Medical Services Advisory Committee (MSAC) Public Summary Document

Application No. 1795 – Positron emission tomography/computed tomography (PET/CT) dopaminergic imaging for evaluating Parkinsonism

Applicant: **Australasian Association of Nuclear Medicine Specialists**

Date of MSAC consideration: **30 July 2026**

Context for decision: MSAC makes its advice in accordance with its Terms of Reference, visit the MSAC website

1. Purpose of application

An application requesting a new Medicare Benefits Schedule (MBS) item for [^{18}F]fluorodopa (FDOPA) positron emission tomography (PET)/computed tomography (CT) dopaminergic imaging for evaluating parkinsonism was received from the Australasian Association of Nuclear Medicine Specialists by the Department of Health, Disability and Ageing.

2. MSAC's advice to the Minister

After considering the strength of the available evidence in relation to comparative safety, clinical effectiveness, cost-effectiveness and total cost, MSAC did not support the public funding of a new MBS item for a fluorodopa positron emission tomography/computed tomography (FDOPA PET/CT) item as a diagnostic imaging test for patients with suspected Parkinsonism, who demonstrate inadequate response to optimised dopaminergic therapy after 12 weeks to 24 months of treatment.

While MSAC acknowledged that there may be a clinical need for this test in the proposed population, MSAC considered that the clinical place of this test in the algorithm for the diagnosis and management of Parkinson's disease was uncertain.

MSAC acknowledged that comparing FDOPA PET/CT against the reference standard of post-mortem neuropathology was difficult due to feasibility issues. Therefore, clinical diagnosis (based on symptoms and signs) was the more pragmatic reference standard. However, even after accounting for this, MSAC considered that the evidence base for test accuracy, comparing FDOPA PET/CT with clinical diagnosis, was highly uncertain given that the populations across studies were heterogeneous, the studies contained small sample sizes, and the studies were classified as being at high risk of bias.

MSAC noted that the patient population in the key Australian study did not align with the proposed population. MSAC noted that while the key study showed that testing was reported to result in a change in management in about 50% of patients, there was no evidence provided linking this change in management to health outcomes, including quality of life outcomes. This led to significant uncertainty in the clinical claim that the test would lead to superior health outcomes compared to standard of care.

MSAC considered that this uncertainty in the clinical claim of effectiveness flowed through to the economic analysis and noted that the economic model was also highly sensitive to its inputs, adding to the overall uncertainty of the cost-effectiveness of the test. MSAC considered that the financial analysis was also highly uncertain due to the uncertainty in the patient population and the test's clinical place, which resulted in uncertain utilisation estimates. MSAC emphasised the importance in resolving these uncertainties given the higher prevalence of Parkinson's disease in the older adult population which could result in a high financial impact in the future, given that Australia has an ageing population.

Consumer summary

This is an application from the Australasian Association of Nuclear Medicine Specialists requesting Medicare Benefits Schedule (MBS) listing of positron emission tomography / computed tomography (PET/CT) dopaminergic imaging using the radiotracer 18F-Fluorodopa (FDOPA) for evaluating parkinsonism.

'Parkinsonism' is a general term for a collection of body movement disorders such as slowness, stiffness and resting tremor. Parkinson's disease (PD) is one form of parkinsonism. Currently, patients are typically diagnosed with PD through clinical diagnosis. This means that they are diagnosed by a doctor based on their symptoms and other signs. However, based on clinical diagnosis alone, it can be difficult to tell the difference between PD and other movement disorders, such as essential tremor.

The application proposes that imaging of the brain using a test called FDOPA PET/CT may help a clinician work out which patients with parkinsonism have PD as opposed to different movement disorders. Working out which movement disorder a patient has, is important to help clinicians choose the right treatment.

In this application, FDOPA PET/CT is used to assess patients who have had a clinical diagnosis of PD, but are not responding to standard PD treatment, after at least 12 weeks but no more than 24 months of treatment. An FDOPA PET/CT scan is a specialised brain scan that uses a radioactive tracer called 18F-Fluorodopa to evaluate brain dopamine function. Dopamine is a chemical messenger in the brain that helps control movement and mood.

During the imaging, patients get a small, safe dose of the radioactive tracer via an injection. This tracer travels to the brain where certain brain cells absorb the tracer and convert it into dopamine. A scanner captures the images which show where and how much dopamine is being made in the brain. Different types of parkinsonism can show different patterns of dopamine activity, which may help doctors better understand the cause of a person's symptoms and guide treatment decisions.

MSAC accepted that the FDOPA PET/CT test is safe. MSAC considered that the evidence on how well FDOPA PET/CT identifies Parkinson's disease was uncertain. The evidence is from a small number of studies, which have small patient populations and participants in the studies have a diverse range of backgrounds, previous treatments, length of treatment, and symptoms. This is not aligned with the application's proposed testing population. MSAC therefore considered there is uncertainty that if the test were applied to the testing population proposed that it would lead to similar accuracy as that reported in the evidence.

MSAC noted the evidence showed there were changes to diagnosis after the FDOPA PET/CT test. Only one of the studies reported changes in management (e.g. medication changes), and no studies were presented to show if changing diagnosis or treatment after the FDOPA PET/CT test resulted in better health outcomes for patients. MSAC considered that if patients were not responding to treatments, they would likely stop or switch treatments anyway, with or without the FDOPA PET/CT test. Therefore, MSAC considered that there was not enough evidence to show that FDOPA PET/CT resulted in reliable changes in treatment or better health outcomes for patients. MSAC considered that these uncertainties in the evidence made it hard to reach a reliable conclusion on whether the FDOPA PET/CT test was good value for money.

Consumer summary
MSAC noted that the test would likely be used in a broader range of patients in clinical practice than what was proposed in the application. This could significantly increase costs to the MBS. MSAC considered that it would need to be more specific on who needed the test in the MBS item descriptor to limit increased costs. Overall, MSAC considered that the evidence and value for money were not adequately demonstrated for FDOPA PET/CT in patients with parkinsonism. MSAC noted that it was not clear who needed this test and what the benefit of the test was. MSAC considered more evidence was needed to address the uncertainty in the clinical, economic and financial analysis. **MSAC's advice to the Commonwealth Minister for Health, Disability and Ageing** MSAC did not support MBS listing of FDOPA PET/CT imaging for evaluating parkinsonism. MSAC accepted that the FDOPA PET/CT procedure was safe, but did not consider that the patient population, clinical place of the test, or its impact on patient outcomes, were clearly defined. Therefore, it was not able to make a recommendation on the effectiveness and value for money of the test.

3. Summary of consideration and rationale for MSAC's advice

MSAC noted that this application from the Australasian Association of Nuclear Medicine Specialists requested a new Medicare Benefits Schedule (MBS) item for positron emission tomography / computed tomography (PET/CT) dopaminergic imaging (FDOPA PET/CT) using the radiotracer 18F-Fluorodopa (FDOPA). Under the proposed item, FDOPA PET/CT would be used to evaluate parkinsonism in patients with suspected Parkinson's disease (PD) who have demonstrated an inadequate response to optimised dopaminergic therapy after 12 weeks to 24 months of treatment.

MSAC noted that the primary purpose of using FDOPA PET/CT in this population is to evaluate presynaptic dopaminergic function in patients with parkinsonism who have not responded to initial dopaminergic therapy, where the imaging results are expected to change diagnosis and management. MSAC noted that currently clinical diagnosis of PD can be difficult, and misdiagnosis can occur. MSAC acknowledged that FDOPA PET/CT was a novel diagnostic imaging modality and noted that there were currently no other imaging techniques to specifically diagnose PD. MSAC acknowledged that there may be a clinical need for FDOPA PET/CT in the proposed population in differentiating between PD and other movement disorders.

MSAC noted that pre-PASC and pre-MSAC consultation feedback indicated strong patient and clinician support for the proposed FDOPA PET/CT service to improve diagnostic certainty in patients with parkinsonism. MSAC acknowledged there were personal and clinical factors in the value of diagnostic technology for patients with parkinsonism. MSAC noted that the feedback often linked improved diagnostic certainty to earlier diagnosis and improved differentiation between Parkinson's disease and related or mimicking conditions. However, MSAC considered that these technologies cannot yet adequately discriminate between PD and atypical parkinsonism.

MSAC noted that currently there are no diagnostic imaging MBS items for the diagnosis of PD. MSAC also noted there are currently no specific MBS items for brain MRI investigation of parkinsonism. MSAC noted that brain MRI is often used to exclude structural causes or other neurological conditions and therefore before patients are referred for a FDOPA PET/CT scan, they

will likely have already undertaken a brain MRI scan. There are existing MBS items for MRI investigation of other brain conditions, and patients may be eligible for an MBS rebate through these items for a prior MRI scan, but eligibility for these MBS rebates would depend on the wording used by the clinician on the request form which outlines the indication for the MRI. There is no specific brain MRI item for an MBS-funded diagnostic work-up for PD.

MSAC noted that the proposed MBS fee of $1,200 aligned with other similar PET/CT scans and reflected the cost of the tracer and ligand. MSAC noted that these costs are largely driven by radiotracer production and distribution, which may contribute to cost variation across providers and locations.

MSAC noted that the patient population in the proposed item did not align with the ratified PICO because it did not clearly restrict FDOPA PET/CT to patients with unresolved diagnostic uncertainty after standard clinical assessment, in whom the result would be expected to change clinical management.

MSAC noted that the comparator was standard of care, consisting mainly of clinical assessment. MSAC considered that this was appropriate and consistent with the ratified PICO. MSAC noted that the PICO confirmation stated the reference standard for PD diagnosis was post-mortem neuropathology. MSAC acknowledged that post-mortem confirmation is generally not feasible in this context and there are few studies available in this area. Therefore, MSAC considered clinical diagnosis to be the more pragmatic reference standard.

MSAC queried whether a brain MRI should be required before FDOPA PET/CT. MSAC considered that a prerequisite brain MRI may help to define the patient population by excluding structural causes of parkinsonism, but noted that MRI for this purpose was not proposed, assessed or costed in the application. MSAC noted that PD-specific MRI sequences, such as nigrosome-1 imaging, which are intended to distinguish degenerative parkinsonism from some non-degenerative causes are not in widespread use and are not funded through a PD-specific MBS item. MSAC further noted the pre-MSAC response stated that while brain MRI should be performed as part of the work-up for PD to assess other pathology and features of atypical PD, sending a patient specifically for a 3T MRI for nigrosome-1 evaluation was not considered necessary. MSAC also noted that the pre-MSAC response was amenable to broadening the item descriptor to allow other dopaminergic radiotracers. MSAC considered that more flexible radiotracer wording would be acceptable if comparative performance (of likely covered radiotracers) could be demonstrated.

MSAC noted that no studies directly addressed the safety of FDOPA PET/CT in the proposed population. However, MSAC accepted that the risks of FDOPA PET are minimal given the low radiation dose (0.03m Sv/MBq), which is comparable to other PET scans. MSAC considered that the direct risks of the scan are likely to be minimal and manageable but noted possible downstream harms from false positive or false negative results leading to inappropriate under-treatment or over-treatment, although the magnitude of this risk is unknown. Therefore, MSAC considered that the overall safety compared to standard of care clinical assessment is likely to be inferior.

MSAC noted that the evidence base for test accuracy was of low confidence. The evidence was based on few studies with heterogeneous patient populations, small sample sizes, single-centre designs and methodological limitations, including lack of blinding in some studies. MSAC noted that FDOPA PET/CT may help distinguish parkinsonian conditions from some non-degenerative causes, such as essential tremor, but is not reliable for differentiating idiopathic PD from atypical parkinsonian disorders.

The key Australian study for change in management was a retrospective study (Yeow et al 2025[1]) with a small sample size (105 patients). MSAC noted that the patient population in this study did not align with the proposed population. The study recruited participants through a single movement disorder clinic, and did not clearly report prior response to dopaminergic medicines or prior brain MRI. The study also included a substantial proportion of patients who had symptoms for more than 5 years. MSAC queried the generalisability of the study population to the broader population proposed in the application and considered that this created low confidence in the clinical evidence.

MSAC noted that the key study showed that FDOPA PET/CT imaging resulted in a change of diagnosis in approximately 33% of patients and/or changed management in approximately 50% of patients. However, there was no follow up on patient health or quality-of-life outcomes to determine whether any of the changes in management were beneficial. MSAC considered that the relationship between FDOPA PET/CT, change in diagnosis, change in management and improved patient outcomes could therefore not be evaluated.

MSAC acknowledged that there was likely a role for FDOPA PET/CT in the clinical management of some patients who are difficult to diagnose. However, MSAC considered that the place of FDOPA PET/CT in the clinical management algorithm was unclear. MSAC noted that in real-world practice, patients may be referred for FDOPA PET/CT later in the management pathway, for example after longer clinical observation, specialist review, brain MRI, Fluorodeoxyglucose (FDG) PET or other investigations. MSAC noted that this population may therefore differ from the proposed population, which consists of patients who have been on treatment for at least 12 weeks but no more than 24 months. MSAC considered this raised further uncertainty about the applicability of the evidence to the proposed population. MSAC note that this had significant flow-on effects when considering patient eligibility and expected utilisation.

MSAC considered that the absence of evidence linking FDOPA PET/CT-related changes in management to improved health outcomes led to significant uncertainty in the clinical claim of superior health outcomes compared with standard of care. MSAC noted that management may change over time based on later clinical assessment even without FDOPA PET/CT. MSAC queried the effectiveness of the proposed changes in management after a FDOPA PET/CT and noted that in some clinical scenarios the result may not change management regardless of the finding. MSAC considered that further evidence would be needed to clarify the clinical place of FDOPA PET/CT in the diagnostic and management pathway.

MSAC considered that uncertainty about the place of FDOPA PET/CT in the clinical management algorithm, and its role as a basis for changing management, flowed through to the economic and financial analysis.

