Protocol

Dopamine Transporter Single-Photon Emission Computed Tomography

(60154)

(Formerly Dopamine Transporter Imaging With Single-Photon Emission Computed Tomography)

Medical Benefit		**Effective Date**: 01/01/15	**Next Review Date**: 09/17
Preauthorization	No	**Review Dates**: 09/14, 09/15, 09/16	

This Protocol considers this test or procedure investigational. If the physician feels this service is medically necessary, preauthorization is recommended.

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 work-up without dopamine transporter single-photon emission computed tomography	Relevant outcomes include: • Test accuracy • Symptoms • Functional outcomes • Medication use
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 work-up without dopamine transporter single-photon emission computed tomography	Relevant outcomes include: • Test accuracy • Symptoms • Functional outcomes • Medication use

Description

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

Summary of Evidence

For individuals who have clinically uncertain Parkinson disease who receive DAT-SPECT, the evidence includes a number of studies from Europe, where a dopamine transporter (DAT) ligand has been available for over a decade. Relevant outcomes are test accuracy, symptoms, functional outcomes, and medication use. In terms of technical performance, the DAT ligand is specific for the striatal DAT, and studies have indicated reliability in assessment of the images when performed by experienced readers. Studies of diagnostic accuracy have reported good specificity for confirming nigrostriatal degeneration, with less sensitivity for ruling out disease; these findings are dependent, however, on a reference standard (clinical diagnosis), which may be flawed, and it

is unknown whether DAT-SPECT would show greater sensitivity than the criterion standard (histopathologic diagnosis). Evidence on clinical utility includes a randomized controlled trial (RCT) that showed more patients evaluated with DAT-SPECT had changes in diagnosis and management than controls without imaging; however, there is limited evidence to evaluate whether these changes improve health outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have clinically uncertain dementia with DLB who receive DAT-SPECT, the evidence includes studies on diagnostic accuracy and its effect on diagnosis and confidence in diagnosis. Relevant outcomes are test accuracy, symptoms, functional outcomes, and medication use. For discriminating between DLB and Alzheimer disease, the sensitivity and specificity of DAT-SPECT is somewhat lower than for parkinsonian syndromes, although the comparison standard used in the available studies may be flawed. Few patients have been evaluated with histopathology as the reference standard. Evidence on clinical utility includes an RCT that showed DAT-SPECT can influence the diagnosis of DLB, particularly when the scan is abnormal. It cannot be determined from this study whether the revised diagnosis was more accurate or resulted in a beneficial change in patient management. The evidence is insufficient to determine the effects of the technology on health outcomes.

Policy

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; OR
- distinguishing between parkinsonian syndromes and essential tremor; OR
- distinguishing between dementia with Lewy bodies and Alzheimers disease; OR
- for monitoring of disease progression.

Background

Parkinsonian syndromes (PS) 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; however, diagnosing PD in the early stage of the disease can be difficult. In addition, other etiologies such as essential tremor (ET), corticobasal degeneration, multisystem atrophy, progressive supranuclear palsy, vascular parkinsonism, and drug-induced parkinsonism can lead to a similar set of symptoms. Even in specialized movement disorders centers, up to 25% of patients may be misclassified, and some patients, such as those with ET who have been diagnosed with PD, may be erroneously treated.[1] This has led to the development of additional tests to improve the accuracy of clinical diagnosis of PD and other PSs. One recent approach is to evaluate the integrity of dopaminergic pathways in the brain using dopamine transporter single-photon emission computed tomography (DAT-SPECT).

DAT-SPECT detects presynaptic dopaminergic deficit by measuring DAT binding. In general, striatal DAT binding is reduced in PD, genetic parkinsonism, DLB, corticobasal degeneration, progressive supranuclear palsy, and multiple system atrophy, while striatal DAT binding is in the normal range in AD, ET, dystonic tremor, orthostatic tremor, drug-induced parkinsonism, psychogenic parkinsonism, and vascular parkinsonism.[2] It is proposed that an abnormal DAT-SPECT supports the diagnosis of PD or other neurodegenerative PS (multisystem atrophy, progressive supranuclear palsy), while a normal DAT-SPECT in a symptomatic patient increases the likelihood of a disease not affecting the nigrostriatal dopaminergic pathway. There is, however, a significant percentage of patients with clinically diagnosed PD who do not show reduced DAT-SPECT binding. These are commonly

referred to as scans without evidence of dopaminergic deficit. Additional research may shed light on these cases.

