NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Donanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of donanemab within its marketing authorisation for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease.

Background

Alzheimer's disease is a progressive neurological disease and is the most common type of dementia, accounting for 50 to 75% of dementia cases.[1] It is thought to be caused by the abnormal build-up of proteins in and around brain cells including beta-amyloid and tau. Deposits of these proteins form plaques around brain cells and disrupt neurone function.[2] Mild cognitive impairment caused by Alzheimer's disease refers to the set of symptoms that occur before the dementia stage of Alzheimer's disease. These can include mild problems with memory, reasoning, attention, language or visuospatial function depth perception. Alzheimer's disease usually develops slowly from these initial symptoms and progression is characterised by deterioration in cognition, functional ability and associated behavioural and psychiatric symptoms. Differential diagnosis of Alzheimer's disease as the cause for people presenting with mild cognitive impairment compared with other causes of mild cognitive impairment is not straightforward from a clinical perspective. However, diagnostics used for Alzheimer's disease, such as positron emission tomography (PET) scan or cerebrospinal fluid (CSF) testing, can be used to differentiate mild cognitive impairment due to Alzheimer's disease from mild cognitive impairment due to other causes.[3]

The number of people with dementia in England was estimated as 748,000 in 2019, with 107,100 cases of mild dementia.[4] Therefore, the number of people diagnosed with mild dementia due to Alzheimer's disease could be up to around 80,000. The largest risk factor for dementia is age, with over 95% of all cases in people aged over 65.[5]

The exact number of people with mild cognitive impairment is unknown. Mild cognitive impairment is prevalent in 5% to 20% of all people over 65. There is a higher risk of developing dementia in people with mild cognitive impairment than people without mild cognitive impairment, with approximately 5% to 20% of people with mild cognitive impairment developing dementia, although there is variation in risk estimates.[6]

There is no cure for Alzheimer's disease. Current management of mild cognitive impairment and mild dementia due to Alzheimer's disease aims to improve cognitive, non-cognitive and behavioural symptoms, but does not slow progression of the underlying disease. [7] NICE guidance (TA217 and NG97) recommends acetylcholinesterase (AChE) inhibitors (donepezil, galantamine and rivastigmine) as options for managing mild to moderate Alzheimer's disease and memantine alone or

in addition to an AChE inhibitor as an option for managing moderate or severe Alzheimer's depending on existing treatment and intolerance to AChE inhibitors. There is no pharmacological management recommended for mild cognitive impairment due to Alzheimer's disease. Non-pharmacological management for mild to moderate Alzheimer's disease includes social support, increasing assistance with day-to-day activities, information and education, carer support groups, community dementia teams, home nursing and personal care, community services, befriending services, day centres, respite care and care homes.

The technology

Donanemab (brand name unknown, Eli Lilly and Company) does not currently have a marketing authorisation in the UK. It has been studied in clinical trials compared with placebo in people with early symptomatic Alzheimer's disease with amyloid and tau pathology, and compared with aducanumab in people with early symptomatic Alzheimer's disease.

Intervention(s)	Donanemab
Population(s)	People with mild cognitive impairment or mild dementia due to Alzheimer's disease
Subgroups	If the evidence allows the following subgroups will be considered: • Mild cognitive impairment due to Alzheimer's disease • Mild dementia due to Alzheimer's disease
Comparators	Established clinical management without donanemab, including but not limited to: • Non-pharmacological management (for mild cognitive impairment due to Alzheimer's disease) • An AChE inhibitor plus non-pharmacological management (for mild dementia due to Alzheimer's disease)
Outcomes	The outcome measures to be considered include: • cognitive and functional impairment • non-cognitive symptoms (e.g. behavioural and psychiatric symptoms) • mortality • ability to remain independent • admission to full-time care • adverse effects of treatment • health-related quality of life

Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The use of donanemab is conditional on the presence of amyloid and tau pathology. The economic modelling should include the costs associated with diagnostic testing for amyloid and tau pathology in people with Alzheimer's disease who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 4.8 of the guidance development manual (available here: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation).
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations	**Related Technology Appraisals:** Donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's disease (2011; updated 2018) NICE technology appraisal guidance 217. **Related technology appraisals in development:** Lecanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease [ID4043] **Related Guidelines:** Dementia: assessment, management and support for people living with dementia and their carers (2018) NICE guideline 97. Dementia, disability and frailty in later life – mid-life approaches to delay or prevent onset (2015) NICE guideline 16 **Related Quality Standards:** Dementia (2019) NICE quality standard 184
Related National Policy	NHS England (2015) Dementia 2020 challenge The NHS Long Term Plan, 2019. NHS Long Term Plan

	NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Department of Health and Social Care (2016-2017) NHS Outcomes Framework: Domain 2

Questions for consultation

Would donanemab be used as an add on treatment to established clinical management? Would donanemab be used in addition to AChE inhibitors or as an alternative to AChE inhibitors?

Have all relevant comparators for donanemab been included in the scope? Which treatments are considered to be established clinical practice in the NHS for symptomatic early Alzheimer's disease?

How should non-pharmacological management be defined?

The eligibility criteria for the clinical trials of donanemab included that people should have confirmed amyloid and tau pathology. Is it expected that this will be a criterion for being eligible for donanemab in clinical practice? Are people with suspected mild cognitive impairment or mild dementia caused by Alzheimer's disease routinely tested for amyloid and tau pathology in the NHS?

Are there any subgroups of people in whom donanemab is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Would donanemab be a candidate for managed access?

Do you consider that the use of donanemab can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which donanemab will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1. Alzheimer's Society: Alzheimer's Society's view on demography. Available at: https://www.alzheimers.org.uk/about-us/policy-and-influencing/what-we-think/demography [Accessed: April 2023].

2. National Health Service (NHS). Alzheimer's disease: Causes. Available at: https://www.nhs.uk/conditions/alzheimers-disease/ [Accessed: April 2023].

3. Albert MS, DeKosky ST, Dickson D, Dubois B, Feldman HH, Fox NC, et al. The diagnosis of mild cognitive impairment due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement. 2011 May;7(3):270–9.

4. The London School of Economics and Political Science - Care Policy and Evaluation Centre. Projections of older people with dementia and costs of dementia care in the United Kingdom, 2019–2040. 2019. Available at: https://www.alzheimers.org.uk/sites/default/files/2019-11/cpec_report_november_2019.pdf. [Accessed: April 2023].

5. Public Health England. Dementia Profile. 2020. Available at: https://www.gov.uk/government/statistics/dementia-profile-updates/statistical-commentary-dementia-profile-april-2020-data-update [Accessed: April 2023].

6. Alzheimer's Society: Mild Cognitive Impairment. Available at: https://www.alzheimers.org.uk/about-dementia/types-dementia/mild-cognitive-impairment-mci [Accessed: April 2023].

7. Alzheimer's Society: Drug treatments and medication for Alzheimer's disease. Available at: https://www.alzheimers.org.uk/about-dementia/treatments/dementia-drugs/drug-treatments-and-medication-alzheimers-disease [Accessed: April 2023].