

## Corporate Medical Policy

### Dopamine Transporter Imaging with Single Photon Emission Computed Tomography

**File Name:** dopamine\_transporter\_imaging\_with\_single\_photon\_emission\_computed\_tomography  
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**Last CAP Review:** 5/2019  
**Next CAP Review:** 5/2020  
**Last Review:** 5/2019

#### Description of Procedure or Service

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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.

##### **Parkinson Disease**

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 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 (eg, those with essential tremor who have been diagnosed with PD) may be erroneously treated. 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.

DaT-SPECT is based on the selective affinity of dopamine transporter ligands for dopamine synthesizing neurons, which allows visualization of deficits in the nigrostriatal dopaminergic pathway. DaT ligands include iodine 123I-2 $\beta$ -carbomethoxy-3 $\beta$ -(4-iodophenyl) tropine (<sup>123</sup>I- $\beta$ -CIT), which is a cocaine analogue with an affinity for both dopamine and serotonin transporters. Intravenous <sup>123</sup>I- $\beta$ -CIT requires a delay between injection and scan of about 24 hours. Iodine-123 N-(3-fluoropropyl)-2 $\beta$ -carbomethoxy-3 $\beta$ -(4-iodophenyl) nortropine (<sup>123</sup>I-FP-CIT) is a fluoropropyl derivate of  $\beta$ -CIT that is selective for brain striatal DaT but can also bind to the serotonin transporter. Intravenous <sup>123</sup>I-FP-CIT can be injected 3 to 6 hours before the scan (DaTscan). Other SPECT ligands with affinity for dopamine transporter include technetium 99m (2 $\beta$ -(N,N $\phi$ -bis(2-mercaptoethyl) ethylene diamino) methyl) and 3 $\beta$ -(4-chlorophenyl) tropine (<sup>99m</sup>Tc-TRODAT-1).

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Binding of ligands with 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.

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 syndrome, 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. 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.

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. 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 DaT-SPECT 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 end point, scans without evidence of dopaminergic deficit are present in 3% to 20% of PD patients. In a study of patients clinically diagnosed with DLB, van der Zande et al (2016) found that 10% of these patients had normal scans. Further research may shed light on these cases.

## Regulatory Status

DaTscan™ (GE Healthcare) was approved by the U.S. Food and Drug Administration (FDA) in 2011 through a new drug application 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. 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.”

**\*\*\*Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

## Policy

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**BCBSNC will provide coverage for Dopamine Transporter Imaging with Single Photon Emission Computed Tomography (DAT-SPECT) when it is determined to be medically necessary because the medical criteria and guidelines shown below are met.**

## Benefits Application

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This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit

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design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

## When Dopamine transporter imaging with single photon emission computed tomography is covered

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

- clinically uncertain Parkinson disease when ordered by a neurologist with expertise in diagnosing and treating movement disorders; or
- clinically uncertain dementia with Lewy bodies, when ordered by a physician with expertise in diagnosing and treating dementia (eg, neurologist, geriatrician).

## When Dopamine transporter imaging with single photon emission computed tomography is not covered

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

## Policy Guidelines

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For individuals who have clinically uncertain Parkinson disease who receive DaT-SPECT, the published evidence includes randomized controlled trials, cohort studies, and case series studies. Relevant outcomes are symptoms, functional outcomes, and treatment-related mortality and morbidity. 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 are limited by gaps in study design, conduct, and relevance. 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. Evidence reported through clinical input augments the published evidence by highlighting that the published randomized controlled trial also reported changes in management following DaT-SPECT imaging that may translate to improvements in health outcomes over time, and the 1-year study follow-up may be too short to demonstrate significant improvement in quality of life in a slowly progressive disease such as Parkinson disease. Clinical input further supports that DaT-SPECT offers clinically valid diagnostic information about the presence or absence of functional loss in the dopamine system (ie, 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 randomized control trials, 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 (ie, 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. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

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## Billing/Coding/Physician Documentation Information

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This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at [www.bcbnsnc.com](http://www.bcbnsnc.com). They are listed in the Category Search on the Medical Policy search page.

