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# MEDICAL POLICY – 6.01.54

# Dopamine Transporter Single-Photon Emission Computed Tomography

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|---|---|---|
| BCBSA Ref. Policy: | 6.01.54 | |
| Effective Date: | Jan. 1, 2025 | RELATED MEDICAL POLICIES: |
| Last Revised: | Dec. 9, 2024 | 7.01.63 Deep Brain Stimulation |
| Replaces: | N/A | |

**Select a hyperlink below to be directed to that section.**

POLICY CRITERIA | DOCUMENTATION REQUIREMENTS | CODING
RELATED INFORMATION | EVIDENCE REVIEW | REFERENCES | HISTORY

Clicking this icon returns you to the hyperlinks menu above.

## Introduction

DAT-SPECT imaging is proposed as a way to look at certain brain functions. In this technique, a chemical containing a tiny amount of radioactivity is injected into a vein. Nerve cells (neurons) in the brain that are associated with dopamine take up this radioactivity. A special camera then captures images of the dopamine neurons. It's known that there is a substantial decrease in the dopamine-producing neurons in Parkinson disease. DAT-SPECT may be medically necessary when a healthcare provider is clinically uncertain of a diagnosis of Parkinson syndrome or dementia with Lewy bodies. DAT-SPECT has also been studied for other conditions, such as essential tremor or Alzheimer disease. DAT-SPECT is considered investigational (unproven) in many situations. This policy describes when DAT-SPECT may be considered medically necessary.

**Note:** The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

## Policy Coverage Criteria

| Imaging | Medical Necessity |
|---|---|
| **Dopamine transporter imaging with single photon emission computed tomography (DaT-SPECT)** | **Dopamine transporter imaging with single-photon emission computed tomography (DaT-SPECT) may be considered medically necessary when used for individuals with:**<br>• Clinically uncertain Parkinson disease;<br>**OR**<br>• Clinically uncertain dementia with Lewy bodies<br><br>**Use of dopamine-transporter imaging with single-photon emission computed tomography is considered investigational for all other indications not included above.** |

| Documentation Requirements |
|---|
| **The individual's medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following:**<br>• Office visit notes that contain the relevant history and physical supporting:<br>  ○ Clinically uncertain Parkinson disease; or<br>  ○ Clinically uncertain dementia with Lewy bodies |

## Coding

| Code | Description |
|---|---|
| **CPT** | |
| 78803 | Radiopharmaceutical localization of tumor, inflammatory process or distribution of radiopharmaceutical agent(s) (includes vascular flow and blood pool imaging, when performed); tomographic (SPECT), single area (e.g., head, neck, chest, pelvis), single day imaging |
| **HCPCS** | |
| A9584 | Iodine I-123 ioflupane, diagnostic, per study dose, up to 5 millicuries |

**Note**: CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

## Related Information

In July 2021, aducanumab (Aduhelm; Biogen), received US Food and Drug Administration (FDA) accelerated approval and in July 2023, lecanemab-irmb- (Leqembi; Esai) received FDA approval as an amyloid beta-targeted antibodies for the treatment of mild cognitive impairment or mild dementia due to Alzheimer disease. A third anti-amyloid antibody product, donanemab-azbt, was approved by the FDA in July 2024. Aducanumab was subsequently discontinued by the manufacturer in 2024. The safety and efficacy of aducanumab or lecanemab in individuals with dementia with Lewy bodies has not been established as participants with any medical or neurological condition other than Alzheimer disease that might be a contributing cause to the subject's cognitive impairment were excluded from trials. The use of dopamine transporter imaging with single-photon emission computed tomography (DaT-SPECT) for the diagnosis, management, or surveillance of Alzheimer disease is considered out of scope for this policy.

### Definition of Terms

**Dopamine:** An organic chemical that acts as a neurotransmitter in the brain and is involved with body movement. Destruction of dopamine neurons produces the symptoms of Parkinson's disease.

**Parkinsonian syndromes (PS):** A group of diseases that share similar fundamental symptoms of slow movement (bradykinesia), rigidity, tremor at rest, and trouble walking.

## Evidence Review

### Description

Dopamine transporter imaging with single-photon emission computed tomography (DaT-SPECT) using radiopharmaceutical ioflupane 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.

# Background

## Parkinsonian Syndromes

Parkinsonian syndromes 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.

