

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

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

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of aducanumab 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 cases¹. It is thought to be caused by the abnormal build-up of proteins in and around the brain cells including beta-amyloid proteins. Deposits of amyloid proteins form plaques around brain cells² and disrupt neurone function. 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 visual depth perception. Alzheimer's disease usually develops slowly from these initial symptoms and progression is characterised by deterioration in cognition, functional ability and behaviour. Differential diagnosis of Alzheimer's disease for people with mild cognitive impairment compared with other types of dementia is not always clearly defined.

The number of people with dementia in England was estimated as 748,000 in 2019, with 107,100 cases of mild dementia.³ Therefore, the number of people diagnosed with mild dementia due to Alzheimer's disease could be up to 80,325. The largest risk factor for dementia is age, with approximately 95% of all cases in people aged over 65.⁴ 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, however not all of these people will go on to develop Alzheimer's disease.⁵ There is a higher risk of developing dementia in people with mild cognitive impairment, even though there is a considerable variability in annual risk estimate of less than 5% to 20%.⁶

There is no cure for Alzheimer's disease. Current management of mild cognitive impairment and mild dementia due to Alzheimer's disease involves symptomatic relief of cognitive, non-cognitive and behavioural symptoms. 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 as an option for managing severe Alzheimer's disease or for people with moderate Alzheimer's disease who are intolerant or have a contraindication to AChE inhibitors. There is no pharmacological management of mild cognitive impairment due to Alzheimer's disease. Non-pharmacological management 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

Aducanumab (Aduhelm, Biogen) is a selective human monoclonal antibody that targets the β -amyloid ($A\beta$) protein in the brain. This reduces the number of amyloid plaques, protein structures present in Alzheimer's disease, in the brain. It is administered intravenously.

Aducanumab does not have a marketing authorisation in the UK for treating mild cognitive impairment or mild dementia due to Alzheimer's disease. It has been studied in clinical trials compared with placebo in patients with early Alzheimer's disease who meet the criteria for mild cognitive impairment due to Alzheimer's disease or mild Alzheimer's disease.

Intervention(s)	Aducanumab plus best supportive care
Population(s)	People with mild cognitive impairment or mild dementia due to Alzheimer's disease, with confirmed amyloid beta pathology.
Comparators	Established clinical management without aducanumab, including but not limited to: <ul style="list-style-type: none"> • For mild cognitive impairment due to Alzheimer's disease: <ul style="list-style-type: none"> ○ Best supportive care (non-pharmacological management) • For mild dementia due to Alzheimer's disease: <ul style="list-style-type: none"> ○ Best supportive care (pharmacological plus non-pharmacological management)
Outcomes	The outcome measures to be considered include: <ul style="list-style-type: none"> • Cognitive and functional impairment • non-cognitive symptoms (e.g. behavioural symptoms) • mortality • ability to remain independent • admission to full-time care • health-related quality of life • adverse effects of treatment.

Economic analysis	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The use of aducanumab is conditional on the presence of beta amyloid. The economic modelling should include the costs associated with diagnostic testing for beta amyloid in people with mild cognitive impairment and mild dementia due to 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 5.9 of the Guide to the Methods of Technology Appraisals'.</p>
Other considerations	<p>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.</p>
Related NICE recommendations and NICE Pathways	<p>Related Technology Appraisals:</p> <p>Donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's disease (2011; updated 2018) NICE Technology Appraisal 217. Static guidance list.</p> <p>Related Guidelines:</p> <p>Dementia: assessment, management and support for people living with dementia and their carers (2018) NICE guideline 97.</p> <p>Dementia, disability and frailty in later life – mid-life approaches to delay or prevent onset (2015) NICE guideline 16</p> <p>Related Quality Standards:</p> <p>Dementia (2019) NICE Quality standard 184</p> <p>Related NICE Pathways:</p> <p>Dementia (2019) NICE pathway</p>
Related National Policy	<p>NHS England (2015) Dementia 2020 challenge</p> <p>The NHS Long Term Plan, 2019. NHS Long Term Plan</p> <p>NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019)</p>

	Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 2, 4 and 5.
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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: December 2020].
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3. 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: December 2020].
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5. Alzheimer's Society: Mild Cognitive Impairment. Available at: <https://www.alzheimers.org.uk/about-dementia/types-dementia/mild-cognitive-impairment-mci> [Accessed: November 2020].
6. Langa KM, Levine DA. The diagnosis and management of mild cognitive impairment: a clinical review. 2014. Available at: <https://jamanetwork.com/journals/jama/fullarticle/2040164>. [Accessed: November 2020].