Protocol

Dopamine Transporter Imaging With Single-Photon Emission Computed Tomography

(60154)

Medical Benefit		**Effective Date**: 04/01/19	**Next Review Date**: 01/21
Preauthorization	No	**Review Dates**: 09/14, 09/15, 09/16, 09/17, 09/18, 01/19, 01/20	

Preauthorization is not required.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.

Populations	Interventions	Comparators	Outcomes
Individuals: • With clinically uncertain Parkinson disease	Interventions of interest are: • Dopamine transporter single-photon emission computed tomography	Comparators of interest are: • Standard diagnostic workup without dopamine transporter single-photon emission computed tomography	Relevant outcomes include: • Symptoms • Functional outcomes • Treatment-related mortality • Treatment-related morbidity
Individuals: • With clinically uncertain dementia with Lewy bodies	Interventions of interest are: • Dopamine transporter single-photon emission computed tomography	Comparators of interest are: • Standard diagnostic workup without dopamine transporter single-photon emission computed tomography	Relevant outcomes include: • Symptoms • Functional outcomes • Treatment-related mortality • Treatment-related morbidity

DESCRIPTION

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

SUMMARY OF EVIDENCE

For individuals who have clinically uncertain Parkinson disease (PD) who receive DaT-SPECT, the published evidence includes randomized controlled trials (RCTs), cohort studies, and case series studies. Relevant outcomes are symptoms, functional outcomes, and treatment-related mortality and morbidity. In populations with clinically apparent PD, studies of diagnostic accuracy have reported high sensitivity and specificity for PD. Studies of clinical validity in the target population of clinically uncertain PD are limited by gaps in study design, conduct, and relevance. Evidence on clinical utility in the target population includes an RCT showing no significant difference in outcomes over time between patients who received a DaT-SPECT scan and those who did not. Evidence reported through clinical input augments the published evidence by highlighting that the published RCT also reported changes in management following DaT-SPECT imaging that may translate to improvements in health

outcomes over time, and the one-year study follow-up may be too short to demonstrate significant improvement in quality of life in a slowly progressive disease such as PD. Clinical input further supports that DaT-SPECT offers clinically valid diagnostic information about the presence or absence of functional loss in the dopamine system (i.e., nigrostriatal degeneration) and is clinically useful for clinically uncertain Parkinson syndrome when a negative result on DaT-SPECT is used to inform treatment decisions by reducing or avoiding unnecessary dopaminergic therapy. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have clinically uncertain dementia with Lewy bodies who receive DaT-SPECT, the published evidence includes RCTs, cohort studies, and case series studies. Relevant outcomes are symptoms, functional outcomes, and treatment-related mortality and morbidity. 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 on health outcomes in the target population. Evidence reported through clinical input augments the published evidence by supporting that DaT-SPECT offers clinically valid diagnostic information about the presence or absence of functional loss in the dopamine system (i.e., nigrostriatal degeneration) and is clinically useful for clinically uncertain dementia with Lewy bodies using a chain of evidence where a positive result on DaTSPECT is used to inform treatment decisions by avoiding potentially harmful use of neuroleptics typically used in dementia patients. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

POLICY

Dopamine transporter imaging with single-photon emission computed tomography may be considered **medically necessary** when used for individuals with:

- clinically uncertain Parkinson disease; or
- clinically uncertain dementia with Lewy bodies.

Use of dopamine transporter imaging with single-photon emission computed tomography is considered **investigational** for all other indications not included above.

BACKGROUND

PARKINSON DISEASE

Parkinsonian syndromes are a group of diseases that share similar cardinal signs, characterized by bradykinesia, rigidity, resting tremor, and gait disturbance. PD is the most common cause of parkinsonism.

Diagnosis

Despite the well-known symptoms of PD, diagnosis is challenging even for experienced clinicians, particularly in the early stages of the disease. In addition, other etiologies such as essential tremor, corticobasal degeneration, multiple system atrophy, progressive supranuclear palsy, vascular parkinsonism, and drug-induced parkinsonism can lead to a similar set of symptoms.

While the criterion standard is postmortem histopathology, clinical diagnosis may be used as an interim reference standard. The accuracy of the diagnosis is influenced by the duration of the symptoms and the clinician's experience. Even in specialized movement disorders centers, up to 25% of patients may be misclassified, and some patients (e.g., those with essential tremor who have been diagnosed with PD) may be erroneously treated.[1] Such misclassifications have led to the call for additional diagnostic tests and biomarkers to improve

the accuracy of clinical diagnosis of PD and other parkinsonian syndromes. One recent approach is to evaluate the integrity of dopaminergic pathways in the brain using dopamine transporter imaging with single-photon emission computed tomography (DaT-SPECT) imaging.

