Dopamine Transporter Imaging with Single-Photon Emission Computed Tomography

Description
Dopamine transporter imaging with single-photon emission computed tomography (DaT-SPECT), using radiopharmaceutical ioflupane (123 I) injection, is a neuro-imaging modality being evaluated to improve the differential diagnosis of parkinsonian syndromes from nonparkinsonian tremor, as well as dementia with Lewy bodies from Alzheimer disease.

FDA REGULATORY STATUS
In 2011, DaTscan™ (GE Healthcare, Chicago, IL) was approved by the U.S. Food Drug Administration through a new drug application and is “indicated for striatal dopamine transporter visualization using single photon emission computed tomography brain imaging to assist in the evaluation of adult patients with suspected parkinsonian syndromes. In these patients, DaTscan may be used to help differentiate ET [essential tremor] from tremor due to parkinsonian syndromes (idiopathic Parkinson's disease, multiple system atrophy and progressive supranuclear palsy). DaTscan is an adjunct to other diagnostic evaluations.” U.S. Food Drug Administration product code: KPS.

POLICY STATEMENT
Dopamine transporter imaging with single-photon emission computed tomography is investigational for all indications, including but not limited to:

- aiding in the diagnosis of patients with clinically uncertain parkinsonian syndromes; OR
- distinguishing between parkinsonian syndromes and essential tremor; OR
- distinguishing between dementia with Lewy bodies and Alzheimer disease; OR
- monitoring of disease progression.

BENEFIT APPLICATION
Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).
FEP 6.01.54 Dopamine Transporter Imaging with Single-Photon Emission Computed Tomography

Rationale

Summary of Evidence

For individuals who have clinically uncertain Parkinson disease who receive DaT-SPECT, the evidence includes randomized controlled trials, cohort studies, and case series studies. Relevant outcomes are symptoms, functional outcomes, and treatment-related mortality and morbidity. Studies of technical validity have shown good interobserver reliability in interpreting images. In populations with clinically apparent Parkinson disease, studies of diagnostic accuracy have reported high sensitivity and specificity for Parkinson disease. Studies of clinical validity in the target population of clinically uncertain Parkinson disease have reported moderate sensitivity and high specificity. These findings are dependent on a reference standard (clinical diagnosis over time), and it is unknown whether DAT-SPECT would show greater sensitivity when assessed by the criterion standard (histopathologic diagnosis). Evidence on clinical utility in the target population includes a randomized controlled trial showing no significant difference in outcomes over time between patients who received a DaT-SPECT scan and those who did not. The evidence is insufficient to determine the effects of this technology on health outcomes.

For individuals who have clinically uncertain dementia with Lewy bodies who receive DaT-SPECT, the evidence includes randomized control trials, cohort studies, and case series studies. Relevant outcomes are symptoms, functional outcomes, and treatment-related mortality and morbidity. Relative to the criterion end point of histopathology, DaT-SPECT has lower sensitivity and higher specificity than expert clinical diagnosis in patients with likely dementia with Lewy bodies. No such studies have been performed in the target population of clinically uncertain dementia with Lewy Bodies. No studies have directly evaluated the effect of DaT-SPECT imaging on health outcomes in the target population. The evidence is insufficient to determine the effects of the technology on health outcomes.

Supplemental Information

Practice Guidelines and Position Statements

American College of Radiology

The American College of Radiology has published appropriateness criteria for dementia and movement disorders, last reviewed in 2015. The College has stated that the diagnosis of idiopathic Parkinson disease (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. The College has also stated that positron emission tomography and single-photon emission computed tomography (SPECT) tracer studies exploring the presynaptic nigrostriatal terminal function and the postsynaptic dopamine receptors have been unable to reliably classify the various parkinsonian syndromes; further, positron emission tomography and SPECT may not even be able to reliably measure disease progression. Use of dopamine transporter (DaT) imaging with SPECT was rated 5 (may be appropriate) to evaluate suspected dementia with Lewy bodies (DLB) and rated 3 (usually not appropriate) to evaluate 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 stated that β-CIT and IBZM (iodobenzamide) SPECT are possibly useful in distinguishing PD from essential tremor (5 class III studies). There was insufficient evidence to determine if these modalities are useful in distinguishing PD from other forms of parkinsonism.
Society of Nuclear Medicine and Molecular Imaging

The Society of Nuclear Medicine, now called the Society of Nuclear Medicine and Molecular Imaging, provided practice guidelines for DaT-SPECT in 2011. The guidelines stated that the main indication for DaT-SPECT is striatal DaT visualization in the evaluation of adults with suspected parkinsonian syndromes to help differentiate essential tremor from tremor due to presynaptic parkinsonian syndromes (PD, multisystem atrophy, progressive supranuclear palsy). Other indications are the early diagnosis of presynaptic parkinsonian syndromes, differentiation of presynaptic parkinsonian syndromes from parkinsonism without presynaptic dopaminergic loss (eg, drug-induced parkinsonism, psychogenic parkinsonism), and differentiation of DLB from Alzheimer disease. The guidance stated 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.

Movement Disorders Society

The Movement Disorder Society's (MDS) diagnostic criteria for PD from 2015 are intended for use in clinical research but can be used to guide clinical diagnosis. 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, anatomic neuroimaging, and methods to detect alpha-synuclein deposition. MDS noted that, although dopaminergic neuroimaging can help to distinguish parkinsonism from PD mimics like essential tremor, "it does not qualify as a criterion for the differentiation of PD from other parkinsonian conditions like atypical parkinsonian syndromes."

European Federation of Neurological Societies and Movement Disorder Society

The European Federation of Neurological Societies and Movement Disorder Society published joint recommendations on the diagnosis of PD in 2013. They provided a level A recommendation for the use of DaT-SPECT in the differential diagnosis between degenerative parkinsonism and essential tremor. The guidelines specified that DaT-SPECT is indicated in the presence of significant diagnostic uncertainty and particularly in patients presenting atypical tremor manifestations.