*Applicable Codes: 78803, 78830, 78831, 78832, 78835*

*There is a specific HCPCS code for DaTscan: A9584*

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

## Scientific Background and Reference Sources

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BCBSA Medical Policy Reference Manual [Electronic Version]. 6.01.54, 8/9/12

BCBSA Medical Policy Reference Manual [Electronic Version]. 6.01.54, 7/11/13

Specialty Matched Consultant Advisory Panel 7/2014

BCBSA Medical Policy Reference Manual [Electronic Version]. 6.01.54, 7/10/14

Specialty Matched Consultant Advisory Panel 6/2015

BCBSA Medical Policy Reference Manual [Electronic Version]. 6.01.54, 11/12/15

BCBSA Medical Policy Reference Manual [Electronic Version]. 6.01.54, 9/08/16

GE Healthcare. DaTscan Ioflupane I123 Injection Full Prescribing Information. 2015: [http://www3.gehealthcare.com/en/products/categories/nuclear\\_imaging\\_agents/datscan](http://www3.gehealthcare.com/en/products/categories/nuclear_imaging_agents/datscan).

BCBSA Medical Policy Reference Manual [Electronic Version]. 6.01.54, 10/12/2017

BCBSA Medical Policy Reference Manual [Electronic Version]. 6.01.54, 11/8/2018

## Policy Implementation/Update Information

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10/16/12 New policy issued. Dopamine transporter imaging with single photon emission computed tomography (DAT-SPECT) is investigational for all indications, including but not limited to, aiding in the diagnosis of patients with clinically uncertain parkinsonian syndromes, essential tremor, or dementia with Lewy bodies, and for the monitoring of disease progression. Medical Director review 10/2012. Notification given 10/16/12 for policy effective date of 1/15/13. (sk)

2/12/13 Added diagnosis codes 331 – 333.99 to Billing/Coding section. (sk)

7/1/13 ICD-10 diagnosis codes added to Billing/Coding section. (sk)

9/10/13 Reference added. No change to Policy guideline. (sk)

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- 8/12/14 Specialty Matched Consultant Advisory Panel review 7/29/14. Removed effective date 10/1/2014 from ICD-10 list. No change to Policy statement. (sk)
- 10/14/14 Reference added. No change to Policy statement. (sk)
- 3/10/15 Added diagnosis code 781.0; as well as ICD-10 diagnosis codes: R25.0, R25.1, R25.2, R25.3, R25.8, R25.9 to the Billing/Coding section. (lpr)
- 7/28/15 Specialty Matched Consultant Advisory Panel review 6/24/2015. No change to policy statement. (lpr)
- 1/26/16 Reference added. Added Alzheimer's disease to list of "including but not limited to" investigational indications under "When Not Covered" section. Sr. Medical Director review 11/2015. (lpr)
- 7/26/16 Specialty Matched Consultant Advisory Panel review 6/29/2016. No change to policy statement. (an)
- 11/22/16 Reference added. (an)
- 6/30/17 Specialty Matched Consultant Advisory Panel review 5/31/2017. No change to policy statement. (an)
- 6/29/18 Description section revised. Policy Guidelines updated. References added. Specialty Matched Consultant Advisory Panel review 5/23/2018. No change to policy statement. (an)
- 7/1/19 Description section revised. Policy statement changed to read: "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 when ordered by a physician with expertise in diagnosing and treating movement disorders or dementia." Policy Guidelines section updated. Reference added. Diagnosis codes removed from Billing/Coding section. Specialty Matched Consultant Advisory Panel review 5/15/2019. (an)
- 12/31/19 Coding section updated to remove deleted code 78607. Added new codes 78830, 78831, 78832, 78835. (eel)
- 1/14/20 Coding section updated to include new code 78803. (eel)

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Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.