MSAC noted that the economic evaluation was a cost-utility analysis which used a Markov model. MSAC noted that in the modelling only patients for whom FDOPA PET/CT would lead to a change in management entered the model, and the changes in management were considered appropriate and translated into improved symptom control and quality-adjusted life years (QALYs). MSAC noted that while this assumption was pragmatic for the purposes of modelling, it was not based on any direct evidence which showed that FDOPA PET/CT-related changes in management improved health outcomes. MSAC also noted other features of the model it considered led to uncertainty, including: that changes in management were not well described or

[1] Yeow, D., et al. (2025). "Clinical utility of (18)F-fluorodopa positron emission tomography in the movement disorder clinic: an Australian experience." Intern Med J 55(2): 207-215.

tracked in the model, different forms of parkinsonism were not explicitly modelled despite being central to the diagnostic purpose of the scan, and that the model did not compare FDOPA PET/CT with alternative diagnostic strategies. MSAC also considered that the applicability of the key Australian retrospective study to the proposed population was a major source of uncertainty in the economic model. MSAC noted the base case incremental cost-effectiveness ratio (ICER) was $18,749 per quality-adjusted life year (QALY) gained. MSAC noted that the economic model was highly sensitive to its inputs, particularly assumptions about the proportion of patients with changes in management, the appropriateness of those changes, and the utility gains from improved symptom control. For instance, the sensitivity analysis demonstrated that if 20% of changes to clinical management were inappropriate or unnecessary, the ICER increased to $80,998 per QALY gained.

MSAC considered that the financial analysis was highly uncertain because of the uncertainty in the proposed population, the clinical place of FDOPA PET/CT and expected utilisation in clinical practice. MSAC noted that the cost to MBS was estimated to be $819,256 in year 1, increasing to $1,679,281 in year 6 (with approximately 500 to 1400 patients per year). However, if FDOPA PET/CT use was extended beyond the base case to all estimated eligible patients not responding to levodopa, and not just those referred via a movement disorder clinic, this would increase to $4,292,900 in year 1 and $8,799,433 in year 6 (approximately 2500 to 7500 patients per year). In addition, since PD is primarily an age-related condition, the patient numbers eligible for access to FDOPA PET/CT could increase substantially in the future. MSAC considered that overall, there would likely be a high financial impact for uncertain clinical effectiveness if the current proposal was MBS-funded.

MSAC considered that there were equity issues which could limit access to FDOPA PET/CT, particularly in rural and remote areas. MSAC considered that specialist imaging sequences and interpretation are not in widespread use, and there may be limited access to neurologists and relevant consultant physicians and specialists in regional and remote areas. MSAC also considered that the short half-life of fluorine-18 (approximately 110 minutes) is a barrier for using FDOPA PET in regional centres, noting that even if there is a suitable PET machine available, the logistical constraints relating to the short half-life could make supply infeasible.

MSAC recommended that any future resubmission would require the following:

- Robust and low-risk-of-bias evidence on FDOPA PET/CT test accuracy, change in management and patient benefit arising from use of the scan.
- Based on this evidence, establish with greater certainty the clinical place of FDOPA PET/CT in the diagnostic and management algorithm.
- Clarify the patient population in whom the scan would be expected to change management and provide improvements in health outcomes.
- Consideration of how other diagnostic tools used to assess movement disorders, including brain MRI and FDG PET, fit in the clinical algorithm for the patient population.
- Redeveloped economic evaluation and financial estimates based on the evidence and the redefined patient population specified above.

4. Background

FDOPA PET/CT has not previously been considered by the Medical Services Advisory Committee (MSAC) for the evaluation of parkinsonism. FDOPA is not registered on the Australian Register of Therapeutic Goods (ARTG) and is currently available only through the Therapeutic Goods

Administration (TGA) Special Access Scheme (SAS) Category B. This is a common regulatory pathway to radiopharmaceutical access for clinical use in Australia.

While FDOPA PET is used internationally for neurodegenerative and neuro-oncological indications, in Australia it is only available at a small number of tertiary centres and research facilities and there are currently no listed MBS items which use this radiopharmaceutical.

What is Parkinson's Disease (PD) and parkinsonism?

PD is a progressive neurodegenerative disorder caused by the loss of dopamine-producing neurons in the substantia nigra and the accumulation of Lewy bodies, leading to classic motor symptoms such as tremor, bradykinesia, rigidity, and postural instability, as well as a wide range of nonmotor symptoms that often appear early and add significantly to disease burden[2]. "Parkinsonism" is a broader clinical syndrome or set of motor symptoms including bradykinesia plus tremor or rigidity.

Types of parkinsonism include:

- PD (also known as idiopathic PD), which is the most common cause of parkinsonism;
- Atypical parkinsonism (otherwise known as atypical PD (APD), or Parkinson's plus), including rare neurodegenerative conditions which show dopaminergic deficits, but progress faster and respond poorly to medication, e.g.:
    - multiple system atrophy (MSA),
    - progressive supranuclear palsy (PSP),
    - corticobasal degeneration (CBD), and
    - dementia with Lewy bodies (DLB).
- Secondary parkinsonisms with non-neurodegenerative causes, which have normal dopaminergic function[3,4]:, such as:
    - vascular parkinsonism,
    - drug-induced parkinsonism, or
    - parkinsonism due to toxic, metabolic, structural or infectious causes (e.g. carbon monoxide poisoning, brain tumours, traumatic brain injury).

The diagnosis of PD is primarily clinical, guided by the Movement Disorder Society (MDS) criteria[5], and requires specialist assessment because no definitive diagnostic test exists. The MDS criteria first establish the presence of parkinsonism (defined as bradykinesia plus either rest tremor or rigidity) and then the PD criteria are used – once the prerequisite "parkinsonism" is met – to evaluate a patient for PD. Clinicians rely on patient history, examination findings, exclusion of "red flags," and assessment of response to levodopa, with two diagnostic certainty levels defined: clinically established PD and clinically probable PD[3]. Supportive features include a clear levodopa response, dyskinesia, rest tremor, and olfactory or cardiac sympathetic

[2] di Biase, L, Pecoraro, PM & Di Lazzaro, V 2025, 'Validating the Accuracy of Parkinson's Disease Clinical Diagnosis: A UK Brain Bank Case-Control Study', *Ann Neurol*, vol. 97, no. 6, Jun, pp. 1110-1121.

[3] Postuma, RB, Berg, D, Stern, M, Poewe, W, Olanow, CW, Oertel, W, Obeso, J, Marek, K, Litvan, I, Lang, AE, Halliday, G, Goetz, CG, Gasser, T, Dubois, B, Chan, P, Bloem, BR, Adler, CH & Deuschl, G 2015, 'MDS clinical diagnostic criteria for Parkinson's disease', *Mov Disord*, vol. 30, no. 12, Oct, pp. 1591-1601.

[4] Waller, S, Williams, L, Morales-Briceño, H & Fung, V 2021, 'The initial diagnosis and management of Parkinson's disease', *Australian Journal of General Practice*, vol. 50, 10/21, pp. 793-800.

[5] Grimes, D, Fitzpatrick, M, Gordon, J, Miyasaki, J, Fon, EA, Schlossmacher, M, Suchowersky, O, Rajput, A, Lafontaine, AL, Mestre, T, Appel-Cresswell, S, Kalia, SK, Schoffer, K, Zurowski, M, Postuma, RB, Udow, S, Fox, S, Barbeau, P & Hutton, B 2019, 'Canadian guideline for Parkinson disease', *Cmaj*, vol. 191, no. 36, Sep 9, pp. E989-e1004.

dysfunction. Features excluding PD include cerebellar signs, gaze palsy, persistent lower-limb–only symptoms, and normal presynaptic dopaminergic imaging.

In Australia, diagnosis and management largely depend on clinical judgement, with general practitioners (GPs) referring suspected cases to neurologists. Access to imaging for the diagnosis of PD is limited. Management remains symptomatic and often requires multidisciplinary care, yet referrals to allied health and support services are suboptimal, with many patients reporting inadequate information provided by their treating physician about PD, limited access to PD nurse specialists, and significant disparities between metropolitan and rural care[6]. The purpose of FDOPA PET is to improve diagnostic certainty for PD and related parkinsonian syndromes, which should improve access to appropriate medical and allied health care with the aim of improving patient outcomes.

5. Prerequisites to implementation of any funding advice

FDOPA is an unapproved radiopharmaceutical requiring TGA approval before routine clinical use. It is currently accessed only under SAS Category B.

FDOPA requires cyclotron-adjacent production due to the short half-life of fluorine-18. Only a limited number of Australian facilities (public and private) have capability, and it is unclear whether all are actively manufacturing FDOPA. National availability would require expansion or stabilisation of supply and good quality assurance processes. PET/CT facilities require appropriately credentialed nuclear medicine physicians, trained technologists, and adherence to harmonisation/quality-control standards for quantitative brain PET imaging.

6. Proposal for public funding

FDOPA PET/CT of the brain is an investigational diagnostic imaging modality used to evaluate presynaptic dopaminergic function within the striatum. It is intended as an adjunctive (triage) test following standard clinical evaluation, magnetic resonance imaging (MRI), and therapeutic trials with dopaminergic agents, when the diagnosis remains unclear. The purpose of the technology is to help distinguish idiopathic PD (iPD) from atypical or non-degenerative parkinsonian conditions, enabling more appropriate treatment decisions and preventing unnecessary escalation of dopaminergic therapy.

A new MBS item is proposed for FDOPA PET/CT as a diagnostic imaging test for patients with parkinsonism, who are suspected of having PD, and who exhibit inadequate response to optimised dopaminergic therapy (Table 1).

The draft item descriptor includes one scan per 12-month period, no more than two scans per lifetime, specialist request required, and clinical criteria (0–30% UPDRS III response after ≥12 weeks' optimisation, within ≤24 months of treatment initiation).

[6] Lang, T, McLean, I, Shin, J, Jackson, V, Lawrenson, I, Zipper, B, Yeung, A, Evans, A & Dewson, G 2025, 'The diagnostic pathway of Parkinson's disease: understanding patient perspectives in Australia', *npj Parkinson's Disease*, vol. 11, no. 1, 2025/04/30, p. 104.

Table 1 Proposed MBS item descriptor and explanatory note for FDOPA PET/CT

Category 5 – DIAGNOSTIC IMAGING SERVICES Group I4 – Nuclear Medicine Imaging Subgroup 2 – PET
MBS Item XXXX FDOPA PET study of the brain, performed for the investigation of parkinsonian symptoms, when: a. the patient has been initially treated for Parkinson's disease but has symptoms which are unresponsive to dopaminergic medication defined as 0%-30% response (Unified Parkinson's Disease Rating Scale) after 12 weeks of treatment optimisation but not greater than 24 months post treatment initiation; and b. further investigation is required to confirm the diagnosis and inform subsequent treatment. Applicable once in any 12-month period. Applicable not more than twice per lifetime (R) Bulk bill incentive
Fee: $1,200 Benefit: 75% = $900 85% = $1095.50*

Source: PICO confirmation MSAC application 1795 April 2025
* Reflects the 1 November 2025 Greatest Permissible Gap (GPG) of $104.50. All out-of-hospital Medicare services which have an MBS fee of $697.00 or more will attract a benefit that is greater than 85% of the MBS fee – being the schedule fee less the GPG amount. The GPG amount is indexed annually on 1 November in line with the Consumer Price Index (CPI) (June quarter).

Draft Explanatory Note
Clinical notes for Item XXXX For Item XXXX, the service includes a semi-quantitative comparison of the results of the study, with the results of an FDOPA PET study of a normal brain from a reference database.

PICO Advisory Subcommittee (PASC) recommended the fee of $1,200 to reflect radiotracer production costs and limiting requests to consultant physicians or GPs in consultation with specialists to minimise inappropriate use.

MSAC may wish to consider whether MRI should be a prerequisite test (where feasible) before FDOPA PET/CT to ensure that structural causes of parkinsonism are excluded and to improve patient selection.

The recommendation to consider requesting by "GPs in consultation with a specialist" is not applicable under the current requesting rights for all MBS-funded nuclear medicine services, including PET, which are all restricted to requesting by consultant physicians and specialists. Clinical advice[7] supports the restriction of requesting rights to consultant physicians and specialists, ideally neurologists or geriatricians.

MSAC may also wish to consider the requirement that patients must be imaged within 24 months of treatment initiation, as this may disadvantage rural patients who experience delays in accessing specialist review.

[7] Personal communication with a neurologist (brain specialist), December 2025.

7. Population

Target population

The target population includes patients suspected of PD who do not respond adequately (defined as ≤30% improvement in symptoms) on the International Movement Disorder Society Unified Parkinson's Disease Rating Scale (UPDRS Part III) after at least 12 weeks of therapy optimisation and within 24 months of starting treatment. If they do not respond to the treatment of PD, PD is not ruled out, but other parkinsonism diagnoses become more likely.

This group includes patients with probable PD with atypical features, equivocal parkinsonism (where patients show parkinsonism symptoms that are too subtle to diagnose a specific condition), and patients insufficiently responsive to levodopa despite diagnostic uncertainty.

An accurate definitive diagnosis is essential, as conditions such as essential tremor (ET)[8], drug-induced parkinsonism, vascular parkinsonism, MSA, PSP, and CBD can resemble PD but require different management approaches. The DCAR of FDOPA PET/CT for parkinsonism addresses most of the Population, Intervention, Comparison, Outcome (PICO) elements that were prespecified in the PICO confirmation that was ratified by PASC.

Population size

PD is the second most common neurodegenerative disorder after Alzheimer's disease and affects over 150,000 Australians, with around 50 new cases diagnosed daily[9]. Its prevalence increases sharply with age, and with Australia's ageing population, both incidence and prevalence are expected to rise significantly. Although PD occurs more often in men, women experience faster progression and higher mortality. Young-onset Parkinson's disease accounts for 10–20% of cases. The population for this application is patients suspected of PD who do not respond to a trial of dopaminergic therapy. This is an estimated 1,500–1,600 people annually who would be eligible for FDOPA PET/CT[10], with expected uptake between 500 and 1,400 per year.

8. Comparator

The comparator as per the PICO Confirmation is standard of care. This consists mainly of clinical assessment, but can also include genetic testing, autonomic function testing, other neuroimaging, olfactory assessment, drug challenge tests, and neurophysiological and neuropsychological evaluations (based on the patient's symptoms).