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. One recent approach to improve the accuracy of clinical diagnosis of PD and other parkinsonian syndromes is to evaluate the integrity of dopaminergic pathways in the brain using 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 can be challenging, particularly when individuals have multiple comorbidities including cerebrovascular disease and/or Alzheimer disease.[1] 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.

## Dopamine Transporter Imaging with Single-Photon Emission Computed Tomography (DaT-SPECT)

DaT-SPECT is based on the selective affinity of dopamine transporter (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 ($^{123}$I-β-CIT), which is a cocaine analogue with an affinity for both dopamine and serotonin transporters. Intravenous

$^{123}$I-β-CIT requires a delay between injection and scan of about 24 hours. Iodine-123 N-(3-fluoropropyl)-2β-carbomethoxy-3β-(4-iodophenyl) nortropane ($^{123}$I-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 $^{123}$I-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 ($^{99m}$Tc-TRODAT-1).[2,3]

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 in Alzheimer disease, essential tremor, dystonic tremor, orthostatic tremor, drug-induced parkinsonism, and psychogenic parkinsonism.[2]

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 individual supports the diagnosis of a disease not affecting the nigrostriatal dopaminergic pathway.

Analysis of DaT-SPECT images can be visual, semiquantitative, or quantitative. In individuals with PD, physical symptoms start after 30% to 50% of dopaminergic neurons have degenerated.[4,5] Symptomatic individuals 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.[6,7,8,9]

Anatomic variation in the brain, including vascular lesions, may interfere with distribution of the iodine-123 tracer and could result in an abnormal scan.[10] 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. Individuals with clinically diagnosed PD or DLB, who present with a normal DaT-SPECT scan, are referred to in the literature as having "scans without evidence of dopaminergic deficit." While many of these individuals are ultimately diagnosed with non-PD syndromes, a portion of individuals 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 end point, scans without evidence of dopaminergic deficit are present in 3% to 20% of PD individuals.[11] In a study of individuals clinically diagnosed

with DLB, van der Zande et al (2016) found that 10% of these individuals had normal scans.[12] Further research may shed light on these cases.

## 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. The 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 individuals who received a DaT-SPECT scan and those who did not. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have clinically uncertain DLB who receive DaT-SPECT, the published evidence includes RCTs, cohort studies, and case series. The relevant outcomes are symptoms, functional outcomes, and treatment-related mortality and morbidity. No studies with the optimal reference standard to assess clinical validity have been performed in the target population of clinically uncertain DLB. No studies have directly evaluated the effect of DaT-SPECT on health outcomes in the target population. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

## Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this policy are listed in **Table 1**.

## Table 1. Summary of Key Trials

| NCT No. | Trial Name | Planned Enrollment | Completion Date |
|---|---|---|---|
| **Ongoing** | | | |

| NCT No. | Trial Name | Planned Enrollment | Completion Date |
|---|---|---|---|
| NCT01453127 | DaTSCAN Imaging in Aging and Neurodegenerative Disease | 500 | Dec 2025 |
| NCT02305147 | Cohort Study to Identify Predictor Factors of Onset and Progression of Parkinson's Disease (ICEBERG) | 360 | Nov 2024 |
| **Unpublished** | | | |
| NCT04193527[a] | A Multicentre, Phase 3, Clinical Study to Compare the Striatal Uptake of a Dopamine Transporter Radioligand, DaTSCAN Ioflupane (123I) Injection, After Intravenous Administration to Chinese Patients With a Diagnosis of Parkinson's Disease, Multiple System Atrophy, Progressive Supranuclear Palsy, or Essential Tremor and to Healthy Controls | 172 | Dec 2021 |

NCT: national clinical trial. [a]Denotes industry sponsored or co-sponsored trial

## Clinical Input Received from Physician Specialty Societies and Academic Medical Centers

### 2018 Input

Clinical input was sought to help determine whether the use of DaT-SPECT in individuals with clinically uncertain PD or clinically uncertain DLB would provide a clinically meaningful improvement in net health outcome and whether the use is consistent with generally accepted medical practice. In response to requests, clinical input was received from three respondents, including one specialty society-level response and two physician-level responses identified through specialty societies.

In individuals who have clinically uncertain PD who receive DaT-SPECT, clinical input supports that DaT-SPECT is clinically useful when a negative result on DaT-SPECT is used to inform treatment decisions by reducing or avoiding unnecessary dopaminergic therapy. Clinical input highlights 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.