Due to the degeneration of nigrostriatal neurons in DLB, DAT-SPECT is also proposed to differentiate DLB from AD. Some note a severe sensitivity to neuroleptics (potentially life-threatening) 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 AD.

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 (ROI) for analysis and the development of an atlas for visual interpretation. Quantitative interpretation may aid visual interpretation and, if performed rigorously, may increase diagnostic accuracy; however, interobserver variability tends to be high with manual ROI-based semiquantification.[3] Semiquantitative analysis also requires normal control values and varies across imaging systems.

DAT ligands include iodine 123 2β-carbomethoxy-3β-(4-iodophenyl) tropane (^{123}I-β-CIT), iodine 123 N-(3-fluoropropyl)-2β-carbomethoxy-3β-(4-iodophenyl) nortropane (^{123}I-FP-CIT), and technetium 99m (2β((N,N'-bis(2-mercaptoethyl) ethylene diamino) methyl), 3β-(4-chlorophenyl) tropane (^{99m}Tc-TRODAT-1).[2] Intravenous ^{123}I-β-CIT requires a delay between injection and scan of about 24 hours. Intravenous ^{123}I-FP-CIT (DaTscan™) is a fluoropropyl derivate of β-CIT that can be injected three to six hours before the scan.

Regulatory Status

DaTscan™ (GE Healthcare) has been in use in Europe since 2000 with a diagnostic indication for use in parkinsonian patients and with expanded use since 2006 in patients suspected of DLB. In 2011, DaTscan™ was approved by the U.S. 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 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."[4] FDA product code: KPS.

Related Protocol

Deep Brain Stimulation

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

References

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

1. Scherfler C, Schwarz J, Antonini A, et al. Role of DAT-SPECT in the diagnostic work up of parkinsonism. Mov Disord. Jul 15 2007; 22(9):1229-1238. PMID 17486648
2. Kagi G, Bhatia KP, Tolosa E. The role of DAT-SPECT in movement disorders. J Neurol Neurosurg Psychiatry. Jan 2010; 81(1):5-12. PMID 20019219
3. Djang DSW, Janssen MJR, Bohnen N. SNM Practice Guideline for Dopamine Transporter Imaging with 123I-Ioflupane SPECT 1.0. 2011; http://interactive.snm.org/docs/123I_ioflupane_SPECT_Practice_Guideline_JNM_Edit_FINAL.pdf. Accessed August 23, 2016.
4. Healthcare G. DaTscan Full Prescribing Information. 2015; http://www3.gehealthcare.com/en/products/categories/nuclear_imaging_agents/datscan. Accessed August 25, 2016.
5. Papathanasiou N, Rondogianni P, Chroni P, et al. Interobserver variability, and visual and quantitative parameters of (123)I-FP-CIT SPECT (DaTSCAN) studies. Ann Nucl Med. Apr 2012; 26(3):234-240. PMID 22237674
6. 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. J Nucl Med. Aug 2014; 55(8):1288-1296. PMID 24925885
7. Prashanth R, Dutta Roy S, Mandal PK, et al. High accuracy classification of Parkinson's disease through shape analysis and surface fitting in 123I-Ioflupane SPECT imaging. IEEE J Biomed Health Inform. Mar 29 2016. PMID 27101625
8. Skanjeti A, Castellano G, Elia BO, et al. Multicenter semiquantitative evaluation of (123)I-FP-CIT brain SPECT. J Neuroimaging. Nov-Dec 2015; 25(6):1023-1029. PMID 25923060
9. Marshall VL, Reininger 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. Mov Disord. Mar 15 2009; 24(4):500-508. PMID 19117369
10. Mo SJ, Linder J, Forsgren L, et al. Accuracy of visual assessment of dopamine transporter imaging in early parkinsonism. Mov Disord Clin Pract. 2015; 2(1):17-23. PMID
11. Brigo F, Matinella A, Erro R, et al. [(1)(2)(3)I]FP-CIT SPECT (DaTSCAN) may be a useful tool to differentiate between Parkinson's disease and vascular or drug-induced parkinsonisms: a meta-analysis. Eur J Neurol. Nov 2014; 21(11):1369-e1390. PMID 24779862
12. Kupsch AR, Bajaj N, Weiland F, et al. Impact of DaTscan SPECT imaging on clinical management, diagnosis, confidence of diagnosis, quality of life, health resource use and safety in patients with clinically uncertain parkinsonian syndromes: a prospective 1-year follow-up of an open-label controlled study. J Neurol Neurosurg Psychiatry. Jun 2012; 83(6):620-628. PMID 22492213
13. Bajaj N, Hauser RA, Seibyl J, et al. Association between Hoehn and Yahr, Mini-Mental State Examination, age, and clinical syndrome predominance and diagnostic effectiveness of ioflupane I 123 injection (DaTSCAN) in subjects with clinically uncertain parkinsonian syndromes. Alzheimers Res Ther. 2014; 6(5-8):67. PMID 25478029