There is no publicly funded dopaminergic imaging in Australia. DAT-SPECT, used in Europe, is not available in Australia and is therefore not considered an appropriate comparator. Fluorodeoxyglucose (FDG) PET has limited relevance due to it measuring regional glucose metabolism (instead of dopaminergic function) and is not indicated for parkinsonism under the MBS.

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[8] Essential tremor (ET) is a neurological disorder defined by an isolated, bilateral action tremor—most commonly of the hands—occurring without other neurological signs such as parkinsonism. Although it is a PD mimic, it is a non-parkinsonian movement disorder and is not classified as a parkinsonism because it lacks bradykinesia.

[9] Parkinson's Australia 2025, *Incidence & prevalence*, viewed 3rd October 2025, <https://www.parkinsons.org.au/information-hub/incidence-prevalence/>.

[10] Based on calculations done during the economic evaluation. More detailed information on this can be found in section 4.2 of the main body of MSAC assessment report 1795.

9. Summary of public consultation input

Consultation input was welcomed from:

1795 – Positron emission tomography / computed tomography (PET/CT) dopaminergic imaging for evaluating Parkinsonism	No. of Inputs Received
Organisations (9)	
I am providing input on behalf of a consumer group or organisation. Consumer organisations are not-for-profit organisations representing the interests of healthcare consumers, their families and carers.	1
I am providing input on behalf of a medical, health, or other (non-consumer) organisation. For example, input on behalf of a group of clinicians, research organisation, professional college, or from an organisation that produces a similar service or technology.	8
Health Professionals (34)	
I am a health professional or health academic working in the area.	34
Consumers (36)	
I have the health condition that this health service or technology is for.	17
I have the health condition that this health service or technology is for and have experience with the proposed health service or technology.	10
I am a parent, partner or another person caring for someone from the above two groups.	5
I am an interested individual who does not fall into any of the above categories.	4
Grand Total	**79**

MSAC received 70 pieces of consultation input from individuals, including 36 from consumers and 34 from health professionals. Additionally, MSAC received eight pieces of input from health organisations and one from a consumer organisation. The organisations that submitted input were:

- Australian and New Zealand Association of Neurologists
- Movement Disorder Association of Australia and New Zealand
- Parkinson's Australia
- Australasian Association of Nuclear Medicine Specialists (AANMS)
- Australian and New Zealand Society of Nuclear Medicine (ANZSNM) (2 inputs)
- Royal Brisbane & Women's Hospital – Department of Neurology, Movement Disorders Service
- Royal Australian and New Zealand College of Radiologists (RANZCR)
- Cyclotek Australia Pty Ltd

Level of support for public funding

Consultation input supported public funding of positron emission tomography / computed tomography (PET/CT) dopaminergic imaging for evaluating Parkinsonism. Approximately 90% of consumers and health professionals indicated support for public funding, with the remainder not answering the question. Inputs described the proposed service as supporting earlier, more accurate or more definitive diagnosis, particularly where current diagnosis is uncertain, reliant on specialist judgement, or tested through medication response. Organisations were also supportive of public funding, however Cyclotek qualified its support, raising concerns about the proposed item descriptor (see below).

Comments on PICO

Population

Inputs were generally supportive of the proposed population, targeting patients with diagnostic uncertainty or atypical clinical features. One respondent recommended that patients need to have had an MRI scan, assessing nigrosome-1 (which should be performed using a 3 Tesla MRI scanner) prior to having an FDOPA-PET, asserting that this can detect many more conditions than the FDOPA-PET, such as brain tumours, vascular Parkinsonism, brain haemorrhages and other Parkinsonian movement disorders such as multiple system atrophy, progressive supranuclear palsy and corticobasal degeneration. AANMS suggested that a new population be included for patients where the clinician suspects a diagnosis of Lewy body dementia, to assess for neurodegeneration.

Intervention

Input was supportive of the proposed intervention, although several inputs, including that from Cyclotek, raised concerns about the proposal to limit assessment of dopaminergic PET/CT to only FDOPA. One respondent noted that various differing tracers are available, and the consideration should go broadly to all DAT scan tracers, FPCIT, F-dopa and others, depending on local availability and familiarity. Cyclotek asserted that restricting the assessment of dopaminergic PET/CT to only FDOPA PET/CT will predictably aggravate radiotracer supply limitations with consequent negative effects on equity of access. While not specifically advocating for inclusion of a broader array of radiopharmaceuticals, RANZCR raised concerns about ongoing radiopharmaceutical supply chain restraints.

Comparator

Inputs agreed that there is no clear universally accepted comparator within the Australian context, with some noting that the current lack of imaging options in Australia (such as dopamine transporter SPECT imaging) is suboptimal. Some input suggested MRI, including nigrosome-1 MRI, as a potential comparator; however, views on this were mixed. Some inputs supported MRI as part of the pathway, while others stated it was not an appropriate comparator.

Outcomes

Input agreed with the outcomes identified by the applicant. Some inputs also identified improved wellbeing for individuals with parkinsonism as an additional outcome, noting the emotional impact of uncertainty on patients and their families.

Perceived Advantages

Inputs consistently identified improved diagnostic certainty as the primary advantage of the proposed service. This was linked to earlier diagnosis and improved differentiation between Parkinson's disease and related or mimicking conditions. Inputs also described benefits for clinical management, including earlier or more appropriate treatment, avoidance of unnecessary therapies, and improved care planning.

Patient and family benefits were also emphasised, including reduced uncertainty, anxiety and distress, improved confidence in diagnosis, and enhanced ability to plan for future care or employment. Some inputs described system-level advantages, including reduced need for repeat consultations or investigations and more efficient use of healthcare resources.

One input noted that these benefits, particularly those related to reassurance and diagnostic certainty, may be difficult to quantify in the absence of high-quality patient-reported outcome data.

Perceived Disadvantages

Many consumer inputs reported minimal or no disadvantages. Where disadvantages were identified, these included out-of-pocket costs, travel burden (particularly for people living in rural/remote Australia), low-level radiation exposure and procedural discomfort such as claustrophobia. Some inputs also noted that receiving a definitive or changed diagnosis may have psychological impacts.

Input described safety concerns as low-level. Some inputs raised potential risks of overuse or inappropriate use, particularly if the service is not clearly targeted to appropriate clinical indications.

Support for Implementation and Issues

Input indicated that implementation was feasible, particularly where PET infrastructure and expertise are already available. However, input identified several challenges, including radiotracer supply and production, transport logistics, availability of trained workforce and reporting capability, and access in rural and regional areas.

MBS Item descriptor

Some input noted that the item descriptor in the MSAC application referred to "dopaminergic imaging of the brain for assessment of Parkinson disease," while the item descriptor in the PICO confirmation refers to "FDOPA PET study of the brain, performed for the investigation of parkinsonian syndromes...". Pre-PASC input from health professionals and organisations (commenting on the item descriptor in the application) were mostly supportive, with AANMS specifically noting that one of the reasons for support was that the descriptor 'is agnostic to the type of PETS radiopharmaceutical used.'

In the pre-MSAC consultation input, several health professionals commented that the item descriptor should include other radiopharmaceuticals, with one stating that it should revert to the original description of 'dopaminergic imaging.' Only ANZSNM and Cyclotek provided pre-MSAC organisational input, with Cyclotek strongly contending that the item should specify predopaminergic or dopaminergic PET/CT and should not be confined to FDOPA PET/CT.

Other comments on the item descriptor included:

- specification of assessment by a neurologist rather than a 'specialist,' although others noted that broader specialties may better support regional and remote access.
- restrictions on repeat testing, with some stating that once every 24 months would be appropriate, while others suggested that fixed intervals may not reflect clinical need.
- a small number of health practitioners advocating for MRI scan, assessing nigrosome-1, prior to accessing Pet/CT.

MBS Fee

There was support for the proposed MBS fee especially the $1,200 suggested by PASC. ANZSNM, AANMS and Cyclotek explicitly cited their support for the fee proposed by PASC of $1,200 with ANZSNM noting that the supply of radiopharmaceutical for the proposed PET scan will have a much higher cost than for standard F-18 FDG.

10. Characteristics of the evidence base

No direct-from-test-to-health-outcomes evidence was identified. Furthermore, no studies were identified that met the inclusion criteria for assessing the test accuracy of FDOPA PET/CT with postmortem neuropathology / autopsy as the reference standard. Three studies were identified investigating the diagnostic accuracy of FDOPA PET with clinical diagnosis or clinical examination

as a reference standard, and four studies were included on change in management. Only one of these studies evaluated change in disease management after FDOPA PET/CT. None of these studies were specific to the target population (or provided subgroup analyses), i.e. those who had failed to respond to a trial of levodopa. See Table 2 below for key features of the included evidence.

No studies met the inclusion criteria for assessing evidence on health outcomes resulting from change in management due to FDOPA PET/CT.

Table 2 Key features of the included evidence

Criterion	Type of evidence supplied	Extent of evidence supplied	Overall risk of bias in evidence base
Performance of the test	Concordance studies with clinical diagnosis as the reference standard.	☒ k=3 n=187	High risk of bias Limited applicability
Change in diagnosis	Before-and-after case series and retrospective cohort study	☒ k=4 n=300	Serious risk of bias Limited applicability
Change in disease management	One retrospective cohort study	☒ k=1 n=105	Serious risk of bias Limited applicability
Health outcomes	N/A	☐ k=0 n=0	N/A
Other - Sensitivity and specificity of comparators for diagnosing parkinsonism	Varying study designs. This evidence did not meet the PICO criteria but was included to estimate the accuracy/performance of the comparator (standard of care).	☒ k=31 n=21,417	N/A

k=number of studies, n=number of patients, N/A=not applicable, PICO=Population/Intervention/Comparator/Outcomes

11. Comparative safety

No studies were identified that addressed the safety of FDOPA PET/CT in patients suspected of PD. No FDOPA-specific safety concerns were identified. Radiation dose is low (~0.03 mSv/MBq) and comparable to other PET tracers, which means risks are limited to standard radiopharmaceutical administration (i.e. there are no special, high-risk hazards associated with FDOPA specifically). There is however potential for downstream harm from false positive or false negative results leading to inappropriate treatment decisions, although the magnitude of this risk is unknown due to limited accuracy data. There is a small, manageable risk of cancer in the long-term from low-risk radiation exposure, which is managed by standard safety protocols (e.g. encouraging hydration to flush the tracer through the kidneys).

Previous MSAC evaluations of PET imaging (e.g. MSAC application 1357) have identified no new or emerging safety issues.

Although the risks of FDOPA are acknowledged to be minimal, the use of FDOPA PET/CT results in likely inferior (but manageable) safety compared with standard of care.

12. Comparative effectiveness

Concordance of FDOPA PET/CT with clinical diagnosis

Three studies (all considered to have a high risk of bias) evaluated FDOPA PET/CT for differentiating PD, APD and ET. All three utilised clinical diagnosis as the reference standard. No studies compared FDOPA PET/CT with the preferred reference standard, neuropathological confirmation at autopsy, limiting the certainty of the findings. Clinical diagnosis, particularly when made early in the disease, is known to be imperfect, and variability in timing (baseline vs follow-up), blinding, and diagnostic criteria likely introduced misclassification bias across studies. None of the studies were specific to those who had failed to respond to a trial of levodopa.

The available evidence indicated that FDOPA PET/CT showed moderate to high agreement with clinical diagnosis, with performance varying by study design, blinding, and reader expertise. The prospective, blinded study by Dhawan et al. (2022) reported moderate positive percent agreement (PPA) (61–73%) but good negative percent agreement (NPA) (87–91%) and highlighted the influence of reader experience on accuracy. The study compared a consensus of the FDOPA results of two non-expert readers (radiologists/nuclear medicine) that had no prior experience in reading FDOPA PET scans with an expert reader's results who had numerous years of experience in reading FDOPA PET scans.

In contrast, the small retrospective study by Ibrahim et al. (2016), in which the final clinical diagnosis (the reference standard) was not blinded to FDOPA PET/CT scan results, reported very high PPA (95%) and NPA (100%), but these estimates are likely inflated due to incorporation bias. The results may therefore be interpreted to mean that clinicians trust the results of FDOPA PET/CT and incorporate the information gained by the imaging into the clinical diagnosis.

The largest prospective study, Sood et al. (2021), focused on using FDOPA PET/CT to differentiate ET from PD or APD using semiquantitative thresholds and reported excellent PPA (100%) and good NPA (84%), with an area under the curve (AUC) of 0.963. However, this study assessed accuracy against the baseline clinical diagnosis rather than clinical assessments performed in the follow-up visits, potentially reducing reliability in early or uncertain cases.

The applicability of these results to the proposed population are limited, as in the study by Ibrahim et al. (2016), only 2/22 patients failed to respond to levodopa. The proportion relevant to the target population from the other studies is unknown.

Across studies, FDOPA PET/CT appears particularly useful for distinguishing ET from parkinsonian conditions, but consistent with known limitations of dopaminergic imaging, it cannot reliably differentiate PD from APD. Variability in reference standards, lack of autopsy validation, and limited sample sizes constrained the robustness of conclusions and suggested moderate overall certainty in the accuracy estimates.

Table 3 FDOPA PET/CT diagnostic accuracy results

Study (N)	Reference Standard	PPA (95% CI)	NPA (95% CI)	Notes
Dhawan et al. 2022 (N=56)[11]	Clinical diagnosis 6–12 months after imaging; blinded assessor	Expert reader: 72.7% (54.5–86.7))	Expert reader: 91.3% (72.0–98.9)	Prospective; blinding; reader expertise impacts accuracy
		Majority read[a]: 60.6% (42.1–77.1)	Majority read[a]: 87.0% (66.4–97.2)	
Ibrahim et al. 2016 (N=28)[12]	Final clinical diagnosis; not blinded to FDOPA PET/CT result	95.4% (75.3–100)	100% (59.0–100)	Retrospective; high risk of incorporation bias; small sample
Sood et al. 2021 (N=103)[13]	Clinical diagnosis at enrolment	100% (ET vs PD/APD at SUR ≥1.35)	84% (ET vs PD/APD at SUR ≥1.35)	Prospective; semiquantitative thresholding; AUC 0.963

APD = atypical parkinsonian disorder; AUC = area under the curve; ET = essential tremor; FDOPA = [18F]fluorodopa; FDOPA PET/CT = [18F]fluorodopa positron emission tomography/computed tomography; N = number of studies; PD = Parkinson's Disease; SUR = specific uptake rate of striatum.

