MSAC Application 1784

Testing options to detect amyloid beta pathology and determine *APOE* genotype in patients with mild cognitive impairment due to Alzheimer's disease, or mild Alzheimer's disease, to determine eligibility for PBS subsidised donanemab treatment

Application for MBS eligible service or health technology

ID:
HPP200168

Application title:
Testing options to detect amyloid beta pathology and determine *APOE* genotype in patients with mild cognitive impairment due to Alzheimer's disease, or mild Alzheimer's disease, to determine eligibility for PBS subsidised donanemab treatment.

Submitting organisation:
ELI LILLY AUSTRALIA PTY LTD

Submitting organisation ABN:
39000233992

Application description

Succinct description of the medical condition/s:
Alzheimer's disease (AD) is a progressive neurodegenerative disease, and the most common form of dementia, accounting for 60-80% of all dementia cases. The pathological hallmark of AD is the accumulation of amyloid beta (Aß) protein plaques, followed by the development of neurofibrillary tangles composed of tau protein within neurons and other characteristic brain changes, resulting in neuronal dysfunction and brain atrophy. The earliest clinical manifestations of AD can be a subjective decline in mental abilities which does not impact performance on objective cognitive tests but as the disease progresses, people living with AD show more advanced symptoms with changes that negatively impact memory and eventually impacting one's ability to perform basic activities of daily living (ADLs), such as cooking and dressing.

Succinct description of the service or health technology:
This application requests an MBS listing for *APOE* testing to determine genotype, and MBS listings for two technologies, Aß positron emission tomography (PET) and cerebrospinal fluid (CSF) AD biomarker immunoassay, to detect Aß pathology. The MBS listings are intended to be used in patients with a clinical diagnosis of mild cognitive impairment (MCI) due to AD, or mild AD to determine eligibility to the drug treatment donanemab. An additional MBS item is also sought to assess amyloid clearance via Aß PET in patients treated with donanemab.

Pharmaceutical Benefits Scheme (PBS) subsidy will be sought for donanemab treatment and proposed restriction criteria will require patients to be redacted, have confirmed evidence of Aß pathology and a diagnosis of MCI or mild AD.

Application contact details

Are you the applicant, or are you a consultant or lobbyist acting on behalf of the applicant?
Applicant

Are you applying on behalf of an organisation, or as an individual?
Organisation

Is the applicant organisation the organisation you are representing in the HPP today?
Yes

Application details

Does the implementation of your service or health technology rely on a new listing on the Pharmaceutical Benefits Scheme (PBS) and/or the Prescribed List?
Yes

Which list/schedule will the other health technologies be listed on?
Pharmaceutical Benefits Scheme

Is the application for a new service or health technology, or an amendment to an existing listed service or health technology?
New

What is the type of service or health technology?
Investigative

Please select the type of investigative health technology:
Other

Please provide details of 'Other' health technology type:
PET scans (Aß PET)
Histopathology and cytology (Aß CSF immunoassay)
Genetic testing (APOE) [molecular diagnostic test; single gene assay]

Can you confirm that the application reflects their perspectives on the use of the proposed health technology or service?
Yes

PICO Sets

Application PICO sets

PICO set number	PICO set name
1	APOE variant and Aß Pathology testing to determine eligibility for donanemab treatment

Testing for Aß Pathology to determine eligibility for donanemab treatment

State the purpose(s) of the health technology for this PICO set and provide a rationale:
Purpose category:
Diagnosis / sub-classification

Purpose description:
To establish a diagnosis or disease (sub)classification in symptomatic or affected patients

Population

Describe the population in which the proposed health technology is intended to be used (5000): Dementia is a broad term used to describe a group of symptoms affecting cognitive and social abilities severely enough to interfere with daily functioning. The most prevalent form of dementia is Alzheimer's Disease (AD), which accounts for 60-80% of all dementia cases (Alzheimer's Association, 2023, Gauthier S, 2022, Tahami Monfared et al., 2022a). AD typically presents with memory loss, but there are many associated cognitive, behavioural and neuropsychiatric features (Knopman et al., 2021). These become more profound as the disease progresses, advancing from more subtle symptoms (such as ability to manage personal finances) to eventually impacting one 's ability to perform basic activities of daily living (ADLs), such as cooking and dressing.