European Association of Nuclear Medicine

The European Association of Nuclear Medicine updated its guidelines on procedures for DaT-SPECT in 2010, based on expert opinion in European countries. The guidelines stated that iodine 123 N-(3-fluoropropyl)-2β-carbomethoxy-3β-(4-iodophenyl)nortropane (123I-FP-CIT) imaging is indicated for detecting loss of functional dopaminergic neuron terminals in the striatum of patients with clinically uncertain parkinsonian syndrome and for the differentiation of DLB from other dementias. Other indications were the early diagnosis of neurodegenerative parkinsonism, assessment of disease severity, and differentiation of presynaptic parkinsonism from other forms of parkinsonism (eg, neuroleptic-induced parkinsonism). The guidelines stated that, in addition to visual interpretation, semiquantitative analysis is recommended to objectively assess striatal DaT binding. Issues requiring further clarification include the assessment of disease progression and effects of treatments and methods for operator-independent definition of region of interest.

National Institute for Health and Care Excellence

The National Institute for Health and Care Excellence published guidance on the diagnosis and management of PD in 2006, which was updated in 2017. The 2006 guidance stated that 123I-FP-CIT SPECT should be considered for people with tremor where essential tremor cannot be clinically differentiated from parkinsonism (based on studies with level of evidence 1a or 1b); this guidance is continued in 2017 recommendations. In addition, the 2006 guidance stated that 123I-FP-CIT SPECT
FEP 6.01.54 Dopamine Transporter Imaging with Single-Photon Emission Computed Tomography

should be available to specialists with expertise in its use and interpretation (based on level of evidence IV, expert opinion); this too was unchanged in the 2017 update. The next expected update is April 2018.

The Institute updated its guidance on dementia in 2016. It recommended that $^{123}$I-FP-CIT SPECT be used to help establish the diagnosis in those with suspected DLB if the diagnosis is in doubt.

**Dementia of Lewy Bodies Consortium**
The Dementia of Lewy Bodies Consortium published clinical guidelines on diagnosis and management in 2017, based on American expert opinion. The guidelines stated that reduced dopamine transporter uptake in basal ganglia demonstrated by SPECT is an indicative biomarker. As such, dementia with abnormal DaT-SPECT imaging would be classified as possible DLB. Presence of an additional core clinical feature (fluctuating cognition, recurrent visual hallucinations, REM sleep disorder, parkinsonism motor abnormalities) in addition to dementia and abnormal DaT-SPECT imaging would allow classification as probable DLB. It was noted that patients with autopsy-confirmed DLB may have normal DaT-SPECT imaging.

**U.S. Preventive Services Task Force Recommendations**

Not applicable.

**Medicare National Coverage**

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

**REFERENCES**

FEP 6.01.54 Dopamine Transporter Imaging with Single-Photon Emission Computed Tomography


32. Tolosa E, Borgho TV, Moreno E. Accuracy of DaTSCAN (123I-ioflupane) SPECT in diagnosis of patients with clinically uncertain parkinsonism: 2-year follow-up of an open-label study. Mov Disord. Dec 2007;22(16):2346-2351. PMID 17914722
33. Galvin JE. Improving the clinical detection of Lewy body dementia with the Lewy Body Composite Risk Score. *Alzheimers Dement (Amst)*. Sep 01 2015;1(3):316-324. PMID 26405688

The policies contained in the FEP Medical Policy Manual are developed to assist in administering contractual benefits and do not constitute medical advice. They are not intended to replace or substitute for the independent medical judgment of a practitioner or other health care professional in the treatment of an individual member. The Blue Cross and Blue Shield Association does not intend by the FEP Medical Policy Manual, or by any particular medical policy, to recommend, advocate, encourage or discourage any particular medical technologies. Medical decisions relative to medical technologies are to be made strictly by members/patients in consultation with their health care providers. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that the Blue Cross and Blue Shield Service Benefit Plan covers (or pays for) this service or supply for a particular member.
FEP 6.01.54 Dopamine Transporter Imaging with Single-Photon Emission Computed Tomography

The policies contained in the FEP Medical Policy Manual are developed to assist in administering contractual benefits and do not constitute medical advice. They are not intended to replace or substitute for the independent medical judgment of a practitioner or other health care professional in the treatment of an individual member. The Blue Cross and Blue Shield Association does not intend by the FEP Medical Policy Manual, or by any particular medical policy, to recommend, advocate, encourage or discourage any particular medical technologies. Medical decisions relative to medical technologies are to be made strictly by members/patients in consultation with their health care providers. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that the Blue Cross and Blue Shield Service Benefit Plan covers (or pays for) this service or supply for a particular member.

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>December 2012</td>
<td>New Policy</td>
<td>Updated policy with literature review. Added reference 19 and 24. No change to policy statement or summary.</td>
</tr>
<tr>
<td>December 2013</td>
<td>Update Policy</td>
<td>Policy updated with literature review; reference 6 added; policy statement unchanged.</td>
</tr>
<tr>
<td>December 2014</td>
<td>Update Policy</td>
<td>Policy updated with literature review; reference 19 and 24. No change to policy statement or summary.</td>
</tr>
<tr>
<td>December 2016</td>
<td>Update Policy</td>
<td>Policy updated with literature review; references 33, 35, 39, 41, and 45 added; reference 38 updated. Policy statement unchanged.</td>
</tr>
<tr>
<td>December 2017</td>
<td>Update Policy</td>
<td>Policy updated with literature review through July 21, 2017; Rationale revised and several references added. Policy statement unchanged.</td>
</tr>
</tbody>
</table>