[a] The study compared the "majority read" -- a consensus of the FDOPA results of two non-expert readers (radiologists/nuclear medicine) that had no prior experience in reading FDOPA PET scans -- with an expert reader's results who had numerous years of experience in reading FDOPA PET scans,

[b] SURs were used to differentiate ET from PD and Parkinson-plus syndrome (PPS). Receiver operating characteristics (ROC) curve was drawn to estimate a cut-off value of mean SURs in both PET and SPECT images for differentiating ET from PD and PPS. In FDOPA images an average SUR of ≥1.35 sensitivity and specificity were 100% and 84%, respectively.

Diagnostic accuracy of standard of care (the comparator)

The interventions described in the body of evidence on diagnostic accuracy of 'standard of care' fall into three broad categories: (1) clinical diagnostic approaches, (2) imaging based interventions, and (3) other tests, such as computational or machine-learning tools. None of the studies focused on the accuracy of the comparative testing strategies were specific to the population of interest (those suspected of PD who have failed to respond to a levodopa trial).

Clinical diagnosis

Accuracy of clinical diagnosis varied widely depending on disease, timing, and specialist expertise. For PD, evidence which had autopsy findings as the reference standard showed generally high accuracy when assessed by movement disorder specialists, with sensitivity typically 82–91% and specificity 85–98%, improving with longer disease duration. Earlier evidence reported lower accuracy (e.g. 76% overall accuracy), suggesting improvements over time with better criteria and increased specialist involvement. Non-specialists tend to overdiagnose PD, producing lower specificity.

Diagnostic accuracy for APD was substantially lower and more variable:

[11] Dhawan, V, Niethammer, MH, Lesser, ML, Pappas, KN, Hellman, M, Fitzpatrick, TM, Bjelke, D, Singh, J, Quatarolo, LM, Choi, YY, Oh, A, Eidelberg, D & Chaly, T 2022, 'Prospective F-18 FDOPA PET Imaging Study in Human PD', *Nucl Med Mol Imaging*, vol. 56, no. 3, 2022-6, pp. 147-157

[12] Ibrahim, N, Kusmirek, J, Struck, AF, Floberg, JM, Perlman, SB, Gallagher, C & Hall, LT 2016, 'The sensitivity and specificity of F-DOPA PET in a movement disorder clinic', *Am J Nucl Med Mol Imaging*, vol. 6, no. 1, 2016, pp. 102-109.

[13] Sood, A, Shukla, J, Shree, R, Vatsa, R, Modi, M & Mittal, BR 2021, 'Comparative Performance of 99mTc-TRODAT-1 SPECT/CT and 18F-FDOPA PET/CT Imaging in Patients With Parkinson's Disease, Parkinson-Plus Syndrome, and Essential Tremor', *Clin Nucl Med*, vol. 46, no. 2, 2021-2-1, pp. 95-102.

- MSA: Sensitivity was <50% at first visit in the majority of cases, improving over time; specificity generally >90%. Autopsy cohorts showed only 62% of clinically diagnosed MSA cases are pathology-confirmed, reflecting high misclassification.
- PSP: Sensitivity ranged 9–84% but specificity was consistently >95%. Misdiagnosis was common, with many cases pathologically shown to be CBD, MSA or LBD.
- DLB: Older criteria showed a low sensitivity (18%), which improved to ~88% under newer criteria, but with reduced specificity.

Overall, clinical diagnosis performs well for PD, but poorly for APD, particularly in early disease, contributing to significant diagnostic uncertainty.

Imaging based interventions

FDG PET: Two autopsy-validated studies assessed FDG PET[14,15]. In patients with clinically uncertain parkinsonism[16], FDG PET correctly classified 80% of cases and distinguished MSA from PSP with 87.5% accuracy, outperforming clinical judgement[14]. A larger autopsy cohort using machine-learning analysis of FDG patterns predicted PSP pathology with 91% accuracy, higher than magnetic resonance parkinsonism index (MRPI) performance[15]. Overall, FDG PET shows strong diagnostic accuracy, especially when paired with computational methods.

MRI: MRI markers were consistently highly specific but poorly sensitive, particularly in early disease. Diffusion-weighted MRI differentiated MSA, parkinsonian type (MSA-P) from PD with 90% sensitivity and 93% specificity[17]. Validation of the 2022 MDS-MSA MRI criteria showed specificity of 99–100%, but sensitivity ranged from 9% in year 1 to 77% later in disease[18]. Classic MRI signs (e.g. the hummingbird[19] sign for PSP, the hot-cross-bun[20] sign and MCP

[14] Schindlbeck, KA, Gupta, DK, Tang, CC, O'Shea, SA, Poston, KL, Choi, YY, Dhawan, V, Vonsattel, JP, Fahn, S & Eidelberg, D 2021, 'Neuropathological correlation supports automated image-based differential diagnosis in parkinsonism', *Eur J Nucl Med Mol Imaging*, vol. 48, no. 11, Oct, pp. 3522-3529.

[15] Braun, AS, Satoh, R, Pham, NTT, Singh-Reilly, N, Ali, F, Dickson, DW, Lowe, VJ, Whitwell, JL & Josephs, KA 2025, 'Machine Learning Models of Voxel-Level [(18)F] Fluorodeoxyglucose Positron Emission Tomography Data Excel at Predicting Progressive Supranuclear Palsy Pathology', *Ann Neurol*, vol. 98, no. 2, Aug, pp. 410-420.

[16] Clinically uncertain parkinsonism means that parkinsonian signs are present, but the cause cannot yet be confidently diagnosed.

[17] Bajaj, S, Krismer, F, Palma, JA, Wenning, GK, Kaufmann, H, Poewe, W & Seppi, K 2017, 'Diffusion-weighted MRI distinguishes Parkinson disease from the parkinsonian variant of multiple system atrophy: A systematic review and meta-analysis', *PLoS One*, vol. 12, no. 12, 2017, p. e0189897.

[18] Wilkens, I, Heine, J, Ruf, VC, Compta, Y, Porcel, LM, Troakes, C, Vamanu, A, Downes, S, Irwin, D, Cohen, J, Lee, EB, Nilsson, C, Englund, E, Nemati, M, Katzdobler, S, Levin, J, Pantelyat, A, Seemiller, J, Berger, S, van Swieten, J, Dopper, E, Rozenmuller, A, Kovacs, GG, Bendahan, N, Lang, AE, Herms, J, Höglinger, G & Hopfner, F 2024, 'Impact of Magnetic Resonance Imaging Markers on the Diagnostic Performance of the International Parkinson and Movement Disorder Society Multiple System Atrophy Criteria', *Mov Disord*, vol. 39, no. 9, Sep, pp. 1514-1522.

[19] The hummingbird sign is a characteristic MRI finding seen in PSP, where selective midbrain atrophy with relative preservation of the pons on a mid-sagittal image creates a brainstem silhouette resembling a hummingbird. It reflects degeneration of the midbrain tegmentum and an imaging clue for PSP.

[20] The hot-cross bun sign is an MRI finding seen on axial T2-weighted images as a cruciform (cross-shaped) hyperintensity within the pons, caused by degeneration of the transverse pontocerebellar fibres with relative preservation of the corticospinal tracts. It is classically associated with the cerebellar subtype of MSA-C, though it can be seen in other disorders affecting pontocerebellar pathways.

hyperintensity for MSA) had excellent specificity (~100%) but modest sensitivity (≤68%)[21]. Overall, MRI is most useful for confirming advanced APD, not early diagnostic differentiation.

Other tests

Emerging computational approaches showed promising accuracy, often exceeding standard clinical assessment. Machine-learning models applied to FDG PET could identify PSP pathology with high accuracy (e.g., 84% sensitivity and 94% specificity)[15], while Bayesian phenotypic models reported >90% sensitivity and specificity for PD and MSA, and strong performance for PSP[22]. These methods are not yet standard clinical tools, but they demonstrate potential to improve diagnostic precision.

Uncertainty in test accuracy

The evidence base for FDOPA PET/CT test accuracy is limited because no studies use the protocol-specified reference standard of postmortem neuropathology, relying instead on imperfect clinical diagnosis that can misclassify cases (particularly early in disease or when distinguishing PD from APD). As a result, concordance between FDOPA PET/CT and clinical diagnosis is difficult to interpret, and biases such as differential misclassification, incorporation bias, small sample sizes, single-centre study designs, lack of blinding, and heterogeneous image reading methods reduce confidence in the accuracy results. Although FDOPA PET/CT can differentiate dopaminergic from nondopaminergic tremor syndromes, its limited ability to distinguish PD from APD restricts its diagnostic utility in the target population.

Comparator evidence is broader but still heterogeneous and indirect, with specialist clinical diagnosis performing reasonably well for PD but less accurately for atypical syndromes, and differences in populations and diagnostic criteria limiting its direct comparability to FDOPA PET/CT evidence.

Linked evidence of change in management

Evidence on the impact of FDOPA PET/CT on clinical management in patients with suspected PD was limited and heterogeneous. Only one Australian study[23] provided detailed, quantifiable data on management change, while other available studies primarily demonstrated diagnostic clarification without clearly reporting downstream treatment consequences.

Across 105 Australian patients, FDOPA PET/CT changed diagnosis in 36% and management in 52% of patients, with the direction and magnitude of impact varying according to scan result. Management changes were more common when scans were consistent with iPD (68%) than when scans were normal (47%) (Table 4). Typical management changes included initiating or escalating dopaminergic therapy, tapering dopaminergic drugs after normal scans, adjustments to antipsychotic medications for suspected drug-induced PD, and in a minority of cases, decisions about advanced therapies such as deep brain stimulation. The applicability of the

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[21] Massey, LA, Micallef, C, Paviour, DC, O'Sullivan, SS, Ling, H, Williams, DR, Kallis, C, Holton, JL, Revesz, T, Burn, DJ, Yousry, T, Lees, AJ, Fox, NC & Jäger, HR 2012, 'Conventional magnetic resonance imaging in confirmed progressive supranuclear palsy and multiple system atrophy', *Mov Disord*, vol. 27, no. 14, Dec, pp. 1754-1762.

[22] Massey, Q, Nihoyannopoulos, L, Zeidman, P, Warner, T, Bhatia, K, Gandhi, S & Lambert, C 2025, 'Refining the diagnostic accuracy of Parkinsonian disorders using metaphenomic annotation of the clinicopathological literature', *NPJ Parkinsons Dis*, vol. 11, no. 1, Nov 10, p. 314.

[23] Yeow, D., et al. (2025). "Clinical utility of (18)F-fluorodopa positron emission tomography in the movement disorder clinic: an Australian experience." Intern Med J 55(2): 207-215.

population in the study by Yeow et al. to the target population in this assessment is unclear, as it was not reported if the patients included in the study had undergone a levodopa trial.

Table 4 Change in provisional diagnosis and management following FDOPA PET/CT stratified by FDOPA PET/CT result, as presented by Yeow et al. (2025)

FDOPA PET/CT result	Number of patients where provisional diagnosis changed (%)	Number of patients where management changed (%)
Consistent with iPD (n=34)	8 (23.5)	23 (67.6)
Normal scan (n=66)	28 (42.4)	31 (47.0)
Atypical FDOPA reduction (n=3)	1 (33.3)	0 (0.0)
Equivocal FDOPA reduction (n=2)	1 (50)	1 (50.0)

FDOPA = [18F]fluorodopa; FDOPA PET/CT = [18F]fluorodopa positron emission tomography/computed tomography; iPD = idiopathic Parkinson disease.

Source: Table 3 of Yeow et al. (2025) and personal communication with Dr. Dennis Yeow (21 January 2026).

Preliminary evidence from the Australian MAP-DOPA study suggested diagnostic impact (redacted), with high concordance between FDOPA findings and subsequent treatment choices (redacted), but it did not report how often management was actually altered. That is, it was unclear whether the changes in diagnosis resulted in treatment changes (and could consequently be expected to impact on health outcomes).[24]

International dual-tracer-tracer PET/CT studies (FDOPA + FDG) similarly showed substantial shifts in diagnostic categorisation, particularly reclassification from iPD to APD, but provided no quantifiable evidence regarding management change.[25,26]

Overall, while FDOPA PET/CT appears to offer meaningful diagnostic value as it provides additional information on presynaptic dopaminergic function that can support or refute a clinical diagnosis of PD or other APD, the current evidence base did not robustly demonstrate a consistent or measurable impact on treatment decisions in real-world practice. Key limitations included retrospective designs, incomplete reporting of prior therapies (notably levodopa trial status), inconsistently defined management outcomes, and lack of applicability to the specific target population of this assessment. These issues substantially limit confidence in the extent to which FDOPA PET/CT changes management in the Australian context.

Linked evidence of health outcomes

No direct evidence was identified to demonstrate that changes in management driven by FDOPA PET/CT based diagnoses improve health outcomes for patients with parkinsonism, and no studies quantified the impact of incorrect, delayed, or revised diagnosis on mortality, function, quality of life, or healthcare utilisation. Although the literature highlighted substantial diagnostic

[24] Dwyer et al. Molecular Algorithms for Parkinsonism: A prospective cohort study to define criteria for the use of 18F-DOPA PET/CT in a movement disorder clinic. – INTERIM RESULTS (MAP DOPA Study). Received via personal communication.

[25] Emsen, B, Villafane, G, David, JP, Evangelista, E, Chalaye, J, Lerman, L, Authier, FJ, Gracies, JM & Itti, E 2020, 'Clinical impact of dual-tracer FDOPA and FDG PET/CT for the evaluation of patients with parkinsonian syndromes', *Medicine (Baltimore)*, vol. 99, no. 45, 2020-11-6, p. e23060.