AD is an age-related progressive neurodegenerative disease, characterised by the accumulation of beta-amyloid (Aß) protein plaques and neurofibrillary tangles (NFTs) in the brain (Demattos et al., 2012, Breijyeh and Karaman, 2020, Knopman et al., 2021). Aß deposition occurs early in the disease process, preceding tau protein aggregation and other pathologies and is believed to initiate the neurodegeneration cascade, clinically manifesting as cognitive and functional impairment (Demattos et al., 2012).

The onset of Aß pathology, the key pathophysiological process of AD, can occur up to 20 years before the clinical onset of AD (Bateman et al., 2012, Busche and Hyman, 2020, Jack Jr et al., 2018) in what is referred to as the preclinical phase of the disease. The earliest clinical manifestations of AD can be a subjective decline in mental abilities which does not impact performance on objective cognitive tests (Knopman et al., 2021a) but as the disease progresses, people living with AD show more advanced symptoms with changes that negatively impact memory and eventually daily functioning, becoming less independent (Alzheimer's Association, 2023)(Knopman et al., 2021b, Weller and Budson, 2018) AD is therefore regarded as a continuum (Jack et al, 2018). There are three broad phases on the continuum, with no sharp demarcation between them: Preclinical AD, MCI due to AD, and dementia due to AD. Dementia due to AD is usually further categorised by severity into mild, moderate, and severe.

Several genes have been shown to increase the risk of AD, with the apolipoprotein E (*APOE*) gene the most characterised. *APOE* ε4 carriers have an increased risk of AD compared to other isoforms, with ε4 homozygotes having the greatest risk of developing AD, however, it is not guaranteed that they will develop AD (Alzheimer's Association 2023; Porsteinsson et al. 2021; Raskin et al. 2015). The causes of AD are not completely understood and multifaceted (Breijyeh and Karaman 2020). *APOE* ε4 is just one of the many risk factors associated with AD. While *APOE* ε4 is not a defining characteristic required for AD diagnosis, *APOE* status will influence treatment eligibility for donanemab. Evidence from the TRAILBLAZER-ALZ 2 trial (the pivotal phase 3 trial which comprises the key clinical trial to be presented in the PBAC submission), found that *APOE* ε4 homozygotes experienced greater ARIA adverse events with donanemab treatment compared to APOE ε4 heterozygotes, and

non-carriers. Redacted.

Patients with a clinical diagnosis of MCI due to AD, or mild AD are the population of interest in this application for the co-dependent technology, *APOE* genotyping followed by testing for Aß pathology, if suitable, to determine eligibility for PBS-subsidised treatment with donanemab.

Search and select the most applicable Medical condition terminology (SNOMED CT):
Alzheimer's disease

Intervention

Name of the proposed health technology:
A test to determine *APOE* genotype and two testing options to assess Aß pathology in patients with a clinical diagnosis of MCI due to AD or mild AD, to determine eligibility for PBS-subsidised donanemab.

Comparator

Nominate the appropriate comparator(s) for the proposed medical service (i.e. how is the proposed population currently managed in the absence of the proposed medical service being available in the Australian health care system). This includes identifying health care resources that are needed to be delivered at the same time as the comparator service (5000):
This application is requesting the following MBS items for use in patients with a clinical diagnosis of MCI due to AD, or mild AD to inform PBS subsidised access to donanemab:
i.   *APOE* genotyping to assess treatment suitability
ii.   a) Aß PET testing and b) CSF AD biomarker immunoassay to assess Aß pathology

The appropriate comparator for APOE genotyping is 'no APOE genotyping'.

The appropriate comparator for Aß PET testing is 'no testing for Aß pathology'.

The appropriate comparators for CSF biomarker testing are 'no testing for Aß pathology' and Aß PET.

The appropriate comparator for donanemab is standard of care, which for patients with a clinical diagnosis of MCI due to AD or mild AD, is instigation of non-pharmaceutical interventions (including encouragement of physical activity, social engagement, maintenance of cognitive stimulation and good nutrition), and for patients with mild AD may also include treatment with AChEI therapy.

