NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Aducanumab for treating mild cognitive impairment in early Alzheimer's disease

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of aducanumab within its marketing authorisation for treating mild cognitive impairment (MCI) in early Alzheimer's disease.

Background

Alzheimer's disease is a progressive neurological disease and is the most common type of dementia accounting for 60 to 70% of dementia cases[1]. It is thought to be caused by the abnormal build-up of proteins in and around the brain cells including amyloid proteins. Deposits of amyloid proteins form plaques around brain cells[2] 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 recorded number of people diagnosed with dementia in England was 471,000 in February 2020.[3] Therefore, the number of people diagnosed with Alzheimer's disease could be up to 329,700. The largest risk factor for dementia is age, with approximately 95% of all cases in people aged over 65.[4] Mild cognitive impairment is prevalent in 10 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%.[5]

There is no cure for Alzheimer's disease. Current management involves the treatment 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. Non-pharmacological treatment 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 (brand name unknown, Biogen) is a selective human antibody that targets the β-amyloid (Aβ) protein in the brain. This reduces the number of amyloid

plaques, protein structures present in Alzheimers disease, in the brain. It is administered intravenously.

Aducanumab does not have a marketing authorisation in the UK for treating mild cognitive impairment 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)	Adacanumab
Population(s)	People with mild cognitive impairment due to Alzheimer's disease or mild Alzheimer's disease
Comparators	Established clinical management without adcanumab including but not limited to: • acetylchlinestrase (AChE) inhibitors o donepezil, galantamine and rivastigmine • memantine • non-pharmacological management
Outcomes	The outcome measures to be considered include: • cognitive 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	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.
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 and NICE Pathways	**Related Technology Appraisals:** Donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's disease (2011; updated 2018) NICE Technology Appraisal 217. Static guidance list. **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 NICE Pathways:** Dementia (2019) NICE pathway
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, NHS Outcomes Framework 2016-2017: Domains 2, 4 and 5.

Questions for consultation

Have all relevant comparators for aducanumab been included in the scope? Which treatments are considered to be established clinical practice in the NHS for mild cognitive impairment caused by Alzheimer's disease?

How should non-pharmacological management be defined?

Are the outcomes listed appropriate?

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

Where do you consider aducanumab will fit into the existing NICE pathway, Dementia?

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 aducanumab 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.

Do you consider aducanumab to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of aducanumab can result in any potential significant and 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 Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

1. EU Joint Programme - Neurodegenerative Disease Research. What is a neurodegenerative disease. 2019. Available from: https://www.neurodegenerationresearch.eu/what/ [Accessed September 2020].

2. National Health Service (NHS). Alzheimer's disease: Causes. 2018. Available from: https://www.nhs.uk/conditions/alzheimers-disease/ [Accessed September 2020].

3. National Health Service (NHS) Digital. Recorded Dementia Diagnoses – February 2020. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/recorded-dementia-diagnoses/february-2020 [Accessed September 2020].

4. Public Health England. Dementia Profile. 2019. Available from: https://www.gov.uk/government/publications/dementia-profile-april-2019-data-update/statistical-commentary-dementia-profile-april-2019-update [Accessed September 2020]

5. Langa KM, Levine DA. The diagnosis and management of mild cognitive impairment: a clinical review. JAMA. 2014;312(23):2551-61. Available from: https://doi.org/10.1001/jama.2014.13806.