[26] Sinisterra Solís, FA, Romero Castellanos, FR, Cortés Mancera, EA, Calderón Ávila, AL, González Rueda, SD, Rosales García, JS, Kerik Rotenberg, NE, Tristán Samaniego, DP & Bonilla Navarrete, AM 2024, 'Brain Evaluation by Dual PET/CT with [(18)F] FDOPA and [(18)F] FDG in Differential Diagnosis of Parkinsonian Syndromes', *Brain Sci*, vol. 14, no. 9, 2024-9-18.

uncertainty and frequent changes in diagnosis, the clinical consequences of misdiagnosis remained unmeasured. No evidence was found to support the idea that starting treatment earlier (based on a diagnosis made with FDOPA PET/CT) leads to better outcomes for patients. Expert clinical advice suggested that a confident diagnosis may improve adherence to dopaminergic therapy and physiotherapy and support better quality of life, while diagnostic errors may delay necessary management for alternative conditions[7]. However, no published evidence was found to substantiate those views. Overall, the evidence base provides no quantifiable health outcome benefits attributable to FDOPA PET/CT, and available insights rely primarily on expert opinion rather than patient-level outcome studies.

Clinical claim

The applicant claimed that use of FDOPA PET/CT would result in more accurate diagnoses of parkinsonian syndromes which in turn would enable superior health outcomes.

Due to significant uncertainty in the evidence base, the claim of superior health outcomes could neither be supported or negated. This uncertainty is caused from the:

- the lack of any data on the accuracy of FDOPA PET/CT versus the reference standard chosen a priori, and
- the lack of information regarding whether the changes in management reported in an Australian trial[23] would result in superior health outcomes.

However, it is plausible based on the identified diagnostic value that the additional information provided by FDOPA PET/CT would help distinguish between types of parkinsonism, and in turn alter management. Therefore, it is plausible that this may be superior to current standard of care.

13. Economic evaluation

Based on the conclusions of the clinical evaluation, FDOPA PET/CT has plausible superior effectiveness and inferior safety (though risks are acknowledged to be minimal). On this basis, a cost-utility analysis (with steps comprising cost effectiveness analysis results) for the addition of FDOPA PET/CT to SOC in patients suspected of PD who had not responded to 12 weeks–2 years of dopaminergic medication was presented.

While this was based on the key Australian change in management study, Yeow et al. (2025)[23], as evidence for performance of FDOPA PET/CT had limited applicability to the evidence for changes in management, and no evidence was identified to support the impact of changes following FDOPA PET/CT, it was unclear whether the changes reported would translate to improvements in patient-relevant outcomes. Given the unproven claim of superior effectiveness, the results of the economic evaluation should be interpreted with caution.

The key components of the economic evaluation are summarised in Table 5.

Table 5 Summary of the economic evaluation

Component	Description
Perspective	Health care system perspective
Population	Patients with parkinsonism who have not responded to 12 weeks to 2 years of dopaminergic medications
Comparator	SOC
Type(s) of analysis	Cost-effectiveness analysis and cost-utility analysis
Outcomes	Change in diagnosis, change in management decisions, LYs on adequate treatment, QALYs due to improved symptom control
Time horizon	3 years in the model base case vs change in management at clinical appointments immediately following results of FDOPA PET/CT, as reported in Yeow et al. (2025)[23].
Computational method	Markov model
Generation of the base case	Modelled economic evaluation, with stepped adjustment of outcomes reported in Yeow et al. (2025)[23]
Health states	Adequate treatment Inadequate treatment Dead
Cycle length	1 month
Transition probabilities	Change in clinical management: 52.4% (Yeow et al. 2025)[23] Adequacy of changes in clinical management: 100%, assumed. Sensitivity analyses presented assuming 80%, based on Dhawan et al. (2022)[11] and 96.6%, based on Ibrahim et al. (2016)[12]. Time to resolution of diagnosis: Rossi et al. (2021)[27] Mortality: ABS life tables, adjusted based on HRs for PD and APD (Fielding et al. 2016)[28]
Utilities	Differential utility weights for the impact of different management strategies on QoL were sourced from the literature. A weighted utility difference was applied based on the distribution of changes in management strategies reported in Yeow et al. (2025)[23].
Costs included	FDOPA PET and co-claimed CT (including professional attendance for review of results) Clinical management pre- and post-FDOPA PET/CT (Yeow et al. 2025)[23] Consultations with managing clinician, assumed to vary between the Adequate and Inadequate treated health states (Chaudhuri et al. 2022)[29] Resolution of diagnosis, assuming FDG-PET (70.7%), brain MRI (29.3%) and professional attendance (100%)
Discount rate	5% for both costs and outcomes
Software	TreeAge Pro and Microsoft Excel

ABS = Australian Bureau of Statistics; APD = atypical parkinsonian disorder; FDG-PET = fluorodeoxyglucose-positron emission tomography; FDOPA PET/CT = [18F]fluorodopa positron emission tomography/computed tomography; MRI = magnetic resonance imaging; PD = Parkinson's Disease; QoL = quality-of-life; SOC = standard of care.

A Markov model was used to generate costs and outcomes due to the use of FDOPA PET/CT. Patients enter health states of the model categorised by adequacy of initial management. Within

[27] Rossi, M, Perez-Lloret, S & Merello, M 2021, 'How much time is needed in clinical practice to reach a diagnosis of clinically established Parkinson's disease?', *Parkinsonism Relat Disord*, vol. 92, Nov, pp. 53-58.

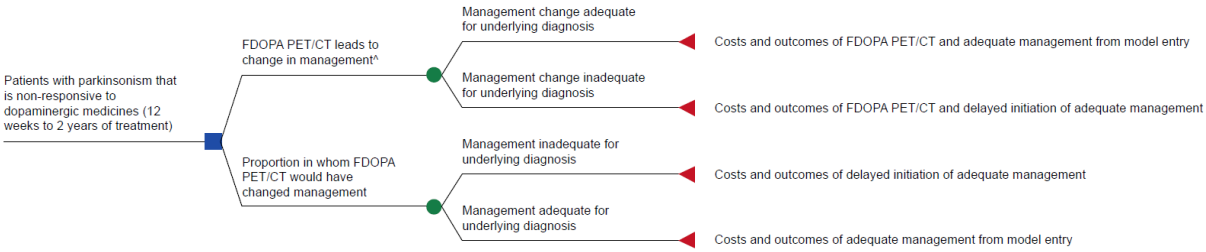
[28] Fielding, S, Macleod, AD & Counsell, CE 2016, 'Medium-term prognosis of an incident cohort of parkinsonian patients compared to controls', *Parkinsonism Relat Disord*, vol. 32, Nov, pp. 36-41.

[29] Chaudhuri, KR, Hand, A, Obam, F & Belsey, J 2022, 'Cost-effectiveness analysis of the Parkinson's KinetiGraph and clinical assessment in the management of Parkinson's disease', *J Med Econ*, vol. 25, no. 1, Jan-Dec, pp. 774-782.

each health state, costs and outcomes of management are quantified until all patients have been diagnostically resolved.

Due to limitations of the data, which did not report changes in management by whether or not the diagnosis was also changed, or report management decisions where these did not change following FDOPA PET/CT, the model was simplified to reflect only those patients where changes in management occurred (with or without a change in diagnosis) (Figure 1). To capture the cost of imaging across all patients, the cost applied reflects that required to identify one patient who experiences a change in management.

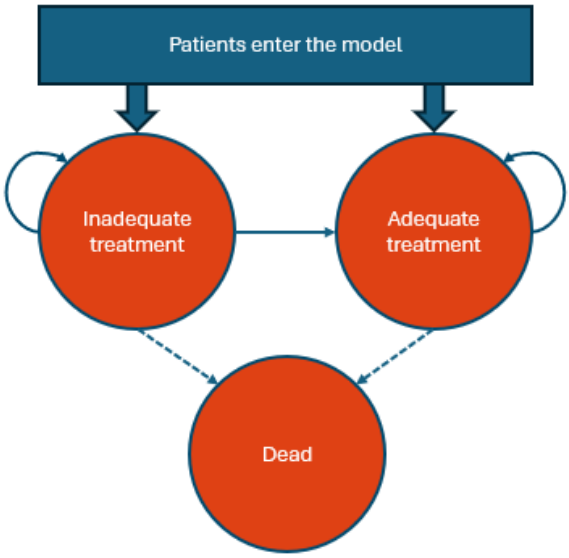
Figure 1 Model structure



FDOPA PET/CT = [18F]fluorodopa positron emission tomography/computed tomography; SOC = standard of care.
^ The cost to identify one patient that FDOPA leads to a change in management is applied.

The model included health states for Adequate treatment, Inadequate treatment and Dead (Figure 2). Patients who are adequately treated from model entry are assumed to remain in this health state, unless they die. Patients who are inadequately treated at model entry remain in this health state, until they have their management adequately changed or die. The risk of death is not assumed to vary between patients who are adequately and inadequately treated, however transitions to death have been included in the analysis so that life years (LYs) on adequate treatment are not overestimated.

Figure 2 Markov model structure



As FDOPA PET/CT is proposed to change clinical management in this population, the distribution across the inadequately and adequately treated health states differed between the intervention and the comparator arms of the model. In the base case analysis, the model assumed that

management changes reported in Yeow et al. (2025)[23] were 100% adequate for managing the patients' underlying diagnoses. While evidence for the performance of FDOPA PET/CT suggested some discordance with clinical diagnosis, the applicability of these results (where interpretation of FDOPA PET/CT was blinded to patients' clinical information) to the proposed setting (where FDOPA PET/CT would provide additional information to SOC) was unclear. Estimates of discordance were explored in sensitivity analyses.

The model time horizon was 3 years, and was based on the MAP-DOPA study[24] which assumed that the combined final clinical diagnosis at 36 months would be taken as ground truth. This was consistent with Rossi et al. (2021)[27] which reported that the time needed to reach a final clinical diagnosis in 95% of patients was 2.75 years. In a subgroup of patients who had not responded to levodopa, 94% had their final clinical diagnosis by 3 years.

The results of the stepped analysis to generate the base case economic evaluation is presented in Table 6.

Table 6 Results of the stepped economic analysis

	FDOPA PET/CT	SOC	Increment
Step 1: Trial-based analysis, based on Yeow et al. (2025)[23] Diagnosis and management decisions at the clinical appointment immediately following results of FDOPA PET/CT. Costs included FDOPA PET and co-claimed CT, including consultation for review of results			
Cost of FDOPA PET/CT, including consultation for review of results	$1,384.40	–	$1,382.40
Changes in diagnosis	36.2%	–	36.2%
Changes in management	52.4%	–	52.4%
ICER per change in management decision			**$2,643**
Step 2: Transformation of changes in management into LYs on adequate treatment Extrapolation to 3 years, including resolution of initially inadequately managed patients. In addition to the costs associated with FDOPA PET/CT, cost of management (adequate or inadequate), costs associated with resolving the diagnosis and implementing adequate management, in patients who were initially inadequately managed were included.			
Total cost	$13,020.63	$11,653.88	$1,366.75
LYs on adequate treatment	2.763	2.030	0.734
ICER per additional LY on adequate treatment			**$1,863**
Step 3: Transformation of LYs on adequate treatment into QALYs Adequate LYs on treatment were transformed into QALYs due to improved symptom control based on published utility values, weighted by the distribution of management changes reported in Yeow et al. (2025)[23].			
Total cost	$13,020.63	$11,653.88	$1,366.75
QALYs due to improved symptom control	0.273	0.200	0.073
ICER per additional QALY gained			**$18,749**

FDOPA PET/CT = [18F]fluorodopa positron emission tomography/computed tomography; ICER = incremental cost-effectiveness ratio; LY = life year; QALY = quality-adjusted life year; SOC = standard of care.

The first step was a trial-based analysis based on Yeow et al. (2025)[23] that included only the cost of FDOPA PET/CT, and reported changes in diagnosis and changes in management decisions. Subsequent modelling steps were presented that transformed the outcome of changes in management into additional LYs on adequate treatment, then additional quality-adjusted life years (QALYs) due to improved symptom control following adequate management.

While FDOPA PET/CT is proposed to increase the proportion of patients who receive adequate treatment, no evidence was identified to support the adequacy of the changes. On this basis, the results of the modelled economic evaluation should be interpreted with caution.

The results of the cost-utility analysis should further be interpreted with the limitations of the utility estimates applied. There is likely to be considerable heterogeneity in patient symptoms and disease severity both across and within diagnoses, and as various sources (from different populations and using different instruments) were used. As a result, comparisons across different management changes are unreliable, and the analysis may be sensitive to the distribution of management changes modelled.

Disaggregated costs and outcomes are presented in Table 7.

Table 7 Disaggregated costs and outcomes

	FDOPA PET/CT	SOC	Increment
Costs			
FDOPA PET/CT cost	$2,642.95	$0.00	$2,642.95
Cost of adequate management	$9,883.59	$8,796.56	$1,087.03
Cost of inadequate management	$0.00	$1,673.09	−$1,673.09
Cost of diagnostic resolution	$0.00	$591.77	−$591.77
Cost of professional attendances for ongoing management	$494.09	$592.46	−$98.37
Total cost	**$13,020.63**	**$11,653.88**	**$1,366.75**
Outcomes			
LYs on adequate treatment	2.763	2.030	0.734
LYs on inadequate treatment	0.000	0.734	−0.734
Total LYs	2.763	2.763	0.000
QALYs due to improved symptom control	0.274	0.201	0.073
QALY decrement for DBS	−0.0012	−0.0013	0.0001
Total QALYs	**0.273**	**0.200**	**0.073**

DBS = deep brain stimulation; FDOPA PET/CT = [18F]fluorodopa positron emission tomography/computed tomography; QALY = quality-adjusted life year; SOC = standard of care.

The incremental cost was driven by the cost of FDOPA PET/CT and adequate management. This was consistent with the claim that FDOPA PET/CT would reduce the delay in time to diagnosis and adequate treatment for managing patient's underlying disease. These costs were offset by a reduction in the cost associated with inadequate management and cost of resources associated with diagnostic resolution.