Outcomes

Outcome description – please include information about whether a change in patient management, or prognosis, occurs as a result of the test information:

Test accuracy outcomes:
- Positive and negative concordance between Aß PET and the evidentiary standard (18florbetapir and 18florbetaben)
- Positive and negative concordance between CSF AD biomarker immunoassay and the evidentiary standard.
- Positive and negative concordance between commercially available CSF AD biomarker immunoassays
- Longitudinal accuracy between CSF AD biomarker immunoassay and the evidentiary standard (if available)

Test related adverse events:
- Safety associated with Aß PET and CSF AD biomarker immunoassay including safety of exposure to radiation during Aß PET and adverse events (AEs) related to lumbar puncture for CSF testing
- Yield of testing

Outcomes related to the therapeutic component:
Clinical effectiveness of the intervention
- Cognitive and functional evaluation, assessed using:
  • Integrated Alzheimer's Disease Rating Scale (iADRS)
  • Clinical Dementia Ratings Scale – Sum of Boxes (CDR-SB)
  • Alzheimer's Disease Assessment – Cognitive subscale (ADAS-Cog13)
  • Clinical Dementia Ratings Scale – Global Score (CDR-G)
  • Alzheimer's Disease Cooperative Study - Activities of Daily Living for Mild Cognitive Impairment (ADCS-iADL)
  • Amyloid Clearance
  • MMSE
- Safety
  • Treatment emergent adverse events: Treatment-related amyloid-related imaging abnormality- (o)edema (ARIA-E) and amyloid-related imaging abnormality haemorrhage (ARIA-H) events.
- Healthcare system
  • Utilisation
  • Healthcare costs
  • Cost effectiveness analysis between Aß PET and CSF AD biomarker immunoassay
  • Total cost to MBS and PBS

Proposed MBS items

Proposed Item AAAAA MBS item number:

Please search and select the proposed category:
DIAGNOSTIC IMAGING SERVICES

Please search and select the proposed group:
NUCLEAR MEDICINE IMAGING

Please search and select the proposed item descriptor or draft a proposed item descriptor to define the population and health technology usage characteristics that would define eligibility for funding:
Beta-amyloid positron emission tomography (PET) study of the brain, with or without quantitative assessment, for the evaluation of patients with a clinical diagnosis of mild cognitive impairment due to Alzheimer's disease or mild Alzheimer's disease, requested by the specialist or consultant physician, to determine if the requirements related to amyloid pathology for access to treatment with donanemab under the Pharmaceutical Benefits Scheme (PBS) are fulfilled.

The patient considered for this service must also meet specific PBS eligibility criteria for treatment with donanemab other than the criterion relating to amyloid pathology.

Applicable not more than X per lifetime

Proposed MBS fee:
$0.00

Indicate the overall cost per patient of providing the proposed health technology:
$0.00

Please specify any anticipated out of pocket costs:
$0.00

Provide details and explain:
Generally, the cost components of performing Aß PET include the Aß PET ligand, PET scan and Aß PET interpretation. To date, all MBS-subsidised PET imaging of the brain has utilised F- 18 fluorodeoxyglucose (FDG), e.g. MBS Item 61559 - FDG PET study of the brain, performed for the evaluation of refractory epilepsy which is being evaluated for surgery (fee: $918) or MBS Item 61560 - FDG PET study of the brain, performed for the diagnosis of Alzheimer's disease (fee: $605.05).

Notably, all amyloid tracers are owned by commercial companies, in contrast to F- 18 FDG which is in the public domain. While current MBS items for FDG-PET may provide comparable costs for performing and interpreting the PET scan, the MBS fee for Aß PET will need to also incorporate the price of the Aß PET ligand which is currently unknown. As such, a MBS fee is not currently proposed.

Proposed Item BBBBB MBS item number:

Please search and select the proposed category:
DIAGNOSTIC IMAGING SERVICES

Please search and select the proposed group:
NUCLEAR MEDICINE IMAGING

Please search and select the proposed item descriptor or draft a proposed item descriptor to define the population and health technology usage characteristics that would define eligibility for funding:
Beta-amyloid positron emission tomography (PET) study of the brain, with or without quantitative assessment, for the evaluation of patients with a clinical diagnosis of mild cognitive impairment due to Alzheimer's disease or mild Alzheimer's disease, requested by the specialist or consultant physician, for assessing response to treatment with donanemab under the Pharmaceutical Benefits Scheme (PBS)

Test must be performed within 18 months of initiating treatment with PBS subsidised donanemab, testing limited to 3 per patient.

