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Subject: Dopamine Transporter Imaging with Single-Photon Emission Computed Tomography

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Position Statement	Billing/Coding	Reimbursement	Program Exceptions	Definitions	Related Guidelines
Other	References	Updates			

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.

Dopamine transporter imaging with single-photon emission computed tomography (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.

Dopamine transporter ligands include iodine 123 2 β -carbomethoxy-3 β -(4-iodophenyl) tropane (123I- β -CIT), which is a cocaine analogue with affinity for both dopamine transporter and serotonin transporters. Intravenous 123I- β -CIT requires a delay between injection and scan of about 24 hours. Iodine 123 N-(3-fluoropropyl)-2 β -carbomethoxy-3 β -(4-iodophenyl)nortropane (123I-FP-CIT) is a fluoropropyl derivate of β -CIT that is selective for brain striatal dopamine transporter, but can also bind to the serotonin transporter. Intravenous 123I-FP-CIT can be injected 3 to 6 hours before the scan (DaTscan). Other ligands with affinity for dopamine transporter include technetium 99m (2 β [(N,N-bis(2-mercaptoethyl) ethylene diamino)methyl) and 3 β -(4-chlorophenyl) tropane (99mTc-TRODAT-1).

Binding of ligands with affinity and specificity for dopamine transporter ligands in the striatum is, in general, reduced in Parkinson disease (PD), genetic parkinsonism, dementia with Lewy bodies (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, psychogenic parkinsonism, and vascular 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. There are, however, a significant percentage of patients with clinically diagnosed PD who do not show reduced DaT-SPECT binding. Patients with clinically diagnosed PD, who present with a normal DaT-SPECT scan, are referred to in the literature as “scans without evidence of dopaminergic deficit” (SWEDD). 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 by the reference standard. Additional research may shed light on these cases.

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 for analysis and the development of an atlas for visual interpretation.

In 2011, the FDA approved [¹²³I]ioflupane ([¹²³I]-fluoropropyl βCIT), a dopamine transporter (DAT) radioligand, for SPECT. DaTscan (Ioflupane I 123 Injection) is a radiopharmaceutical 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.

POSITION STATEMENT:

Dopamine transporter imaging with single-photon emission computed tomography (DaT-SPECT) **meets the definition of medical necessity** when used for members with the following:

- Clinically uncertain Parkinson disease; **OR**
- Clinically uncertain dementia with Lewy bodies.

Dopamine transporter imaging with single-photon emission computed tomography (DaT-SPECT) for all other indications, including but not limited to monitoring of disease progression is considered **experimental or investigational**. The evidence is insufficient to determine the effects of dopamine transporter imaging with single-photon emission computed tomography (DaT-SPECT) on health outcomes.

BILLING/CODING INFORMATION:

CPT Coding:

There is no specific CPT code for dopamine transporter imaging.

HCPCS Coding:

A9584	Iodine I-123 ioflupane, diagnostic, per study dose, up to 5 millicuries
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ICD-10 Diagnosis Codes That Support Medical Necessity:

G20	Parkinson's disease
G21.0-G21.9	Secondary parkinsonism
G31.83	Dementia with Lewy bodies

REIMBURSEMENT INFORMATION:

Refer to section entitled [POSITION STATEMENT](#).

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage products: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) was found at the time of the last guideline reviewed date.

DEFINITIONS:

Parkinsonian syndromes: a group of movement disorders characterized by tremor, bradykinesia, and rigidity.

RELATED GUIDELINES:

[FDG-SPECT, 04-78000-15](#)

OTHER:

Other names used to report Dopamine transporter imaging with single-photon emission computed tomography (DaT-SPECT):

Note: The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.

DaT neuroimaging
DaTscan
DAT-SPECT
DaT SPECT scan
Dopaminergic neuroimaging
Dopamine transporter imaging
Dopamine transporter (DaT) scan
Dopamine transporter scan (DaTSCAN)

REFERENCES:

1. Adler CH, Beach TG, Hentz JG et al. Low clinical diagnostic accuracy of early vs advanced Parkinson disease: clinicopathologic study. *Neurology*. 2014 Jul; 83(5): 406-412.