Therefore, assumptions regarding the appropriateness of management following FDOPA PET/CT are a key driver of the incremental cost, in addition to the assumption that adequate management would largely be delayed in the SOC arm (increasing the cost of adequate management under SOC, and reducing the incremental cost of adequate management). Due to a lack of evidence to support the extent of adequate changes in management following FDOPA PET/CT, or the delay in adequate treatment under SOC, the results are subject to considerable uncertainty.

Disaggregation of LYs showed that the incremental LYs on adequate treatment gained were all due to a reduction in LYs spent on inadequate treatment. No difference in LYs was modelled

between FDOPA PET/CT and SOC. Incremental QALYs were driven by improved symptom control, due to increased time spent on adequate treatment.

The key drivers of the primary analysis are presented in Table 8.

Table 8 Key drivers of the model

Description	Method/Value	Impact Base case: $18,749/QALY gained
Proportion of incorrect FDOPA PET/CT changes in management	0% (assumption)	High, favours FDOPA PET/CT Assuming 20% of changes were inadequate, based on Dhawan et al. (2022)[11], increased the ICER to $80,998/QALY gained. Assuming 3.4% of changes were inadequate, based on Ibrahim et al. (2016)[12], increased the ICER to $25,533/QALY gained.
Proportion of patients with a change in clinical management	52.4% (Yeow et al. 2025)[23]	High, direction uncertain. Reducing the proportion with a change in management to 40% increased the ICER to $29,970/QALY gained. Increasing this proportion to 60% reduced to ICER to $14,145/QALY gained.
Utility of symptom control in PD by pharmacotherapy	0.0853 (Chaudhuri et al. 2022)[29]	High, direction uncertain. Reducing the utility to 0.0210 increased the ICER to $27,010/QALY gained. Increasing the utility to 0.1325 reduced the ICER to $15,311/QALY gained.
Utility of symptom control in ET	0.220 (Herceg et al. 2012)[30]	High, direction uncertain. Reducing the utility to 0.110 increased the ICER to $24,718/QALY gained. Reducing the utility to 0.165 increased the ICER to $21,323/QALY gained.

ET = essential tremor; FDOPA PET/CT = [18F]fluorodopa positron emission tomography/computed tomography; ICER = incremental cost-effectiveness ratio; PD = Parkinson's Disease; QALY = quality-adjusted life year.

The results of key univariate sensitivity analyses are summarised in Table 9. ***The results in bold italics reflect post-ESC work requested as per the ESC discussion.***

[30] Herceg, M, Nagy, F, Pal, E, Janszky, J, Kesmarky, I, Komoly, S & Kovacs, N 2012, 'Pramipexole may be an effective treatment option in essential tremor', *Clin Neuropharmacol*, vol. 35, no. 2, Mar-Apr, pp. 73-76.

Table 9 Key univariate sensitivity analyses

	Inc. cost	Inc. QALYs	ICER per additional QALY	% change
Base case	**$1,366.75**	**0.073**	**$18,749**	–
Change in management (base case: 52.4%, Yeow et al. 2025)				
40%	$2,184.80	0.073	$29,970	+60%
45%	$1,800.25	0.073	$24,695	+32%
50%	$1,492.60	0.073	$20,475	+9%
55%	$1,240.89	0.073	$17,022	−9%
60%	$1,031.14	0.073	$14,145	−25%
Proportion of incorrect FDOPA PET/CT changes in management (base case: 0%, assumption)				
20% (Dhawan et al. 2022)[11]	$3,526.11	0.044	$80,998	+332%
3.4% (Ibrahim et al. 2016)[12]	$1,733.84	0.068	$25,533	+36%
Exclude proportion of changes that relate to starting levodopa [a]	$1,240.40	0.074	$16,675	−11%
Utility of symptom control in PD by pharmacotherapy (base case: 0.085) [b]				
0.1325	$1,366.75	0.089	$15,311	−18%
0.021	$1,366.75	0.051	$27,010	+44%
0.023	$1,366.75	0.051	$26,645	+42%
Utility of symptom control in ET (base case: 0.22) [c]				
0.11	$1,366.75	0.055	$24,718	+32%
0.165	$1,366.75	0.064	$21,323	+14%
Distribution of management changes [d] ***(base case: 47.3% symptom control of PD, 20.0% symptom control of ET, 32.7% others*** [e]***).***				
53.2% symptom control of PD, 10.0% symptom control of ET, 36.8% others [f]***.***	$1,300.72	0.062	$21,040	+12%
35.5% symptom control of PD, 40.0% symptom control of ET, 24.5% others [g]***.***	$1,498.80	0.095	$15,768	−16%

ET = essential tremor; FDOPA PET/CT = [18F]fluorodopa positron emission tomography/computed tomography; ICER = incremental cost-effectiveness ratio; MRgFUS = Magnetic Resonance-guided Focused Ultrasound; PD = Parkinson's Disease; QALY = quality-adjusted life year; SOC = standard of care.

[a] Some changes in management reported in Yeow et al. (2025)[23] included the commencement of dopaminergic medicines. As the proposed item descriptor requires a prior trial of dopaminergic medication, this sensitivity analysis excludes these changes in management changing both the absolute proportion of changes in management following FDOPA PET/CT, and the distribution of management changes.

[b] All utility values explored were sourced from Chaudhuri et al. (2022)[29]. The base case applied the difference in utility between Controlled (0.1451) and Uncontrolled (0.0598) PD health states, under SOC management, based on UK estimates. The upper estimate (0.1365) reflected the difference between health states in patients monitored with a wrist-worn device (also based on UK estimates). The lower estimates were based on differences between health states using the EQ-5D European Index (difference: 0.021) and German Index (difference: 0.023).

[c] Base case utility was derived from Herceg et al. (2012)[30] and reflected a significant improvement in EQ-5D using Hungarian norms in patients with a significant improvement in Fahn-Tolosa-Marin Tremor Rating Scale due to pramipexole treatment. This estimate was applied in subsequent studies to reflect the utility of marked improvement in symptoms following MRgFUS neurosurgery (Li et al. 2019; Jameel et al. 2022)[31,32]. These studies also applied a 0.11 utility increment to reflect mild to moderate improvement in symptoms following MRgFUS neurosurgery, assumed to be between baseline and marked improvement after surgery. The average of mild-moderate (0.11) and marked improvement (0.22) was tested in a further analysis.

[31] Li, C, Gajic-Veljanoski, O, Schaink, AK, Higgins, C, Fasano, A, Sikich, N, Dhalla, I & Ng, V 2019, 'Cost-Effectiveness of Magnetic Resonance-Guided Focused Ultrasound for Essential Tremor', *Mov Disord*, vol. 34, no. 5, May, pp. 735-743.

[32] Jameel, A, Meiwald, A, Bain, P, Patel, N, Nandi, D, Jones, B, Weston, G, Adams, EJ & Gedroyc, W 2022, 'The cost-effectiveness of unilateral magnetic resonance-guided focused ultrasound in comparison with unilateral deep brain stimulation for the treatment of medically refractory essential tremor in England', *Br J Radiol*, vol. 95, no. 1140, Dec 1, p. 20220137.

[d] The sensitivity analyses presented varied the proportion of changes that resulted in symptom control in ET, with the distribution of the remaining changes in management maintained. The cost and utility of the respective management changes were also maintained.
[e] Base case distribution of other management changes included: weaned levodopa and proceeded with ventriculoperitoneal shunt (1.8%), proceeded with DBS workup (9.1%), recommendation to psychiatrist to consider weaning anti-psychotic (5.5%), proceeded with gamma knife workup (1.8%), started benzhexol and botulinum toxin injections (1.8%) and cessation of treatment (12.7%).
[f] Distribution of other management changes included: weaned levodopa and proceeded with ventriculoperitoneal shunt (2.0%), proceeded with DBS workup (10.2%), recommendation to psychiatrist to consider weaning anti-psychotic (6.1%), proceeded with gamma knife workup (2.0%), started benzhexol and botulinum toxin injections (2.0%) and cessation of treatment (14.3%).
[g] Distribution of other management changes included: weaned levodopa and proceeded with ventriculoperitoneal shunt (1.4%), proceeded with DBS workup (6.8%), recommendation to psychiatrist to consider weaning anti-psychotic (4.1%), proceeded with gamma knife workup (1.4%), started benzhexol and botulinum toxin injections (1.4%) and cessation of treatment (9.5%).

The analyses were most sensitive to the proportion of patients with a change in management, the proportion of changes by FDOPA PET/CT that were inadequate for achieving symptom control, and utility estimates applied for symptom control in ET and by pharmacotherapy in PD. In the analyses that varied the proportion of patients with a change in management, incremental QALYs were not observed to change. This was due to the model reflecting only those patients with a change in management (and so in the proportion in whom there was not a change, no difference in outcomes was assumed).

The analysis was highly sensitive to the proportion of management changes by FDOPA PET/CT that were inadequate. The performance data used in the sensitivity analysis reflected discordance with clinical diagnosis, which is acknowledged to be imperfect, and particularly the more extreme assumption of FDOPA inaccuracy, was considered unlikely to reflect performance of FDOPA PET/CT when used in addition to SOC (as seen in Dhawan et al. (2022)[11], where the readers of FDOPA PET/CT were blinded to patients' clinical data).

14. Financial/budgetary impacts

An epidemiological approach was used to estimate the use and cost of FDOPA PET/CT to the MBS in patients suspected of PD, who had an inadequate response to dopaminergic therapies within two years of initiating treatment. A summary of the data sources used to estimate the impact is presented in Table 10.

Table 10 Key data sources and parameter values applied in the utilisation and financial estimates

Data	Value (source)
No. patients initiating one line of levodopa-based therapy, 2024–25	14, 479 (PBS data [a] for the number of incident patients initiated on levodopa and benserazide, levodopa and carbidopa or levodopa, carbidopa and entacapone, and who had received only one line of therapy, 2024–25)
Proportion of patients who initiate levodopa-based therapy, 2020–21 to 2024–25, who receive only one line of treatment	84.6% (PBS data [a] of the number of patients who had received only one line of therapy (levodopa and benserazide, levodopa and carbidopa or levodopa, carbidopa and entacapone), 2020–21 to 2024–25, as a proportion of all patients who initiated a levodopa-based therapy in the same time period)
Annual growth in the no. patients who initiate levodopa-based treatment	Decreasing from 1.78% in 2025–26 to 0.71% in 2031–32 (Mellick 2024)[33]
Proportion of patients who do not respond to dopamine treatment	46.3% (Merello et al. 2002)[34]
Proportion referred to movement disorder specialist	100% (assumption)
Proportion of patients who require further investigation to confirm diagnosis and inform subsequent treatment	19.1% (assumption based the 1795 Application Summary that 10% of patients referred to a movement disorder clinic would benefit from FDOPA PET/CT, assuming that benefit is defined as having a change in management).
Proportion of patients with a change in management	52.4% (Yeow et al. 2025)[23]
Uptake of FDOPA PET/CT	30% in Year 1, increasing to 90% in Year 6 (uptake estimated in the 1795 Application Summary, Years 1–3: 30%, Year 4: 70%)
Proportion of patients who uptake FDOPA PET/CT within first year of levodopa treatment initiation	50% (assumption)
Reduction in use of brain MRI on SOC resolution of diagnosis	30% of patients with a change in management, over the first three years after FDOPA PET/CT, based on Section 3
Proportion of patients who reduce DBS due to FDOPA PET/CT	1.8% of patients who have a change in management following FDOPA PET/CT (Yeow et al. 2025)[23]
FDOPA PET schedule fee and MBS benefits	Proposed schedule fee: $1,200.00 75% benefit: $900.00 85% benefit: $1,095.50
Co-claimed CT attenuation item	MBS item 61505 schedule fee $95[b] 75% benefit: $71.25 85% benefit: $80.75
Proportion of MBS-eligible FDOPA PET/CT services that receive the 85% benefit	100.0% (assumption)

DBS = deep brain stimulation; FDOPA PET/CT = [18F]fluorodopa positron emission tomography/computed tomography; MRI = magnetic resonance imaging; SOC = standard of care.
[a] PBS data for items: 2225D, 2226E, 2227F, 2228G, 2229H, 2231K, 8218M, 8219N, 14356N, 14387F, 14388G, 14428J, 14455T, 14551W, 14552X, 1242J, 1245M, 14427H, 14454R, 1255C, 14322T, 8797B, 8798C, 8799D, 9292C, 9344T, 9345W, 14357P, 14456W, 14457X, 14498C, 14527N, 14554B for financial years 2020–21 to 2024–25.
[b] As a result of Clause 1.2.21(1) of the *Health Insurance (Diagnostic Imaging Services Table) Regulations*, whenever a practitioner provides two or more diagnostic imaging services for the same patient on the same day, the fee for any item other than the highest fee item is reduced by $5.

The financial implications to the MBS resulting from the proposed listing of FDOPA PET/CT are summarised in Table 11.

[33] Mellick, G 2024, *Ecosystem of Parkinson's in Australia Project Part 3: Modelling geographic distributions & future*, Parkinson's Australia Ltd, Canberra.

[34] Merello, M, Nouzeilles, MI, Arce, GP & Leiguarda, R 2002, 'Accuracy of acute levodopa challenge for clinical prediction of sustained long-term levodopa response as a major criterion for idiopathic Parkinson's disease diagnosis', *Mov Disord*, vol. 17, no. 4, Jul, pp. 795-798.