In individuals who have clinically uncertain DLB who receive DaT-SPECT, clinical input supports that DaT-SPECT is clinically useful when a positive result on DaT-SPECT is used to inform treatment decisions by avoiding potentially harmful use of neuroleptics which may be used in dementia patients. Clinical input noted 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 DLB using a chain of evidence where a positive result on DaT-SPECT is used to inform treatment decisions by avoiding potentially harmful use of neuroleptics typically used in dementia patients.

## Practice Guidelines and Position Statements

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Guidelines or position statements will be considered for inclusion if they were issued by, or jointly by, a US professional society, an international society with US representation, or the National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

## American College of Radiology

In 2019, the American College of Radiology updated the appropriateness criteria for movement disorders and neurodegenerative diseases.[42] The College categorized Ioflupane SPECT/CT as 'may be appropriate' for initial imaging of Parkinsonian syndrome. A strength of evidence rating was not given for this statement.

The American College of Radiology (2019) updated the appropriateness criteria for dementia.[43,] The College categorized Ioflupane SPECT or SPECT/CT brain as 'may be appropriate' for initial imaging for suspected DLB. A strength of evidence rating was not given for this statement.

## Dementia of Lewy Bodies Consortium

In 2017, the Dementia of Lewy Bodies Consortium published clinical guidelines on diagnosis and management, based on American expert opinion.[44] The guidelines stated that reduced DaT 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. The presence of another core clinical feature (fluctuating cognition, recurrent visual hallucinations, rapid eye-movement sleep disorder, parkinsonism motor abnormalities) in addition to dementia and abnormal DaT-SPECT imaging would allow classification as probable DLB. It was noted that individuals with autopsy-confirmed DLB may have normal DaT-SPECT imaging.

## Movement Disorders Society

In 2015, the Movement Disorders Society's (MDS) diagnostic criteria for PD are intended for use in clinical research but may be used to guide clinical diagnosis.[15] The MDS considers clinical expert opinion to be the criterion standard to diagnose PD and that diagnoses are usually made clinically without ancillary diagnostic testing. Methods that may become available as knowledge advances are diagnostic biochemical markers, anatomic neuroimaging, and methods to detect alpha-synuclein deposition. Normal functional neuroimaging of the presynaptic dopaminergic system, if performed, is listed as an absolute exclusion criterion for PD. 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." Normal functional neuroimaging of the presynaptic dopaminergic system is also listed as criteria for exclusion from diagnosis of PD in individuals with early/de novo PD.[45]

In 2023, the MDS published a statement on the biological definition, staging and classification of PD.[46] The document mentions dopamine imaging but states that its use is not widespread enough to be included in a staging or classification schema.

## National Institute for Health and Clinical Evidence

In 2006, the NICE published guidance on the diagnosis and management of PD[47], which was updated in 2017.[48,49] The 2006 guidance stated that iodine 123 N-(3-fluoropropyl)-2β-carbomethoxy-3β-(4-iodophenyl) nortropane ($^{123}$I-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 recommendation is continued in 2017 guidance. Also unchanged was the recommendation that $^{123}$I-FP-CIT SPECT should be available to specialists with expertise in its use and interpretation (based on level of evidence IV, expert opinion).

The NICE updated its 2016 guidance on dementia in 2018.[50] It recommended that $^{123}$I-FP-CIT SPECT be used to help establish the diagnosis in those with suspected DLB if the diagnosis is uncertain.

## Society of Nuclear Medicine and Molecular Imaging et al

In 2020, the Society of Nuclear Medicine and Imaging and the European Association of Nuclear Medicine published a joint practice guideline and procedure standard for dopaminergic imaging in Parkinsonian syndromes.[51] The guideline indicated presynaptic dopaminergic imaging for "detecting loss of nigrostriatal dopaminergic neuron terminals of patients with parkinsonian syndromes, especially:

- To support the differential diagnosis between essential tremor and neurodegenerative parkinsonian syndromes. Note that presynaptic dopaminergic imaging is unable to distinguish IPD [idiopathic Parkinson disease] and DLB [dementia with Lewy bodies] from PSP [progressive supranuclear palsy], CBD [corticobasal degeneration], or putaminal variant of MSA [multiple system atrophy];
- To help distinguish between dementia with Lewy bodies and other dementias (in particular, Alzheimer's disease, AD);
- To support the differential diagnosis between parkinsonism due to presynaptic degenerative dopamine deficiency and other forms of parkinsonism, e.g., between IPD and drug-induced, psychogenic, or vascular parkinsonism;
- To detect early presynaptic parkinsonian syndromes."