Proposed MBS fee:
$0.00

Indicate the overall cost per patient of providing the proposed health technology:
$0.00

Please specify any anticipated out of pocket costs:
$0.00

Provide details and explain:
Generally, the cost components of performing Aß PET include the Aß PET ligand, PET scan and Aß PET interpretation. To date, all MBS-subsidised PET imaging of the brain has utilised F- 18 fluorodeoxyglucose (FDG), e.g. MBS Item 61559 - FDG PET study of the brain, performed for the evaluation of refractory epilepsy which is being evaluated for surgery (fee: $918) or MBS Item 61560 - FDG PET study of the brain, performed for the diagnosis of Alzheimer's disease (fee: $605.05).

Notably, all amyloid tracers are owned by commercial companies, in contrast to F- 18 FDG which is in the public domain. While current MBS items for FDG-PET may provide comparable costs for performing and interpreting the PET scan, the MBS fee for Aß PET will need to also incorporate the price of the Aß PET ligand which is currently unknown. As such, a MBS fee is not currently proposed.

Proposed Item CCCCC MBS item number:

Please search and select the proposed category:
PATHOLOGY SERVICES

Please search and select the proposed group:
IMMUNOLOGY

Please search and select the proposed item descriptor or draft a proposed item descriptor to define the population and health technology usage characteristics that would define eligibility for funding:

Quantification by immunoassay of ß-amyloid and tau protein concentration in a sample of cerebrospinal fluid from a patient with a clinical diagnosis of mild cognitive impairment due to Alzheimer's disease or mild Alzheimer's disease, requested by the specialist or consultant physician, to determine if the requirements related to amyloid pathology for access to treatment with donanemab under the Pharmaceutical Benefits Scheme (PBS) are fulfilled.

The patient considered for this service must also meet specific PBS eligibility criteria for treatment with donanemab other than the criterion relating to amyloid pathology.

Applicable not more than X per lifetime

Proposed MBS fee:
$0.00

Indicate the overall cost per patient of providing the proposed health technology:
$0.00

Please specify any anticipated out of pocket costs:
$0.00

Provide details and explain:
At present, Aß CSF immunoassay is performed at The National Dementia Diagnostics Laboratory (NDDL), located at The Florey in Melbourne for a non-rebated fee of $400. A MBS fee will be proposed in the ADAR

Proposed Item DDDDD MBS item number:

Please search and select the proposed category:
PATHOLOGY SERVICES

Please search and select the proposed group:
GENETICS

Please search and select the proposed item descriptor or draft a proposed item descriptor to define the population and health technology usage characteristics that would define eligibility for funding:
Genetic testing to determine apolipoprotein E ε4 (APOE ε4) genotype as requested by a specialist or consultant physician for patients with Mild Cognitive Impairment (MCI) due to Alzheimer's disease and Mild Alzheimer's dementia who are being considered for therapy with donanemab.

The patient considered for this service must also meet specific PBS eligibility criteria for treatment with donanemab other than the criterion relating to APOE genotype.

Proposed MBS fee:
$154

Indicate the overall cost per patient of providing the proposed health technology:
$154

Please specify any anticipated out of pocket costs:
$0.00

Provide details and explain:
Currently, private pathology providers offer APOE genetic testing for a non-rebated fee of around $154 (Sonic Genetics 2023).

How is the technology/service funded at present? (For example: research funding; State-based funding; self-funded by patients; no funding or payments):
At present, a clinical diagnosis of AD is made through a comprehensive medical evaluation, and there is currently no requirement for patients to be screened for *APOE* ε4, or investigated for Aß pathology. As such, *APOE* genotyping and tests for assessing presence of Aß pathology are not currently MBS funded.