Table 11 Net financial implications of FDOPA PET/CT to the MBS

	2026-27 (Year 1)	2027-28 (Year 2)	2028-29 (Year 3)	2029-30 (Year 4)	2030-31 (Year 5)	2031-32 (Year 6)
No. patients initiated on levodopa trial	17,720	18,024	18,329	18,633	18,937	19,072
No. patients who do not respond to levodopa (46.3%)	8,204	8,345	8,486	8,627	8,768	8,831
No. patients who require additional investigation to confirm diagnosis and inform subsequent treatment (19.1%)	1,566	1,593	1,619	1,646	1,673	1,685
Proportion of patients eligible who uptake FDOPA PET/CT	30.0%	30.0%	30.0%	70.0%	80.0%	90.0%
No. of patients who do not respond to levodopa therapy who uptake FDOPA PET/CT	470	478	486	1,152	1,339	1,517
- no. who uptake within first year of initiating levodopa (50.0%)	235	239	243	576	669	758
- no. who uptake in second year of initiating levodopa (50.0%)	462 [a]	235	239	243	576	669
No. patients who uptake FDOPA PET/CT [A]	696	474	482	819	1,246	1,428
Cost of FDOPA PET/CT to the MBS ($1176.25 per patient) [b]	**$819,256**	**$557,242**	**$566,731**	**$963,531**	**$1,465,066**	**$1,679,281**
Additional consultations to review FDOPA PET/CT results (A × 100%)	696	474	482	819	1,246	1,428
Cost of additional consultations to the MBS (item 116, average $76.00 per patient) [b]	**$52,934**	**$36,005**	**$36,618**	**$62,256**	**$94,661**	**$108,502**
No. with change in management (A × 52.4%) [B]	365	248	252	429	652	748
No. who reduce use of brain MRI (30.0%)	107	73	74	126	191	219
- first year (72.0%)	77	52	53	90	137	158
- second year (17.0%)		18	12	13	21	32
- third year (5.4%)			6	4	4	7
Reduction in use of brain MRI	77	70	71	107	163	197
Reduction in cost of brain MRI to the MBS (item 63004, average $384.25 per service) [b]	**$29,542**	**$27,069**	**$27,396**	**$41,076**	**$62,565**	**$75,633**
No. who appropriately avoid DBS (B × 1.8%)	7	5	5	8	12	14
No. treated in MBS eligible scenarios (93.1%)	6	4	4	7	11	13
Reduction in cost of DBS to the MBS [c]	**$54,160**	**$36,838**	**$37,466**	**$63,697**	**$96,853**	**$111,014**
Net impact to the MBS	**$788,488**	**$529,339**	**$538,487**	**$921,013**	**$1,400,308**	**$1,601,136**

DBS = deep brain stimulation; FDOPA PET/CT = [18F]fluorodopa positron emission tomography/computed tomography; MRI = magnetic resonance imaging.

[a] Incident patients in the previous year who meet the eligibility criteria and uptake

[b] Assuming 100% of services are provided out-of-hospital with the Greatest Permissible Gap applied, and that CT attenuation Item 61505 is co-claimed with every service.

[c] Each patient was assumed to reduce the use of one 63010, one 21922 and one 23035 for DBS planning by MRI; and one 40851, one 40852, two 40860, one 20210 and one 23240 services for implantation of the device and leads. All services were assumed to receive the 75% level of MBS benefit.

There may be variations in practice regarding the interpretation of the proposed restriction that FDOPA PET/CT be used where 'further investigation is required to confirm the diagnosis and inform subsequent treatment'. While requests for FDOPA PET/CT were referred from movement disorder clinics in the key clinical evidence (Yeow et al. 2025)[23] and ongoing MAP-DOPA[24] study, in practice, referrals may be requested from a broader range of requestors. The base case assumed likely use within patients referred to movement disorder clinics, however as an upper limit, a scenario analysis assumed that all patients who do not respond to levodopa-based therapy could be eligible for FDOPA PET/CT. This was associated with a 5-fold increase in the cost to the MBS (Table 12). Changes in use of other affected MBS services were not estimated for the scenario due to uncertain applicability in the estimates of change in management to the broader population eligible for FDOPA PET/CT.

Table 12 Scenario analysis, assuming all patients who do not respond to levodopa-based therapy are eligible

	2026-27 (Year 1)	2027-28 (Year 2)	2028-29 (Year 3)	2029-30 (Year 4)	2030-31 (Year 5)	2031-32 (Year 6)
No. patients who do not respond to levodopa (46.3%)	8,204	8,345	8,486	8,627	8,768	8,831
Proportion of patients who uptake FDOPA PET/CT	30.0%	30.0%	30.0%	70.0%	80.0%	90.0%
No. of patients who do not respond to levodopa therapy who uptake FDOPA PET/CT	2,461	2,504	2,546	6,039	7,014	7,947
- no. who uptake within first year of levodopa (50.0%)	1,231	1,252	1,273	3,019	3,507	3,974
- no. who uptake in second year of levodopa (50.0%)	2,419 [a]	1,231	1,252	1,273	3,019	3,507
No. patients who uptake FDOPA PET/CT	3,650	2,482	2,525	4,292	6,527	7,481
Cost to the MBS ($1176.25 per patient) [a]	**$4,292,900**	**$2,919,946**	**$2,969,670**	**$5,048,900**	**$7,676,944**	**$8,799,433**

FDOPA PET/CT = [18F]fluorodopa positron emission tomography/computed tomography.
[a] All patients diagnosed in year prior to listing who would uptake FDOPA PET/CT are assumed to uptake
[b] Assuming 100% of services are provided out-of-hospital with the Greatest Permissible Gap applied, and that CT attenuation Item 61505 is co-claimed with every service.
(100% × ($1,176.25) + 0% × ($900.00 + $71.25)).

Analyses were most sensitive to changes in estimates used to determine the size of the eligible population (e.g. proportion that do not respond to levodopa-based therapy and proportion who require further testing) and also to the extent of uptake, particularly in the initial years, where low uptake in the population eligible had been assumed.

As FDOPA PET/CT is proposed as an additional test, no changes in the use or financial impact of substituted tests was assumed, though there may be changes in use of consultations to review FDOPA PET/CT results and downstream health technologies related to resolving the diagnosis under SOC (brain MRI) and avoidance of inadequate management (driven by assumed appropriate avoidance of DBS use, based on Yeow et al.[23]).

While FDOPA PET/CT was also modelled to increase the use of adequate management, changes in the use of these health technologies were not considered in the financial analysis. Estimates of the multiple treatment changes at a micro-costing level across a population would not be accurate and in the majority of cases the changed resource use pattern following FDOPA PET/CT

simply represents bringing forward the change in service use by 0–3 years, rather than adding/off-setting different future associated services. This approach may slightly underestimate the overall financial impact of FDOPA PET/CT changes (assuming these are considered appropriate).

The impact of listing FDOPA PET/CT on state government budgets and private health insurers was also considered. Changes in use of services borne by state government budgets included a reduction in use of FDG-PET to resolve diagnosis and inform subsequent treatment under SOC and avoidance of DBS in patients managed in the public setting. The resulting reduction in cost per year was estimated to increase from $134,000 to $333,000 over the projected period.

For private health insurers, a reduction in cost due to avoided DBS procedures (including device components) was assumed. The estimated reduction in cost increased from $210,000 in the first year of listing, to $430,000 by year six.

15. Other relevant information

Equity and accessibility: Access to FDOPA PET/CT may be limited by the technical and logistical challenges of producing fluorine-18, which typically requires onsite hospital-based or nearby manufacturing. This creates equity concerns, particularly for patients in rural and remote areas who already face delays in diagnosis and specialist referral. The proposed requirement that patients have ≤24 months of levodopa exposure may unintentionally disadvantage these groups.

Restricting claims to consultant physicians and making brain MRI a prerequisite test (for those able to have MRI) may help target the test to patients most likely to benefit, as a brain MRI can rule out other conditions (e.g. tumours, strokes, vascular PD) and be useful in discriminating PD from APDs.

All PET services listed on the MBS are restricted to requesting by consultant physicians and specialists, as the health practitioners most suited to manage the client's treatment depending on the outcomes of the scan. However, it is known that this may introduce additional delays due to consultation wait times and increase demand on specialist services.

Environmental factors: FDOPA is used in very small amounts and poses minimal direct environmental risk because fluorine18 has a short half-life. However, its production requires strict environmental and radiation safety controls. Manufacturing involves radioactive waste handling, energy-intensive cyclotron operation, and cleanroom processes. Despite these factors, overall environmental impacts are well managed through established radiopharmaceutical regulations and internationally recognised safety standards.

Value of knowing: Even without disease-modifying treatments, a clearer diagnosis can improve understanding of prognosis, support planning for future care, and reduce anxiety associated with uncertain or conflicting clinical information.

16. Committee-in-confidence information

redacted

17. Key issues from ESC to MSAC

Main issues for MSAC consideration

Clinical issues:

- The reference standard for testing for parkinsonism is post-mortem neuropathology, which was not used in the department contracted assessment report (DCAR) due to lack of available evidence. The evidence supporting the accuracy of FDOPA PET/CT was instead based on comparisons against clinical diagnosis, with methodological limitations and heterogeneity across studies regarding what clinical diagnosis comprised. The benefit of the intervention is therefore unclear, although more extensive data from the MAP-DOPA study with a better-characterised study population might be helpful.
- The Australian study (Yeow et al., 2025) showed use of FDOPA PET/CT led to a change in diagnosis in about 33% of cases and change in management in about 50% of cases, but it is unknown if these changes were clinically appropriate and if they led to improved health outcomes.
- That study (Yeow, et al.) also may not align well with the PICO population as the proportion previously treated with dopaminergic medicines is unclear and around 40% of the patients had had symptoms for >5 years. The other studies that assessed change in diagnosis also did not report the proportion of patients with no prior response to dopaminergic medicines. The applicant's pre-ESC response stated that it may be difficult to obtain ethics approval for a trial comparing FDOPA scans in those treated or not treated, however ESC noted that an observational study could report such information. The prospective MAP-DOPA study may have recorded prior treatments.
- The DCAR reported that most patients in the study by Yeow et al would have had an MRI prior to their FDOPA PET/CT scan to exclude structural causes of parkinsonism. The results from Yeow therefore reflect the additional diagnostic information from FDOPA PET/CT in those undergoing previous MRIs, which should be considered in the interpretation of that study's results.
- ESC noted the applicant's pre-ESC response that a brain MRI will usually be performed as part of the diagnostic work-up of parkinsonism to exclude other pathology. ESC considered that, as there is no specific MBS item for the investigation of parkinsonism, it is unclear if such scans are being claimed via the MBS (e.g. via MRI items for tumours, stroke, inflammation or demyelinating conditions of the brain). The applicant's pre-ESC response also noted that brain MRI can include an assessment of nigrosome-1 (a potential investigation of parkinsonism), however ESC considered that this requires specific MRI hardware (3T MRI scanner) and appropriate expertise to interpret the scan, which may not be widely available and may be less informative than the FDOPA scan. There is no specific MBS item for nigrosome-1 assessment.

Economic issues:

- The applicability of the study relied on for the economic model was uncertain as it did not contain critical information on the population (for instance, as discussed previously, the proportion of patients with no response to dopaminergic medicines), and due to its retrospective nature, management changes could not be attributed to FDOPA PET/CT results alone.
- It is uncertain whether the 'change in management' estimate translates to patient health outcomes (and resulting Quality Adjusted Life Years) because it is based on the assumption that management changes improve symptom control, and improved symptom control then improves quality of life rather than on any direct evidence that FDOPA PET/CT–related management improves patient health outcomes. MSAC may wish to review previous PET/CT

or similar applications in which translation to health benefits has been assumed to occur from imaging.

- The small sample size of the change in management data relied on in the economic model means that the estimated proportions for different types of management change are likely to be highly uncertain.

Financial issues:

- Serious concerns exist about the applicability of the evidence to the proposed population, resulting in uncertain patient eligibility. Patient numbers have a large impact on the financial estimates.
- The wording in the item descriptor may need to be tightened to link the FDOPA PET scan to the initial course of dopaminergic treatment where the scan will have more clinical benefit, and to stipulate the type of requestor, to better predict patient numbers and utilisation.

Other issues:

- The short half-life of the isotope (110 minutes) is a barrier for using FDOPA PET/CT in regional centres, even if they have a suitable PET machine.

ESC discussion

ESC noted that this application from the Australasian Association of Nuclear Medicine Specialists was for Medicare Benefits Schedule (MBS) listing of positron emission tomography / computed tomography (PET/CT) dopaminergic imaging (FDOPA PET/CT) for evaluating parkinsonism in those who have not responded adequately to standard Parkinson's disease (PD) treatment after 12 weeks of therapy. The proposed use was in patients with persistent diagnostic uncertainty, specifically in those with limited response after ≥ 12 weeks optimised dopaminergic treatment (where limited response was defined as 0% to 30% response on the Unified Parkinson's Disease Rating Scale) and within 24 months of treatment initiation, where further investigation was required to inform a possible differential diagnosis and management. ESC noted that the radiopharmaceutical used in the proposed technology is not included in the Australian Register of Therapeutic Goods (ARTG). Access is therefore limited to supply under the Therapeutic Goods Administration (TGA) Special Access Scheme (SAS), whereby registered health practitioners may arrange access to unapproved therapeutic goods for individual patients on an individual basis. The Department clarified that patient access to FDOPA PET/CT is currently through the SAS, which is a common pathway to access radiopharmaceuticals in Australia. The Department noted that MBS listing may result in greater uptake of the radiopharmaceutical and provide an incentive for ARTG registration.

ESC noted that parkinsonism is a clinical syndrome comprising motor symptoms including bradykinesia (slowness in initiating movement) and tremor or rigidity. PD is a specific form of parkinsonism caused by progressive neurodegeneration resulting in loss of dopamine-producing neurons and accumulation of Lewy bodies. Misdiagnosis occurs in 14% to 29% of patients with parkinsonism, and some people with PD have limited response to therapy.

ESC noted and welcomed the public consultation inputs (49 inputs received pre-PASC and 18 received pre-MSAC). The feedback was largely supportive. Parkinson's Australia stated that the scan would provide more certainty in diagnoses, which would lead to better treatments. Feedback was also provided that the diagnosis would improve the value of knowing so that patients could understand their diagnosis and plan for their future care, thus reducing anxiety. Some feedback expressed concern that FDOPA PET/CT would not change clinical management.

ESC noted the proposed MBS item descriptor and fee. ESC considered it appropriate to amend the item descriptor wording from 'further investigation is required to confirm the diagnosis and inform subsequent treatment' to 'further investigation is required to *consider an alternative*

diagnosis where the results of imaging are expected to change treatment'. This would help to tighten the eligible patient population. ESC agreed with PASC that the fee of $1,200 is appropriate, reflecting increases in the costs of the radioisotope.