In 2011, the Society of Nuclear Medicine, now called the Society of Nuclear Medicine and Molecular Imaging, provided practice guidelines for DaT-SPECT.[52] 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, multiple-system atrophy, progressive supranuclear palsy). Other indications are the early diagnosis of presynaptic parkinsonian syndromes, differentiation of presynaptic parkinsonian syndromes from parkinsonism without a presynaptic

dopaminergic loss (e.g., 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.

## Medicare National Coverage

There is no national coverage determination.

## Regulatory Status

In 2011, DaTscan (GE Healthcare) was approved by the US Food Drug Administration (FDA) 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 individuals with suspected parkinsonian syndromes. In these individuals, 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."[13] In 2022, DaTscan was approved for use in patients with suspected dementia with Lewy bodies.

In July 2021, aducanumab (Aduhelm; Biogen), an amyloid beta-targeted antibody, was approved for the treatment of mild cognitive impairment or mild dementia due to Alzheimer disease. In July 2023, lecanemab-irmb (Leqembi; Esai) received FDA approval as amyloid beta-targeted antibodies for the treatment of mild cognitive impairment or mild dementia due to Alzheimer disease. A third anti-amyloid antibody product, donanemab-azbt, was approved by the FDA in July 2024. Aducanumab was subsequently discontinued by the manufacturer in 2024. The safety and efficacy of aducanumab, lecanemab, or donanemab in individuals with DLB has not been established as individuals with any medical or neurological condition other than Alzheimer disease that might be a contributing cause to the subject's cognitive impairment were excluded from trials. The use of DaT-SPECT for the diagnosis, management, or surveillance of Alzheimer disease is considered out of scope for this policy.

FDA product code: KPS.

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## History

| Date | Comments |
|---|---|
| 10/15/12 | New policy. Policy created with literature review through March 2012; considered investigational. |
| 09/27/13 | Policy updated with literature review through May 28, 2013; references 19 and 23 added; policy statement unchanged. |

| Date | Comments |
|---|---|
| 09/23/14 | Annual Review. Policy updated with literature review through June 6, 2014; reference 6 added; policy statement unchanged. |
| 12/08/15 | Annual Review. Policy updated with literature review through June 4, 2015; references 5, 7, 10-11, 13, 15, 22-25, 31, and 33 added. Clinical input reviewed. Policy statement unchanged. |
| 11/01/16 | Annual Review, approved October 11, 2016. Added related policy 6.01.502. Policy updated with literature review through July 24, 2016; references added. Policy statement unchanged. |
| 12/01/17 | Annual Review, approved November 9, 2017. Policy updated with literature review through July 21, 2017; Several references added. Policy statement unchanged. |
| 01/01/19 | Annual Review, approved December 13, 2018. Policy updated with literature review through August 2018. Policy updated with clinical input and change to policy statements to medically necessary for clinically uncertain Parkinson disease and clinically uncertain dementia with Lewy bodies; reference 39 added; references 26 and 43 updated. |
| 12/01/19 | Annual Review, approved November 6, 2019. Policy updated with literature review through July 2019; no references added. Policy statements unchanged. |
| 01/01/20 | Coding update, added note that CPT code 78607 terminated 1/1/20. |
| 02/01/20 | Coding update, added CPT code 78803. |
| 01/01/21 | Annual Review, approved December 17, 2020. Removed CPT code 78607. |
| 01/01/22 | Annual Review, approved December 2, 2021. Policy updated with literature review through August 20, 2021; reference added. Policy statements unchanged. |
| 08/01/22 | Minor edit. Removed 6.01.502 Single Photon Emission Computed Tomography (SPECT) for Non-cardiac Indications from related policies due to archival. |
| 01/01/23 | Annual Review, approved December 12, 2022. Policy updated with literature review through September 6, 2022; no references added. Policy statements unchanged. Changed the wording from "patient" to "individual" throughout the policy for standardization. |
| 01/01/24 | Annual Review, approved December 11, 2023. Policy updated with literature review through August 28, 2023; no references added. Policy statements unchanged. |
| 01/01/25 | Annual Review, approved December 9, 2024. Policy updated with literature review through August 26, 2024; references added. Policy statements unchanged. Title changed to Dopamine Transporter Single-Photon Emission Computed Tomography. |

and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). 

**Scope**: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.