NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Hydromethylthionine mesylate for treating mild cognitive impairment or mild or moderate dementia caused by Alzheimer's disease ID6343

Draft scope

Draft remit/evaluation objective

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

Background

Alzheimer's disease is a progressive neurological disease and is the most common cause of dementia.[1] It is thought to be caused by the abnormal build-up of proteins in and around brain cells. These proteins are called beta-amyloid and tau. Deposits of amyloid proteins form plaques around brain cells.[1] Tau can aggregate into neurofibrillary tangles that form within brain cells.[1]

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. Dementia caused by Alzheimer's disease usually develops slowly from these initial symptoms. Progression from mild to moderate dementia is characterised by further deterioration in cognition, functional ability and associated behavioural and psychiatric symptoms. 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 or dementia due to Alzheimer's disease from mild cognitive impairment or dementia due to other causes.[2,3]

The exact number of people with mild cognitive impairment caused by Alzheimer's disease is unknown. Approximately 210,000 people in England have mild cognitive impairment, present to the healthcare system, and have clinical suspicion of Alzheimer's disease.[4]

The number of people with dementia in England was estimated as 748,000 in 2019, with 107,100 cases of mild and 206,300 cases of moderate dementia.[5] Alzheimer's disease causes around 60 to 70% of cases of dementia.[6] The largest risk factor for dementia is age, with over 95% of all cases in people aged over 65.[1]

There is no cure for Alzheimer's disease and there are currently no disease modifying treatments approved for use in the UK. Current management of mild cognitive impairment and mild or moderate dementia caused by Alzheimer's disease aims to improve cognitive, non-cognitive and behavioural symptoms, but does not slow progression of the underlying disease.[7,8] NICE guidance (TA217 and NG97) recommends:

- acetylcholinesterase (AChE) inhibitors (donepezil, galantamine and rivastigmine) as options for managing mild to moderate Alzheimer's disease,

- memantine monotherapy as an option for managing moderate Alzheimer's disease for people who are intolerant or have a contraindication to AChE inhibitors,

- memantine in addition to an AChE inhibitor for managing moderate Alzheimer's disease for people who are already taking an AChE inhibitor.

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 risk factor modification, 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

Hydromethylthionine mesylate (brand name unknown, TauRx Therapeutics) does not currently have a marketing authorisation in the UK for treating Alzheimer's disease. It has been studied in clinical trials compared with placebo in people with mild cognitive impairment and mild to moderate dementia caused by Alzheimer's disease.

Intervention(s)	Hydromethylthionine mesylate
Population(s)	People with mild cognitive impairment or mild or moderate dementia caused by Alzheimer's disease
Subgroups	If the evidence allows the following subgroups will be considered: • Apolipoprotein E 4 (ApoE4) gene carrier status • Mild cognitive impairment caused by Alzheimer's disease • Mild dementia caused by Alzheimer's disease • Moderate dementia caused by Alzheimer's disease

Comparators	Established clinical management without hydromethylthionine mesylate, including but not limited to:
	• For mild cognitive impairment due to Alzheimer's disease:
	  ○ Non-pharmacological management
	  ○ Donanemab (subject to NICE evaluation)
	  ○ Lecanemab (subject to NICE evaluation)
	• For mild dementia due to Alzheimer's disease:
	  ○ Non-pharmacological management
	  ○ AChE inhibitors
	  ○ Donanemab (subject to NICE evaluation)
	  ○ Lecanemab (subject to NICE evaluation)
	• For moderate dementia due to Alzheimer's disease:
	  ○ Non-pharmacological management
	  ○ AChE inhibitors
	  ○ Memantine monotherapy (for people who are intolerant of or have a contraindication to AChE inhibitors)
	  ○ Memantine plus an AChE inhibitor

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 availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability and cost of biosimilar and generic products should be taken into account. The economic modelling should include the costs associated with diagnostic testing for amyloid 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:** Donanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease [ID6222]. Publication expected September 2024. Lecanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease [ID4043]. Publication expected publication July 2024. **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 (2023) Manual for prescribed specialist services (2023/2024) Department of Health and Social Care (2016-2017) NHS Outcomes Framework: Domain 2

Questions for consultation

Have all relevant comparators for hydromethylthionine mesylate been included in the scope?

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

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

Where do you consider hydromethylthionine mesylate will fit into the existing care pathway for Alzheimer's disease?

Would hydromethylthionine mesylate be used as an add on treatment to established clinical management? Would hydromethylthionine mesylate be used in addition to AChE inhibitors, memantine, lecanemab or donanemab (subject to NICE's ongoing appraisals) or as an alternative?

Please select from the following, would hydromethylthionine mesylate be:
A. Prescribed in primary care with routine follow-up in primary care
B. Prescribed in secondary care with routine follow-up in primary care
C. Prescribed in secondary care with routine follow-up in secondary care
D. Other (please give details):
For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

Would hydromethylthionine mesylate be a candidate for managed access?

Do you consider that the use of hydromethylthionine mesylate 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 hydromethylthionine mesylate 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. National Health Service (NHS). Alzheimer's disease. Available at: https://www.nhs.uk/conditions/alzheimers-disease/ [Accessed: April 2024].

2. 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.

3. McKhann GM, Knopman DS, Chertkow H et al. (2011) The diagnosis of dementia 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 7(3):263-9.

4. Wailoo A. (2023) Estimates of the size of the English eligible population in for amyloid targeting therapies in Alzheimer's Disease. NICE DSU Report. Available at: https://www.nice.org.uk/Media/Default/About/what-we-do/HTA%20Lab/Appendix-D.pdf

5. 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 2024].

6. World Health Organization. (2023) Dementia fact sheet. Available at: https://www.who.int/news-room/fact-sheets/detail/dementia [Accessed: April 2024]

7. Alzheimer's Society: Mild Cognitive Impairment. Available at: https://www.alzheimers.org.uk/about-dementia/types-dementia/mild-cognitive-impairment-mci [Accessed: April 2024].

8. 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 2024].