ESC considered that geriatricians and neurologists should be included in the list of requestors of the service, to improve access in regional and rural areas. However, ESC also noted that broadening the requestors may increase uptake and utilisation. Furthermore, all the patients in the study underpinning the economic analysis were referred for the scan by neurologists specialising in movement disorders; hence the change in management observed in the study may not be observed in practice if requested by different providers in different settings. ESC considered the requirement for scanning within 2 years of treatment initiation to be appropriate noting that most referrals for scans would be expected to be semi-urgent and that extension of the timeframe could inappropriately increase utilisation. ESC also advised that the proposed limitation of no more than 2 services per patient over a lifetime should be retained while noting there was no clear evidence supporting two scans.

ESC further considered that the wording in the descriptor may need to be tightened to link the FDOPA PET scan to the initial course of dopaminergic treatment where the scan will have most benefit. ESC considered that this was needed in order to exclude patients who fail to respond to second- or third-line treatments being sent for FDOPA PET scans because they were technically within the 24 months post treatment initiation condition.

ESC queried the feasibility of performing FDOPA PET/CT scans in regional centres. The pre-ESC response correctly stated that many regional centres have PET machines, but ESC considered the short half-life of the isotope (110 minutes) to be a major barrier to using this technology outside of metropolitan clinics as any flight to transport the radiopharmaceutical from a metropolitan manufacturer to a regional centre is likely to be longer than 110 minutes.

ESC noted the clinical management algorithm. To be eligible for the proposed treatment, patients are required to trial, and show no improvement after using, dopaminergic drugs for 12 weeks to 2 years.

ESC considered whether magnetic resonance imaging (MRI) of the brain should be a prerequisite test prior to FDOPA PET/CT to improve patient selection. ESC noted that brain MRI would typically be performed prior to FDOPA PET/CT in clinical practice to exclude structural causes of parkinsonism, as outlined in the pre-ESC response. Where patients meet the relevant item requirements, this imaging may be undertaken using one of the existing MBS-listed brain MRI items, however there is no MBS-listed MRI item specifically for investigation of parkinsonism. Setting aside the potential use of existing MBS-funded MRI items to exclude structural causes of parkinsonism, ESC noted that the question of whether there should be a prior brain MRI for specific investigation of PD was outside the scope of the existing application as this was not part of the PICO of the current application and therefore has not been assessed within the DCAR. ESC noted the pre-ESC response's statement that a brain MRI for this specific indication could include nigrosome-1 imaging (subregion within the substantia nigra that contains dopaminergic neurons), however this technology and the radiology expertise required to interpret this type of imaging is not widely available.

ESC considered the evidence base to be a major source of uncertainty. The principal concern was that diagnostic accuracy evidence compared FDOPA PET/CT to clinical diagnosis rather than the reference standard of post-mortem neuropathology. ESC noted that clinical diagnosis was not an appropriate reference standard for establishing the true test accuracy of FDOPA PET/CT, although ESC recognised the practical limitations of obtaining neuropathological confirmation. ESC considered the overall evidence for accuracy was low certainty, based on small samples, from single centres only, was methodologically heterogeneous, and not directly aligned with the

proposed population, particularly because prior response to levodopa or other dopaminergic therapy was often not clearly reported in the studies.

ESC considered the safety of the FDOPA PET/CT scan and considered there was insufficient evidence to support conclusions of superiority, inferiority or non-inferiority. ESC considered it plausible that better pharmacological management resulting from more accurate diagnosis could improve safety, such as from reduction in falls, better fitness, less ineffective medicine use, and less anxiety (from greater diagnostic certainty). ESC considered any possible harms from radiation exposure to be limited and well managed clinically. ESC acknowledged there may be possible harms from false positive or false negative results leading to either over- or under-treatment, but there were no data to support this. Overall, ESC agreed with the clinical claim that the use of FDOPA PET/CT results in likely inferior (but well understood and manageable) safety compared with standard of care.

ESC considered that the included studies assessing diagnostic accuracy were of variable certainty, with heterogeneous populations, and issues with bias (for example, lack of blinding). The sensitivity and specificity reported were also variable, and ESC determined that the reason for this was uncertain. One possible explanation for the heterogeneity of results could be the different methods and timing used to establish clinical diagnoses across studies, varying reader expertise in interpreting FDOPA PET/CT, or the scan's inability to differentiate between PD and atypical Parkinson's Disease (APD). ESC considered it a limitation that FDOPA PET/CT imaging is unable to differentiate between different forms of degenerative parkinsonism (PD vs types of APD). Overall, ESC considered that the concordance between clinical diagnosis and scan diagnosis was uncertain.

ESC then considered the evidence for change in clinical management. ESC noted that the unpublished Australian MAP-DOPA study and two non-Australian studies focused on change in diagnosis and did not report change in management. These studies therefore could not be directly compared with the sole published Australian study, Yeow et al. (2025)[35], which reported both change in diagnosis and change in management. It was also unknown if a change in diagnosis and change in management led to improved health outcomes including quality of life, as these were not measured in any of the studies. In addition, ESC noted that patients with atypical PD do not respond well to treatments and therefore may continue to have limited treatment options following FDOPA PET/CT. ESC also noted that the study populations do not align with the PICO – for example, in two of the studies some patients had dual imaging (FDOPA PET/CT and FDG PET/CT), and in the sole published Australian study ~ 40% of included patients had long-term symptoms (>5 years). The proportion of patients with no response to dopaminergic medicines prior to FDOPA PET/CT is also not reported in the published Australian study and therefore it is unclear if study populations met this criterion. The pre-ESC response stated that it may be difficult to obtain ethics approval for such a study. ESC noted the MAP-DOPA study may have recorded prior treatments and once published, could provide outcomes for this population.

ESC noted that the sole published Australian study (Yeow) reported that FDOPA PET/CT changed diagnosis in about one-third of cases and management in about one-half of cases; however, it remained uncertain whether these management changes were clinically appropriate and whether they translated into improved patient outcomes. ESC noted that, as it was likely that most patients in the Australian studies would have received MRI of the brain before progressing to FDOPA PET/CT (as per the applicant's pre-ESC response), this would likely have had a selection effect on this set of patients. The results from Yeow therefore reflect the additional diagnostic

[35] Yeow, D, Fielder, M, Hynard, S, Adam, R, Katz, M, Lehn, A, Thomas, P & O'Sullivan, JD 2025, 'Clinical utility of (18)F-fluorodopa positron emission tomography in the movement disorder clinic: an Australian experience', Intern Med J, vol. 55, no. 2, 2025-2, pp. 207-215.

information from the FDOPA PET/CTs in those patients with prior MRI, which should be considered in the interpretation of those results. However, the percentage of patients receiving prior MRI was not reported in these studies.

ESC accepted that more accurate diagnosis and more appropriate management could plausibly improve outcomes, reduce ineffective medicine use and possibly reduce anxiety through greater diagnostic certainty, but considered the size and reliability of such benefits to be highly uncertain. Overall, ESC considered that the clinical evidence supported at most a plausible but uncertain diagnostic and management benefit, with no direct evidence that this translated into superior health outcomes. ESC considered that in light of the uncertainties associated with the evidence the value of knowing benefits highlighted in the consultation feedback were not strongly supported by the evidence,

ESC noted that the economic evaluation used a Markov model with 3 health states – adequate treatment, inadequate treatment, or dead – followed by a stepwise analysis.

ESC also noted some key structural model assumptions:

- Different conditions and types of PD are not modelled, although the purpose of FDOPA PET/CT is to distinguish between conditions, accurately diagnose and treat appropriately. While ESC considered this to be an acceptably pragmatic approach, it does provide any granularity for the economic analysis.
- Only patients for whom FDOPA PET/CT would lead to a change in management enter the model. However, the cost of screening multiple patients to identify one patient in whom a management change would occur is applied on model entry, which accounts for the costs incurred for patients for whom there is no change in management. ESC considered this to be an acceptably pragmatic approach due to limited available data.
- The base case assumes that all changes in management due to FDOPA/PET CT lead to an adequate change in management while the sensitivity analysis assumes that FDOPA PET/CT leads to an inadequate change in management in a proportion of patients where 'adequacy' refers to whether the symptoms of parkinsonism are controlled or uncontrolled. However, it is possible that neither FDOPA PET/CT nor standard of care are 'adequate' in this sense. No evidence was available to explore other diagnoses or management strategies in the analysis.
- It is assumed that most diagnoses are resolved after 3 years and most patients are managed adequately. However, in reality, some cases remain missed. ESC considered this to be an acceptably pragmatic approach due to limited available data.
- Adequate treatment is not assumed to be life-extending, and there is no transition from the adequately to inadequately treated health states. ESC considered this to be acceptable because diagnosis appears to be resolved within the first 3 years after intervention.

ESC noted the following considerations regarding the applicability of the Yeow study which informed the economic model:

- Referral to FDOPA PET/CT: Cases in the Yeow et al. study reflect patients with significant diagnostic uncertainty presenting to a movement disorder clinic or to a movement disorder neurologist. In practice, claims for this item would likely reflect the study population in Yeow et al. if referral to FDOPA PET/CT is restricted to particular specialists and consultant physicians.
- MRI of the brain as a prerequisite before the FDOPA PET/CT scan: The Yeow et al. study likely included patients who underwent a brain MRI before the FDOPA PET/CT scan. The number of patients increases if brain MRI is not done first. The model assumed MBS item 63004 – MRI for inflammation of the brain - was used for the prior brain MRI.

- Duration of disease and prior dopaminergic medication use: The Yeow et al. study did not define whether patients were treated with dopaminergic medications before the intervention and for how long. It may be different to the proposed setting.
- Distribution of underlying diagnoses: The limited and selected mix of underlying diagnoses of patients in the Yeow et al. study may be narrower than what might be encountered in wider clinical practice. Therefore in practice, there may be a significantly different magnitude of percentage change in management than what is reported in Yeow et al.
- Reported changes in management: It is unknown which changes in management occurred. A small range of changes in management, such as medicines and surgery were documented, but other management changes such as allied health services (e.g. physiotherapy) were not included. The Yeow et al. study does not describe this well i.e. because the study was a retrospective chart review, it was not possible to determine whether the reported management changes were driven by FDOPA PET/CT results alone or by other clinical information.

ESC noted that the base case incremental cost-effectiveness ratio (ICER) was $2,643 per change in management decision. When extrapolated to 3 years, the ICER for transformation of changes in management into life years (LYs) on adequate treatment was $1,863. The ICER per additional quality-adjusted LY (QALY) gained was $18,749.

ESC noted that uncertainty analyses revealed that the key driver of the ICER was the proportion of incorrect FDOPA PET/CT changes in management – assuming a proportion of 20% of scan resulted in inappropriate changes in management (base case was 0%) increased the ICER to $80,998 per additional QALY.

ESC also noted that the results of the economic evaluation are driven by health-related utility of the changes. Symptom control of essential tremor has a 0.22 incremental utility applied, compared to symptom control of PD which is assigned an incremental utility of 0.0853. This reflects the model's assumption that, because PD is more severe, the treatment benefit (from symptom control) is not as large. Because the model is designed to have a weighted utility average, ESC considered that this should be further explored as well.

ESC noted the uncertainty around whether the intervention results in improved health outcomes. Any health benefit in the model is assumed to arise because FDOPA PET/CT changes management, those management changes improve symptom control, and improved symptom control then improves quality of life. ESC considered this pathway plausible, but uncertain, because there was no direct evidence that FDOPA PET/CT–related management changes improved patient health outcomes. ESC noted that MSAC has previously accepted this kind of uncertainty for Application 1195 (use of PET to diagnosis Alzheimer's disease), as well as other applications regarding PET for cancer. However, for the previous cancer imaging applications, ESC noted that these were largely accepted by MSAC based on budget neutrality (due to the proposed imaging replacing other imaging) and superior diagnostic accuracy with the intervention. ESC considered that such precedents did not remove the need to address the specific evidentiary weaknesses in the current application.

ESC considered this uncertainty was amplified by the change-in-management evidence, which relied on Yeow et al. (2025), a small retrospective study of 105 scan results. Because of the small sample size, the estimated proportions for different types of management change are likely to be highly uncertain.

ESC noted that the base case financial impact was, appropriately, an epidemiological approach, with utilisation estimated at 500 in year 1 and increasing to 1,400 by year 6 (noting about 1,500 to 1,600 patients would be eligible each year). This results in a net cost to the MBS of $788,488

in year 1, increasing to $1,601,136 in year 6. Costs to the Pharmaceutical Benefits Scheme (PBS) would also increase due to increased treatment use.

ESC noted that these base case financial impacts are limited to non-responding patients who are referred to movement disorder clinics. Including all non-responders to levodopa increases the eligible population to about 8,500 patients per year, which results in a much larger financial impact to the MBS: $4.3 million in year 1 to $8.8 million in year 6. ESC therefore considered that patient numbers, leakage and clarity of the restriction were major issues for decision making. As discussed previously, serious concerns exist about the applicability of the evidence from Yeow to the proposed population, resulting in uncertain patient eligibility which may have a large impact on the financial estimates. ESC also noted that the financial estimates did not include reduced use of substituted tests, but considered this likely to have only a minor effect compared with the larger uncertainty around eligible numbers and uptake.

Overall, ESC considered that there is a plausible case for diagnostic and management benefit from the use of FDOPA PET/CT, but that the evidence remained insufficient to establish the magnitude of patient benefit or the reliability of the economic and financial estimates with confidence. ESC considered that additional work before MSAC deliberation would be helpful. In particular, ESC considered that more extensive and better characterised data from the MAP-DOPA study would be valuable, especially if it more clearly described prior dopaminergic treatment, symptom duration, prior magnetic resonance imaging, the distribution of underlying diagnoses, the nature and appropriateness of management changes, and any subsequent patient outcomes.

18. Applicant comments on MSAC's Public Summary Document

The applicant had no comment.

19. Further information on MSAC

MSAC Terms of Reference and other information are available on the MSAC Website: visit the MSAC website