Claims

In terms of health outcomes (comparative benefits and harms), is the proposed technology claimed to be superior, non-inferior or inferior to the comparator(s)?
Superior

Please state what the overall claim is, and provide a rationale (2000):
This application proposes that the co-dependent technology, *APOE* genotyping to assess treatment suitability, and Aß testing (via either Aß PET or CSF) to assess Aß pathology, followed by therapy with donanemab and standard of care in patients with confirmed evidence of Aß, results in superior health outcomes, and manageable safety outcomes compared to no testing and standard of care in patients with a clinical diagnosis of MCI due to AD, or mild AD.

This clinical claim is justified by acceptable safety and analytical performance of *APOE* screening and Aß testing (via either Aß PET or CSF), superior efficacy with a manageable safety profile of donanemab treatment compared to standard of care in patients with MCI due to AD or mild AD and confirmed evidence of Aß pathology (as supported by the phase 3, double-blind placebo-controlled study TRAILBLAZER-ALZ 2 trial and subgroup analysis for patients who are *APOE* ε4 redacted, and the clinical utility of the co-dependent technology.

Estimated utilisation

Estimate the prevalence and/or incidence of the proposed population:
The proposed population for Aß testing is patients with a clinical diagnosis of MCI due to AD or mild AD. A funnel-based approach has been used to estimate the number of patients with either mild AD or patients with mild cognitive impairment (MCI) due to AD. The size of these two populations are estimated separately, as shown hereafter. Notably, the estimates presented here are considered preliminary and will be further examined within the ADAR.

Mild AD population estimates
The epidemiology of AD is entangled with that of all-cause dementia (Knopman et al., 2021). There are many forms of dementia, with AD being the most prevalent (AIHW 2023).

As AD is the leading cause of dementia, the number of people with dementia in Australia have been sourced from the AIHW report 'Dementia in Australia' (AIHW 2023). However, the exact population size may vary depending on the data sources used to derive patient dementia prevalence rates and the approach taken to generate these estimates. Therefore, other sources will be examined for the dossier development.

Based on the AIHW 2022 report, the rate of dementia rises with age, with prevalence rates reported from 1.5% for Australians aged 60 to 64 years to 42.9% for Australian aged 90 and over (AIHW 2023). In 2022, it was estimated that there were 401,300 Australians living with dementia (AIHW 2023). These numbers are expected to increase from 438,978 in 2025 to 531,701 by 2030 (see attached excel).

AIHW data presents data on the severity of disease for dementia only, with 55% of dementia cases being classified as mild (AIHW 2012). Among patients with mild dementia, it was assumed that 75% of these cases will be due to AD as reported by the Australian Dementia Network Registry (ADNeT) ((Ward SA and Arsenova V, 2023). The population of patients with mild AD is depicted in attached excel workbook. Further data sources will be explored as part of the dossier development to validate the population estimates.

MCI due to AD population estimates
As described above, the population of patients with MCI due to AD is estimated separately from patients with confirmed mild AD. At present, identified literature sources report a wide range of prevalence rates for MCI (Sachdev et al., 2015). These heterogenous results can be attributed to differences in study populations, diagnostic criteria and methodology (Sachdev et al., 2015). Sachdev and authors (2015) estimated that the proportion of patients with amnestic MCI (aMCI) was 2.0%. The same publication also reports prevalence estimates from two Australian studies, i.e. the Sydney Memory and Ageing Study (MAS) (3.6%; Sachdev PS 2010), and the Personality and Total Health Through Life Project (PATH) (1.0%, Anstey KJ 2012). For the purpose of this application, overall prevalence rates were applied (i.e. 2 %) but other rates will be explored for the submission dossier.

The ADNeT 2022 report estimated that 72% of MCI cases are due to AD. As presented in the attached excel workbook, this proportion was applied to the MCI population estimates to determine the number of patients with MCI suspected due to AD. At present, these population estimates are considered indicative and further data sources will be examined as part of the submission

Provide the percentage uptake of the proposed health technology by the proposed population:

Year 1 estimated uptake(%):
36

Year 2 estimated uptake(%):
36

Year 3 estimated uptake(%):
36

Year 3 estimated uptake(%):
36

Estimate the number of patients who will utilise the proposed technology for the first full year:
see attached excel

Optionally, provide details:
Sources that estimate the number of patients who will utilise the proposed technology (i.e. biomarker testing are limited and there will be a proportion of patients with mild AD or MCI due to AD who will remain undetected in the Australian community. For the purpose of this application, the proportion of patients who will be identified with mild AD or MCI due to AD and receive subsequent cognitive screening was determined using inputs from the RAND Australia research report (Baxi et al., 2019).