2. Akahoshi M, Abe K, Uchiyama Y et al. Attenuation and scatter correction in I-123 FP-CIT SPECT do not affect the clinical diagnosis of dopaminergic system neurodegeneration. *Medicine* 2017 Nov; 96(45): e8484.
3. American College of Radiology ACR Appropriateness Criteria® Clinical Condition: Dementia and Movement Disorders, Date of origin: 1996; Last review date: 2015.
4. Ba F, Martin WR. Dopamine transporter imaging as a diagnostic tool for parkinsonism and related disorders in clinical practice. *Parkinsonism Related Disorders*. 2015 Feb; 21(2):87-94.
5. Badoud S, Van De Ville D, Nicastro N et al. Discriminating among degenerative parkinsonisms using advanced (123I)-ioflupane SPECT analyses. *NeuroImage Clinical*. 2016.Jul; 12:234-240.
6. Bajaj N, Hauser RA, Grachev ID. Clinical utility of dopamine transporter single photon emission CT (DaT-SPECT) with (123I) ioflupane in diagnosis of parkinsonian syndromes. *Journal of Neurology Neurosurgery Psychiatry*. 2013 Nov; 84(11): 1288–1295.
7. Bega D, Gonzalez-Latapi P, Zadikoff C et al. Is There a Role for DAT-SPECT Imaging in a Specialty Movement Disorders Practice? *Neuro-Degenerative Diseases*. 2015; 15(2):81-86.
8. Berardelli A, Wenning GK, Antonini A et al. EFNS/MDS-ES/ENS [corrected] recommendations for the diagnosis of Parkinson's disease. *European Journal of Neurology*. 2013 Jan;20(1):16-34.
9. Blue Cross Blue Shield Association Evidence Positioning System®. 6.01.54 Dopamine Transporter Imaging with Single-Photon Emission Computed Tomography, 10/19.
10. Booth TC, Nathan M, Waldman AD et al. The role of functional dopamine-transporter SPECT imaging in parkinsonian syndromes, part 1. *AJNR American Journal of Neuroradiology* 2015 Feb; 36 (2): 229-235.
11. Booth TC. The role of functional dopamine-transporter SPECT imaging in parkinsonian syndromes, part 2. *AJNR American Journal Neuroradiology* 2015 Feb;36(2):236-44.
12. Catafau AM, Tolosa E; DaTSCAN Clinically Uncertain Parkinsonian Syndromes Study Group. Impact of dopamine transporter SPECT using 123I-IOFLUPANE on diagnosis and management of patients with clinically uncertain Parkinsonian syndromes. *Movement Disorders*. 2004 Oct; 19(10):1175-82.
13. Colloby SJ, McParland S, O'Brien JT et al. Neuropathological correlates of dopaminergic imaging in Alzheimer's disease and Lewy body dementias. *Brain*. 2012 Sep; 135(Pt 9): 2798-2808.
14. Covington MF, Sherman S, Lewis D et al. Patient Survey on Satisfaction and Impact of 123I-Ioflupane Dopamine Transporter Imaging. *PLoS One*. 2015 Jul 30; 10(7):e0134457.
15. Cummings JL, Fine MJ, Grachev ID et al. Effective and efficient diagnosis of parkinsonism: the role of dopamine transporter SPECT imaging with ioflupane I-123 injection (DaTscan™). *American Journal of Managed Care* 2014 March; 20(5 Suppl):S97-109.
16. Djang DS, Janssen MJ, Bohnen N et al. SNM practice guideline for dopamine transporter imaging with 123I-ioflupane SPECT 1.0. *Journal of Nuclear Medicine*. 2012 Jan; 53(1):154-16.
17. Georgiopoulos C, Davidsson A, Engström M et al. The diagnostic value of dopamine transporter imaging and olfactory testing in patients with parkinsonian syndromes. *Journal of Neurology*. 2015 Sep; 262(9):2154-2163.
18. Grosset DG, Tatsch K, Oertel WH et al. Safety analysis of 10 clinical trials and for 13 years after first approval of ioflupane 123I injection (DaTscan). *Journal of Nuclear Medicine*. 2014 Aug; 55(8):1281-1287.
19. Hauser RA, Bajaj N, Marek K et al. Sensitivity, Specificity, Positive and Negative Predictive Values and Diagnostic Accuracy of DaTscan™ (Ioflupane I123 Injection): Predicting Clinical Diagnosis in Early Clinically Uncertain Parkinsonian Syndrome. *Journal of Neurology & Stroke* 2014; 1(1):00003.
20. Hirsch L, Jette N, Frolkis A et al. The Incidence of Parkinson's Disease: A Systematic Review and Meta-Analysis. *Neuroepidemiology*. 2016;46(4):292-300.