14. Hauser RA, Bajaj N, Marek K, et al. Sensitivity, specificity, positive and negative predictive values and diagnositic accuracy of DaTscan(TM) (Ioflupane I123 injection): Predicting clinical diagnosis in early clinically uncertain parkinsonian syndrome. J Neurol Stroke. 2014; 1(1):00003.
15. Benamer TS, Patterson J, Grosset DG, et al. Accurate differentiation of parkinsonism and essential tremor using visual assessment of [123I]-FP-CIT SPECT imaging: the [123I]-FP-CIT study group. Mov Disord. May 2000; 15(3):503-510. PMID 10830416
16. 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; 4(7):e005122. PMID 24993764
17. Vlaar AM, de Nijs T, Kessels AG, et al. Diagnostic value of 123I-ioflupane and 123I-iodobenzamide SPECT scans in 248 patients with parkinsonian syndromes. Eur Neurol. 2008; 59(5):258-266. PMID 18264015
18. Adler CH, Beach TG, Hentz JG, et al. Low clinical diagnostic accuracy of early vs. advanced Parkinson disease: clinicopathologic study. Neurology. Jul 29 2014; 83(5):406-412. PMID 24975862
19. Joutsa J, Gardberg M, Roytta M, et al. Diagnostic accuracy of parkinsonism syndromes by general neurologists. Parkinsonism Relat Disord. Aug 2014; 20(8):840-844. PMID 24816002
20. Kupsch A, Bajaj N, Weiland F, et al. Changes in clinical management and diagnosis following DaTscan SPECT imaging in patients with clinically uncertain parkinsonian syndromes: a 12-week follow-up study. Neurodegener Dis. May 8, 2013; 11(1):22-32. PMID 22571977
21. Catafau AM, Tolosa E. Impact of dopamine transporter SPECT using 123I-Ioflupane on diagnosis and management of patients with clinically uncertain Parkinsonian syndromes. Mov Disord. Oct 2004; 19(10):1175-1182. PMID 15390019
22. Tolosa E, Borght 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
23. Bairactaris C, Demakopoulos N, Tripsianis G, et al. Impact of dopamine transporter single photon emission computed tomography imaging using I-123 ioflupane on diagnoses of patients with parkinsonian syndromes. J Clin Neurosci. Feb 2009; 16(2):246-252. PMID 19097795
24. Sixel-Doring F, Liepe K, Mollenhauer B, et al. The role of 123I-FP-CIT-SPECT in the differential diagnosis of Parkinson and tremor syndromes: a critical assessment of 125 cases. J Neurol. Dec 2011; 258(12):2147-2154. PMID 21547379
25. Bega D, Gonzalez-Latapi P, Zadikoff C, et al. Is there a role for DAT-SPECT Imaging in a specialty movement disorders practice? Neurodegener Dis. 2015; 15(2):81-86. PMID 25592727
26. Sadasivan S, Friedman JH. Experience with DaTscan at a tertiary referral center. Parkinsonism Relat Disord. Jan 2015; 21(1):42-45. PMID 25465746
27. Oravivattanakul S, Benchaya L, Wu G, et al. Dopamine transporter (DaT) scan utilization in a movement disorder center. Mov Disord Clin Pract. 2015; 3(1):31-35. PMID
28. Seifert KD, Wiener JI. The impact of DaTscan on the diagnosis and management of movement disorders: A retrospective study. Am J Neurodegener Dis. 2013; 2(1):29-34. PMID 23515233
29. Thiriez C, Itti E, Fenelon G, et al. Clinical routine use of dopamine transporter imaging in 516 consecutive patients. J Neurol. Apr 2015; 262(4):909-915. PMID 25649832