This report assessed the preparedness of the Australian health care system infrastructure for an AD modifying therapy (Baxi et al., 2019). In the clinical pathway proposed by Baxi et al it was assumed, based on expert clinical advice, that 80% of Australian patients aged 50 years and over would be screened each year in general practice and 50% of those who screen positive for MCI would be followed up with a dementia specialist evaluation. It is assumed these patients who are assessed by a dementia specialists are referred for *APOE* testing Redacted. Therefore, approximately 90% of patients who are evaluated by a specialist would receive Aß testing. Accordingly, it is currently assumed that 36% of patients with mild AD or MCI due to AD will access biomarker testing (Aß PET or CSF AD biomarker testing). However, this will be further assessed in the ADAR, with further consideration to capacity constraints with regard to AD biomarker testing, particularly for Aß PET. Therefore, these proposed utilisation estimates are considered indicative and will be further explored in the ADAR.

Notably, only those patients with confirmed evidence of Aß pathology would be considered eligible for treatment with donanemab. The estimated uptake and utilisation of donanemab treatment will be presented in the ADAR.

Will the technology be needed more than once per patient?
Yes, multiple times

Over what duration will the health technology or service be provided for a patient? (preferably a number of years):
see below

Optionally, provide details:

What frequency will the health technology or service be required by the patient over the duration? (range, preferably on an annual basis):
see below

Optionally, provide details (5000):
Test frequency: Patients with a clinical diagnosis of MCI due to AD, or mild AD (meeting clinical criteria for treatment with donanemab) will be eligible for *APOE* screening to determine whether they are *APOE* ε4 redacted and suitable for treatment. Redacted. As *APOE* genotype will not change, this precludes patients from receiving treatment according

to the current proposed TGA label. If the results from the *APOE* screen are suitable, patients will be eligible for testing with one of the proposed technologies: Aß PET or CSF AD biomarker immunoassay, to confirm Aß pathology, and thus determine eligibility for treatment with PBS-subsidised donanemab. If a patient is determined to be negative for Aß pathology, the implication would be that any current cognitive impairment is as a result of something other than AD, however, it is noted that this would not preclude the possibility of AD dementia in the future. As such, a patient may be eligible for subsequent testing for Aß pathology. Limitations on the number of tests for assessing Aß pathology have not been proposed in this application but will be discussed in the ADAR.

Assessment of amyloid clearance: In Australian clinical practice, it is expected that donanemab treatment will continue up to a maximum treatment duration of 18 months, with a potential for earlier treatment completion if amyloid plaque clearance can be assessed and is achieved. At present, Aß PET is the only method for assessing amyloid clearance in AD patients and in the TRAILBLAZER-ALZ 2 trial was assessed at 24, 52 and 76 weeks. A separate MBS item is proposed to assess amyloid clearance in patients treated with donanemab. Currently, a maximum of three uses of this MBS item is proposed with a requirement to be utilized within 18 months of donanemab treatment initiation, which aligns with the Aß PET monitoring schedule within the TRAILBLAZER-ALZ 2 trial. Alternative Aß PET monitoring schedules will be explored in the ADAR. The distribution of patients treated with either a treat-to-amyloid-clearance approach (and hence requiring Aß PET monitoring) compared to a fixed treatment duration of 18 months will also be explored within the ADAR.

Consultation

List all appropriate professional bodies / organisations representing the group(s) of health professionals who provide the health technology/service:

Professional body name:
Australasian Association of Nuclear Medicine Specialists (AANMS)

Rationale:
A professional body representing medical practitioners working in the field of nuclear medicine diagnosis and therapy

Professional body name:
Australian and New Zealand Society of Nuclear Medicine (ANZSNM)

Rationale:
A professional society for people working across all areas of professional practice in nuclear medicine across Australia and New Zealand

Professional body name:
The Royal College of Pathologists of Australasia (RCPA)

Rationale:
A professional organisation representing Pathologists and Senior Scientists in Australasia

List all appropriate professional bodies / organisations representing the group(s) of health professionals who request the health technology/service:

Professional body name:
Australian and New Zealand Association of Neurologists (ANZAN)

Rationale:
A professional organisation for neurologists in Australia and New Zealand

Professional body name:
Australian and New Zealand Society for Geriatric Medicine (ANZSGM)

Rationale:
A professional society for geriatricians and other medical practitioners involved health care of older persons in Australia and New Zealand.

