
E76.03	Scheie's syndrome	G96.9	Disorder of central nervous system, unspecified
P07.30	Preterm newborn, unspecified weeks of gestation	G98.8	Other disorders of nervous system
P07.31	Preterm newborn, gestational age 28 completed weeks	P07.3	Preterm [premature] newborn [other]
P07.32	Preterm newborn, gestational age 29 completed weeks	P83.2	Hydrops fetalis not due to hemolytic disease
P07.33	Preterm newborn, gestational age 30 completed weeks	Q01.0	Feeding problems of newborn
P07.34	Preterm newborn, gestational age 31 completed weeks	Q01.1	Frontal encephalocele
P07.35	Preterm newborn, gestational age 32	Q01.2	Nasofrontal encephalocele

	completed weeks		
P07.36	Preterm newborn, gestational age 33 completed weeks	Q01.8	Occipital encephalocele
P07.37	Preterm newborn, gestational age 34 completed weeks	Q01.9	Encephalocele of other sites
P07.38	Preterm newborn, gestational age 35 completed weeks	Q02	Encephalocele, unspecified
P07.39	Preterm newborn, gestational age 36 completed weeks	Q03.0	Microcephaly
Q06	Other congenital malformations of spinal cord	Q03.1	Malformations of aqueduct of Sylvius
Q06.0	Amyelia	Q03.8	Atresia of foramina of Magendie and Luschka
Q06.1	Hypoplasia and dysplasia of spinal cord	Q03.9	Other congenital hydrocephalus
Q06.2	Diastematomyelia	Q04.0	Congenital hydrocephalus, unspecified
Q06.3	Other congenital cauda equina malformations	Q04.1	Arhinencephaly
Q06.4	Hydromyelia	Q04.2	Holoprosencephaly
Q06.8	Other specified congenital malformations of spinal cord	Q04.3	Other reduction deformities of brain
Q92.6	Marker chromosomes	Q04.4	Septo-optic dysplasia of brain
Q93	Monosomies and deletions from the autosomes, not elsewhere classified	Q04.5	Megalencephaly
Q93.51	Angelman syndrome	Q04.6	Congenital cerebral cysts
Q93.59	Other deletions of part of a chromosome	Q04.8	Other specified congenital malformations of brain
Q93.8	Other deletions from the autosomes	Q04.9	Congenital malformation of brain, unspecified
Q93.82	Williams syndrome	Q05.0	Cervical spina bifida with hydrocephalus
D82.1	Di George's syndrome	Q05.1	Thoracic spina bifida with hydrocephalus
E75.0	GM2 gangliosidosis	Q05.2	Lumbar spina bifida with hydrocephalus
E75.00	GM2 gangliosidosis, unspecified	Q05.3	Sacral spina bifida with hydrocephalus

E75.01	Sandhoff disease	Q05.4	Unspecified spina bifida with hydrocephalus
E75.02	Tay-Sachs disease	Q05.5	Cervical spina bifida without hydrocephalus
E75.09	Other GM2 gangliosidosis	Q05.6	Thoracic spina bifida without hydrocephalus
E75.1	Other and unspecified gangliosidosis	Q05.7	Lumbar spina bifida without hydrocephalus
E75.10	Unspecified gangliosidosis	Q05.8	Sacral spina bifida without hydrocephalus
E75.11	Mucolipidosis IV	Q05.9	Spina bifida, unspecified
E75.19	Other gangliosidosis	Q06.9	Congenital malformation of spinal cord, unspecified
E75.2	Other sphingolipidosis	Q07.00	Arnold-Chiari syndrome without spina bifida or hydrocephalus
E75.21	Fabry (-Anderson) disease	Q07.01	Arnold-Chiari syndrome with spina bifida
E75.22	Gaucher disease	Q07.02	Arnold-Chiari syndrome with hydrocephalus
E75.23	Krabbe disease	Q07.03	Arnold-Chiari syndrome with spina bifida and hydrocephalus
E75.25	Metachromatic leukodystrophy	Q07.8	Other specified congenital malformation of nervous system
E75.26	Sulfatase deficiency	Q07.9	Congenital malformation of nervous system, unspecified
E75.29	Other sphingolipidosis	Q90.0	Trisomy 21, nonmosaicism (meiotic nondisjunction)
E75.4	Neuronal ceroid lipofuscinosis	Q90.1	Trisomy 21, mosaicism (mitotic nondisjunction)
E78.71	Barth syndrome	Q90.2	Trisomy 21, translocation
E78.72	Smith-Lemli-Opitz syndrome	Q90.9	Down syndrome, unspecified
F70	Mild intellectual disabilities	Q91.0	Trisomy 18, nonmosaicism (meiotic nondisjunction)
F71	Moderate intellectual disabilities	Q91.1	Trisomy 18, mosaicism (mitotic nondisjunction)
F72	Severe intellectual disabilities	Q91.2	Trisomy 18, translocation
F73	Profound intellectual disabilities	Q91.3	Trisomy 18, unspecified
F78	Other intellectual disabilities	Q91.4	Trisomy 13, nonmosaicism (meiotic nondisjunction)
F79	Unspecified intellectual disabilities	Q91.5	Trisomy 13, mosaicism (mitotic nondisjunction)
F82	Specific developmental disorder of motor	Q91.6	Trisomy 13, translocation