30. Hubbuch M, Farmakis G, Schaefer A, et al. FP-CIT SPECT does not predict the progression of motor symptoms in Parkinson's disease. Eur Neurol. 2011; 65(4):187-192. PMID 21412004
31. Vogt T, Kramer K, Gartenschlaeger M, et al. Estimation of further disease progression of Parkinson's disease by dopamine transporter scan vs. clinical rating. Parkinsonism Relat Disord. Jul 2011; 17(6):459-463. PMID 21515087
32. McKeith I, O'Brien J, Walker Z, et al. Sensitivity and specificity of dopamine transporter imaging with 123I-FP-CIT SPECT in dementia with Lewy bodies: a phase III, multicentre study. Lancet Neurol. Apr 2007; 6(4):305-313. PMID 17362834
33. Brigo F, Turri G, Tinazzi M. 123I-FP-CIT SPECT in the differential diagnosis between dementia with Lewy bodies and other dementias. J Neurol Sci. Dec 15 2015; 359(1-2):161-171. PMID 26671107
34. 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; 3(4). PMID 23572198
35. van der Zande JJ, Booij J, Scheltens P, et al. [(123)]FP-CIT SPECT scans initially rated as normal became abnormal over time in patients with probable dementia with Lewy bodies. Eur J Nucl Med Mol Imaging. Jun 2016; 43(6):1060-1066. PMID 26830298
36. 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. Br J Psychiatry. Feb 2015; 206(2):145-152. PMID 25431431
37. Kemp PM, Clyde K, Holmes C. Impact of 123I-FP-CIT (DaTSCAN) SPECT on the diagnosis and management of patients with dementia with Lewy bodies: a retrospective study. Nucl Med Commun. Apr 2011; 32(4):298-302. PMID 21278615
38. American College of Radiology (ACR). ACR Appropriateness Criteria®: Dementia and Movement Disorders. 2015; https://acsearch.acr.org/docs/69360/Narrative/. Accessed August 23, 2016.
39. Wippold FJ, 2nd, Brown DC, Broderick DF, et al. ACR Appropriateness Criteria Dementia and Movement Disorders. J Am Coll Radiol. Jan 2015; 12(1):19-28. PMID 25557568
40. 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. Apr 11 2006; 66(7):968-975. PMID 16606907
41. Postuma RB, Berg D, Stern M, et al. MDS clinical diagnostic criteria for Parkinson's disease. Mov Disord. Oct 2015; 30(12):1591-1601. PMID 26474316
42. Berardelli A, Wenning GK, Antonini A, et al. EFNS/MDS-ES recommendations for the diagnosis of Parkinson's disease. Eur J Neurol. Jan 2013; 20(1):16-34. PMID 23279440
43. Darcourt J, Booij J, Tatsch K, et al. EANM procedure guidelines for brain neurotransmission SPECT using (123)I-labelled dopamine transporter ligands, version 2. Eur J Nucl Med Mol Imaging. Feb 2010; 37(2):443-450. PMID 19838702
44. National Institute for Health and Clinical Excellence (NICE). Parkinson's disease in over 20s: Diagnosis and management [CG35]. 2006; https://www.nice.org.uk/guidance/cg35/chapter/1-Guidance#diagnosing-parkinsons-disease. Accessed August 23, 2016.
45. National Institute for Health and Clinical Excellence (NICE). Parkinson's disease (update) [GID-CGWAVE0698]. 2016; https://www.nice.org.uk/guidance/indevelopment/GID-CGWAVE0698. Accessed August 23, 2016.

46. National Institute for Health and Clinical Excellence (NICE). Dementia: supporting people with dementia and their careers in health and social care [CG42]. 2016; https://www.nice.org.uk/guidance/CG42/chapter/1-Guidance#diagnosis-and-assessment-of-dementia. Accessed August 23, 2016.