List all appropriate professional bodies / organisations representing the group(s) of health professionals that may be impacted by the health technology/service:

Professional body name:
Australasian Association of Nuclear Medicine Specialists (AANMS)

Rationale:
A professional body representing medical practitioners working in the field of nuclear medicine diagnosis and therapy

Professional body name:
Australian and New Zealand Association of Neurologists (ANZAN)

Rationale:
A professional organisation for neurologists in Australia and New Zealand

Professional body name:
Australian and New Zealand Society for Geriatric Medicine (ANZSGM)

Rationale:
A professional society for geriatricians and other medical practitioners involved health care of older persons in Australia and New Zealand.

Professional body name:
Australian and New Zealand Society of Nuclear Medicine (ANZSNM)

Rationale:
A professional society for people working across all areas of professional practice in nuclear medicine across Australia and New Zealand

Professional body name:
The Royal College of Pathologists of Australasia (RCPA)

Rationale:
A professional organisation representing Pathologists and Senior Scientists in Australasia

List the patient and consumer advocacy organisations or individuals relevant to the proposed health technology:

Number of organisations listed: 1

Professional body name:
Dementia Australia

Rationale:
Dementia Australia is the national peak body supporting people living with dementia, their families and carers

List the relevant sponsor(s) and / or manufacturer(s) who produce similar products relevant to the proposed service or health technology:

Professional body name:
Cyclotek

Rationale:
Commercial manufacturer of three Aβ PET radiotracers commercially in Australia (and New Zealand): 18F-florbetaben (Neuraceq®), 18F-florbetapir (Amyvid®) and 18F-flutemetamol (Vizamyl®)

Professional body name:
Roche Diagnostics

Rationale:
Sponsor of TGA registered CSF AD biomarker immunoassays (Elecsys® β-Amyloid (1-42) CSF, Elecsys® Phospho-Tau (181P) CSF, Elecsys® Total -Tau CSF)

Regulatory information

Would the proposed health technology involve the use of a medical device, in-vitro diagnostic test, radioactive tracer or any other type of therapeutic good?
Yes

Has it been listed or registered or included in the Australian Register of Therapeutic Goods (ARTG) by the Therapeutic Goods Administration (TGA)?
No

Is the therapeutic good classified by the TGA as either a Class III or Active Implantable Medical Device (AIMD) against the TGA regulatory scheme for devices?
No

Is the therapeutic good to be used in the service exempt from the regulatory requirements of the Therapeutic Goods Act 1989?
Yes

Codependent details

Will a submission be made to the Pharmaceutical Benefits Advisory Committee (PBAC)?
Yes

Please select the PBAC meeting date relevant for this codependent application:
12/03/2025

Please provide a rationale for the codependency and indicate how the proposed PBS restriction would reference the intervention(s) proposed for MSAC consideration:
The requested MBS listing for *APOE* genotyping is for the purpose of assessing donanemab suitability. The MBS listings for beta-amyloid (Aß) PET and CSF Alzheimer's Disease (AD) biomarker immunoassay, are for the purposes of assessing Aß pathology in patients. The requested MBS listings are intended for use in patients with mild cognitive impairment (MCI) due to AD or mild AD, to determine eligibility for PBS-subsidised treatment with donanemab.

Donanemab is an immunoglobulin G1 antibody which specifically targets an N-terminal pyroglutamate amyloid-ß epitope found exclusively in mature brain amyloid plaques. By binding to the N-terminal truncated form of Aß, donanemab facilitates plaque removal through microglial- mediated phagocytosis. The proposed PBS restriction for donanemab will require patients with MCI due to AD or mild AD to have confirmed evidence of Aß pathology.