	function		
F84	Pervasive development disorders	Q91.7	Trisomy 13, unspecified
F84.0	Autistic disorder	Q92.0	Whole chromosome trisomy, nonmosaicism (meiotic nondisjunction)
F84.2	Rett's syndrome	Q92.1	Whole chromosome trisomy, mosaicism (mitotic nondisjunction)
F84.3	Other childhood disintegrative disorder	Q92.2	Partial trisomy
F84.5	Asperger's syndrome	Q92.5	Duplications with other complex rearrangements
F84.8	Other pervasive developmental disorders	Q92.61	Marker chromosomes in normal individual
F84.9	Pervasive developmental disorder, unspecified	Q92.62	Marker chromosomes in abnormal individual
F88	Other disorders of psychological development	Q92.7	Triploidy and polyploidy
F89	Unspecified disorder of psychological development	Q92.8	Other specified trisomies and partial trisomies of autosomes
F90	Attention-deficit hyperactivity disorders	Q92.9	Trisomy and partial trisomy of autosomes, unspecified
F98.2	Other feeding disorders of infancy and childhood	Q93.0	Whole chromosome monosomy, nonmosaicism (meiotic nondisjunction)
F98.9	Unspecified behavioral and emotional disorders with onset usually occurring in childhood and adolescence	Q93.1	Whole chromosome monosomy, mosaicism (mitotic nondisjunction)
G11.1	Early-onset cerebellar ataxia	Q93.2	Chromosome replaced with ring, dicentric or isochromosome
G12.0	Infantile spinal muscular atrophy, type I [Werdnig-Hoffman]	Q93.3	Deletion of short arm of chromosome 4
G12.1	Other inherited spinal muscular atrophy	Q93.4	Deletion of short arm of chromosome 5
G31.84	Mild cognitive impairment, so stated	Q93.5	Other deletions of part of a chromosome
G71.0	Muscular Dystrophy	Q93.7	Deletions with other complex rearrangements
G71.00	Muscular dystrophy, unspecified	Q93.81	Velo-cardio-facial syndrome

G71.01	Duchenne or Becker muscular dystrophy	Q93.88	Other microdeletions
G71.02	Facioscapulohumeral muscular dystrophy	Q93.89	Other deletions from the autosomes
G71.09	Other specified muscular dystrophies	Q93.9	Deletion from autosomes, unspecified
G71.11	Myotonic muscular dystrophy	Q95.2	Balanced autosomal rearrangement in abnormal individual
G71.12	Myotonia congenita	Q95.3	Balanced sex/autosomal rearrangement in abnormal individual
G71.13	Myotonic chondrodystrophy	Q99.2	Fragile X chromosome
G71.14	Drug induced myotonia	Q99.8	Other specified chromosome abnormalities
G71.19	Other specified myotonic disorders	Q99.9	Chromosomal abnormality, unspecified
G71.2	Congenital myopathies	R27.9	Unspecified lack of coordination
G80.0	Spastic quadriplegic cerebral palsy	R62.0	Delayed milestone in childhood
G80.1	Spastic diplegic cerebral palsy	R62.50	Unspecified lack of expected normal physiological development in childhood
G80.2	Spastic hemiplegic cerebral palsy	R62.51	Failure to thrive (child)
G80.3	Athetoid cerebral palsy	R62.59	Other lack of expected normal physiological development in childhood
G80.4	Ataxic cerebral palsy	R63.3	Feeding difficulties
G80.8	Other cerebral palsy	T74.4XXA	Shaken infant syndrome, initial encounter
G80.9	Cerebral palsy, unspecified	T74.4XXD	Shaken infant syndrome, subsequent encounter
		T74.4XXS	Shaken infant syndrome, sequela