21. Hughes AJ, Daniel SE, Kilford L et al. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. *Journal of Neurology, Neurosurgery and Psychiatry* 1992. Mar; 55(3): 181-184.
22. Jakobson S, Linder J, Forsgren L, et al. Accuracy of visual assessment of dopamine transporter imaging in early parkinsonism. *Movement Disorders*. 2014; 8:1-7.
23. Jung Y, Jordan LG, Lowe VJ et al. Clinicopathological and 123I-FP-CIT SPECT correlations in patients with dementia. *Annals of Clinical and Translational Neurology*. 2018. Mar; 5(3): 376-381.
24. Marshall VL, Reiningner CB, Marquardt M et al. Parkinson's disease is overdiagnosed clinically at baseline in diagnostically uncertain cases: a 3-year European multicenter study with repeat [123I] FP-CIT SPECT. *Movement Disorders*. 2009 Mar; 24(4):500-508.
25. Marsili L, Rizzo G, Colosimo C. Diagnostic Criteria for Parkinson's Disease: From James Parkinson to the Concept of Prodromal Disease. *Frontiers in Neurology*. 2018, Mar 23; 9: 156.
26. McKeith IG, Boeve BF, Dickson DW et al. Diagnosis and management of dementia with Lewy bodies: Fourth consensus report of the DLB Consortium. *Neurology*. 2017 Jul ;89(1):88-100.
27. National Institute for Health and Care Excellence): Dementia: supporting people with dementia and their carers in health and social care Clinical guideline [CG42] Published: 22 November 2006
28. National Institute for Health and Care Excellence): Parkinson's disease in adults NICE guideline [NG71] Published date: July 2017.
29. Nuvoli S, Spanu A, Piras MR et al. 123I-ioflupane brain SPECT and 123I-MIBG cardiac planar scintigraphy combined use in uncertain parkinsonian disorders. *Medicine (Baltimore)*. 2017 May; 96(21):e6967.
30. O'Brien JT, Oertel WH, McKeith IG et al. Is ioflupane I123 injection diagnostically effective in patients with movement disorders and dementia? Pooled analysis of four clinical trials. *BMJ Open*. 2014 Jul 3; 4(7):e005122.
31. Oravivattanakul S, Benchaya L, Wu G et al. Dopamine transporter (DaT) scan utilization in a movement disorder center. *Movement Disorders Clinical Practice* 2016 Jan/Feb 3 (1); 31-35.
32. Postuma RB, Berg D2, Stern M et al. MDS clinical diagnostic criteria for Parkinson's disease. *Movement Disorders*. 2015 Oct;30(12):1591-601.
33. Rajput AH, Offord KP, Beard CM et al. Essential tremor in Rochester, Minnesota: a 45-year study. *Journal of Neurology, Neurosurgery, and Psychiatry*. 1984 May; 47 (5): 466-704.
34. Schrag A, Ben-Shlomo Y, Quinn N. How valid is the clinical diagnosis of Parkinson's disease in the community? *Journal of Neurology, Neurosurgery, and Psychiatry*. 2002 Nov; 73 (5): 529-534. Seifert KD, Wiener JI. The impact of DaTscan on the diagnosis and management of movement disorders: A retrospective study. *American Journal of Neurodegenerative Disease* 2013; 2(1):29-34.
35. Seibyl JP, Kupsch A, Booij J et al. Individual-reader diagnostic performance and between-reader agreement in assessment of subjects with Parkinsonian syndrome or dementia using 123I-ioflupane injection (DaTscan) imaging. *Journal of Nuclear Medicine*. 2014 Aug; 55(8):1288-1296.
36. Siepel FJ, Rongve A, Buter TC et al. (123I)FP-CIT SPECT in suspected dementia with Lewy bodies: a longitudinal case study. *BMJ Open*. 2013 Apr 8; 3(4).
37. Sierra M, Martinez-Rodriguez, Sanchez-Juan P et al. Prospective clinical and DaT-SPECT imaging in premotor LRRK2 G2019S-associated Parkinson disease. *Neurology* 2017. Aug; 89(5): 439-444.
38. Suchowersky O, Reich S, Perlmutter J et al. Practice Parameter: diagnosis and prognosis of new onset Parkinson disease (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 2006 Apr ;66(7):968-975.
39. Thomas AJ, Attems J, Colloby SJ et al. Autopsy validation of 123I-FP-CIT dopaminergic neuroimaging for the diagnosis of DLB. *Neurology*. 2017 Jan; 88 (3): 276-283.

40. Uyama N, Otsuka H, Shinya T et al. The utility of the combination of a SPECT study with [123I]-FP-CIT of dopamine transporters and [123I]-MIBG myocardial scintigraphy in differentiating Parkinson disease from other degenerative parkinsonian syndromes. Nuclear Medicine Communications. 2017 Jun; 38(6):487-492.
41. van der Zande JJ, Booij J, Scheltens P et al. [(123)I]FP-CIT SPECT scans initially rated as normal became abnormal over time in patients with probable dementia with Lewy bodies. European Journal of Nuclear Meicine and Nuclear Medicine 2016. Jun; 43(6): 1060-1066.
42. Vlaar AM, van Kroonenburgh MJ, Kessels AG et al. Meta-analysis of the literature on diagnostic accuracy of SPECT in parkinsonian syndromes. BMC Neurology. 2007 Sep ;7:27.
43. Walker Z, Moreno E, Thomas A et al. Clinical usefulness of dopamine transporter SPECT imaging with 123I-FP-CIT in patients with possible dementia with Lewy bodies: randomised study. British Journal of Psychiatry. 2015 Feb; 206(2):145-152.
44. Ziebell M, Anderson BB, Thomsen G et al. Predictive value of dopamine transporter SPECT imaging with [123I]PE2I in patients with subtle parkinsonian symptoms. European Journal of Nuclear Medicine and Molecular Imaging 2012 Feb; 39:242–250.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the BCBSF Medical Policy & Coverage Committee on 12/03/20.

GUIDELINE UPDATE INFORMATION:

02/15/18	New Medical Coverage Guideline.
11/15/18	Review; no change to position statement, Updated references.
12/15/18	Revision; added position statement for clinically uncertain Parkinson disease and clinically uncertain dementia with Lewy bodies. Revised experimental investigational position statement. Added diagnoses codes (G20, G21.0-G21.9, G31.83). Updated references.
12/15/20	Review/revision; no change to position statement. Deleted code 78607. Updated references.