DEMENTIA WITH LEWY BODIES

Dementia with Lewy bodies (DLB) is a type of dementia characterized by parkinsonism, visual hallucinations, cognitive fluctuation, sleep disorders, and severe neuroleptic sensitivity. DLB is the second most common form of degenerative dementia; Alzheimer disease, which can have similar symptoms at onset, is the most common.

Diagnosis

Diagnosis can be challenging, particularly when patients have multiple comorbidities including cerebrovascular disease and/or Alzheimer disease.[2] As with PD, DLB is characterized by the degeneration of nigrostriatal neurons; as such, DaT-SPECT is also proposed to differentiate DLB from Alzheimer disease. Misdiagnosis of DLB is concerning because some have noted a severe sensitivity (potentially life-threatening) to neuroleptics 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 Alzheimer disease.

DaT-SPECT

DaT-SPECT is based on the selective affinity of DaT ligands for dopamine-synthesizing neurons, which allows visualization of deficits in the nigrostriatal dopaminergic pathway.

DaT ligands include iodine 123I-2β-carbomethoxy-3β-(4-iodophenyl) tropane (123I-β-CIT), which is a cocaine analogue with an affinity for both dopamine and serotonin transporters. Intravenous 123I-β-CIT requires a delay between injection and scan of about 24 hours. Iodine-123 N-(3-fluoropropyl)-2β-carbomethoxy-3β-(4-iodophenyl) nortropane (123I-FP-CIT) is a fluoropropyl derivate of β-CIT that is selective for brain striatal DaT but can also bind to the serotonin transporter. Intravenous 123I-FP-CIT can be injected three to six hours before the scan (DaTscan). Other SPECT ligands with affinity for dopamine transporter include technetium 99m (2β((N,N¢-bis(2-mercaptoethyl) ethylene diamino)methyl) and 3β-(4-chlorophenyl) tropane (99mTc-TRODAT-1).[3,4]

Binding of ligands with an affinity for DaT ligands in the striatum is, in general, reduced in PD, genetic parkinsonism, DLB, corticobasal degeneration, progressive supranuclear palsy, and multiple system atrophy. In contrast, striatal DaT ligand binding is expected to be within the normal range of Alzheimer disease, essential tremor, dystonic tremor, orthostatic tremor, drug-induced parkinsonism, and psychogenic parkinsonism.[3]

Visualization of striatal dopamine transporter binding, through DaT-SPECT, permits assessment of presynaptic dopaminergic deficit. It is proposed that an abnormal DaT-SPECT scan supports the diagnosis of PD, DLB, or other neurodegenerative parkinsonian syndromes, while a normal DaT-SPECT scan in a symptomatic patient supports the diagnosis of a disease not affecting the nigrostriatal dopaminergic pathway.

Analysis of DaT-SPECT images can be visual, semiquantitative, or quantitative. In patients with PD, physical symptoms start after 30% to 50% of dopaminergic neurons have degenerated.[5,6] Symptomatic patients with PD would be thus expected to have sufficient abnormality on DaT-SPECT for visual analysis to be adequate for interpretation. 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 for analysis and the development of an atlas for visual interpretation. Several research centers are developing quantitative and semiquantitative classification methods for the evaluation of DaT-SPECT images.[7-10]

Anatomic variation in the brain, including vascular lesions, may interfere with the distribution of the iodine-123 tracer and could result in an abnormal scan.[11] Dopamine agonists and levodopa may also affect DaT expression, which could influence the ability of DaT-SPECT to monitor the progression of disease unless these agents are discontinued prior to imaging. Patients with clinically diagnosed PD or DLB, who present with a normal

DaTSPECT scan, are referred to in the literature as having "scans without evidence of dopaminergic deficit." While many of these patients are ultimately diagnosed with non-PD syndromes, a portion of patients with normal DaT-SPECT imaging are confirmed to have PD or DLB by the reference standard. In studies where clinical diagnosis is used as an endpoint, scans without evidence of dopaminergic deficit are present in 3% to 20% of PD patients.[12] In a study of patients clinically diagnosed with DLB, van der Zande et al (2016) found that 10% of these patients had normal scans.[13] Further research may shed light on these cases.

REGULATORY STATUS

In 2011, DaTscan™ (GE Healthcare) 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."[14]

U.S. Food Drug Administration product code: KPS.

RELATED PROTOCOL

Deep Brain Stimulation

Services that are the subject of a clinical trial do not meet our Technology Assessment and Medically Necessary Services Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment and Medically Necessary Services Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

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We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

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