Navigating Health Technology Assessment Requirements: The Current Landscape of Alzheimer's Disease Modifying Treatments

HTA244

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Introduction

- The prevalence of dementia worldwide is projected to reach 78 million cases by 2030.[1]
- Alzheimer's disease (AD) is the most common form of dementia and accounts for up to 70% of all cases.[2]
- As of September 2025 (**Figure 1**), two disease-modifying treatments (DMTs) for AD have received authorisations in Europe, the US, and Australia: lecanemab (Leqembi) and donanemab (Kinsula).

Figure 1. Regulatory approvals of DMTs across the MHRA, FDA and TGA

MHRA[3]	FDA[4,5]	TGA[6]
Approval **Lecanemab**: August 2024 **Donanemab**: October 2024	**Approval** **Lecanemab**: July 2023 **Donanemab**: July 2024	**Approval** **Lecanemab**: September 2025 (initial rejection October 2024) **Donanemab**: May 2025
Indication For use in the early stages of Alzheimer's disease	**Indication** For treating early-stage Alzheimer's disease by targeting and clearing amyloid plaques	**Indication** For use in early Alzheimer's disease

Abbreviations: DMT = disease modifying treatment; FDA = Food and Drug Administration; MHRA = Medicines and Healthcare Products Regulatory Agency; TGA = Therapeutic Goods Administration

Objectives

- **Our research aims to provide an overview of DMT health technology assessment (HTA) appraisals and highlight the challenges faced by manufacturers when the clinical value and cost-effectiveness of DMTs for AD are under evaluation.**

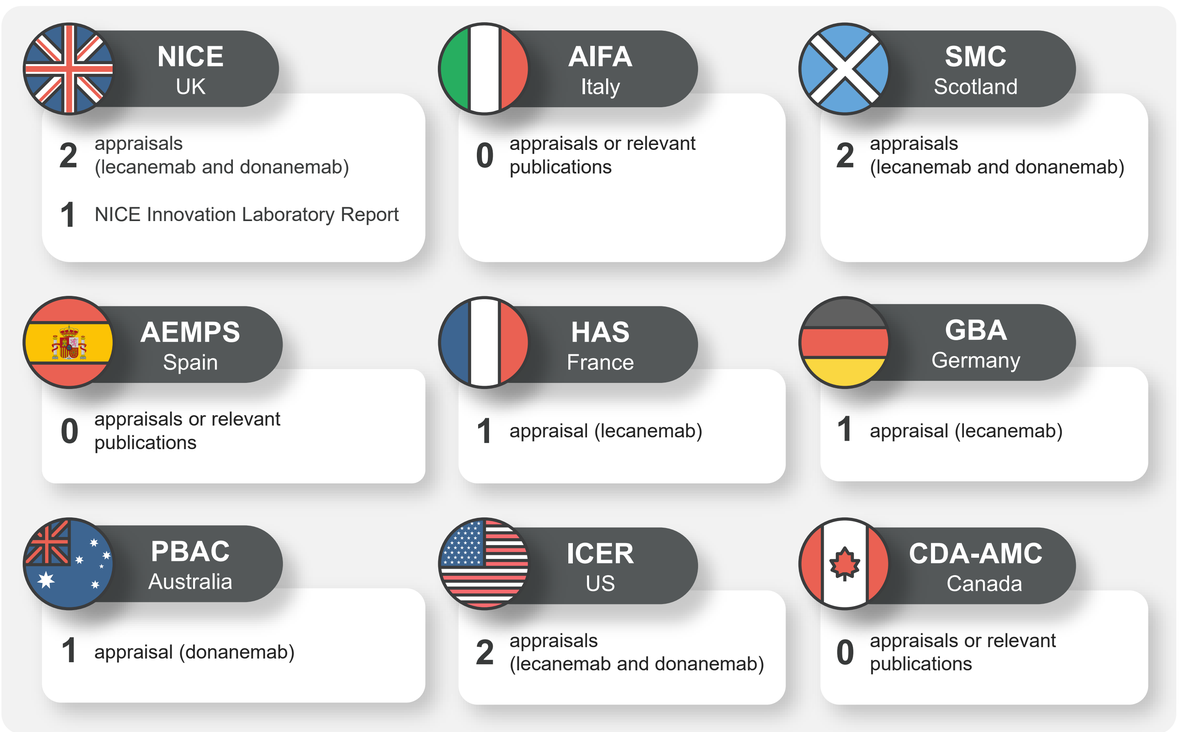
Methods

- We conducted a targeted search for published materials on the assessment of DMTs in AD, including HTA appraisals, press releases, and reports in the EU4, the UK, Australia, Canada, and the US.
- Searches were run on 18 September 2025 across nine HTA body websites.

Results

- The results of the searches are presented in **Figure 2**.
  - We identified nine appraisals in total (two for National Institute for Health and Care Excellence [NICE], two for Scottish Medicines Consortium [SMC], two for Institute for Clinical and Economic Review [ICER], and one each for Gemeinsamer Bundesausschuss [G-BA], Haute Autorité de Santé [HAS], and the Pharmaceutical Benefits Advisory Committee [PBAC]).
  - We did not identify any published DMT appraisals for AD in Italy, Spain, or Canada.
- Our search identified one NICE Innovation Laboratory report that highlighted potential challenges faced by manufacturers when DMTs are assessed for dementia.[3]
  - Key uncertainties included prevalence estimates for the eligible treatment population, long-term treatment benefit, whether trial outcomes are clinically meaningful, and the additional cost of service implications.
  - The report concluded that while multiple challenges may arise during the evaluation of DMTs, NICE's approach is appropriate for their assessment.

Figure 2. Overview of relevant publications identified in the TLR



Abbreviations: AEMPS = Agencia Española de Medicamentos y Productos Sanitarios; AIFA = Agenzia Italiana del Farmaco; CDA-AMC = Canada's Drug Agency; G-BA = Gemeinsamer Bundesausschuss; HAS = Haute Autorité de Santé; ICER = Institute for Clinical and Economic Review; NICE = National Institute for Health and Care Excellence; PBAC = Pharmaceutical Benefits Advisory Committee; SMC = Scottish Medicines Consortium; TLR = targeted literature search

Results (cont.)

- An overview of HTA recommendations is presented in **Table 1**.

Table 1. Overview of HTA recommendations for DMTs in the treatment of AD

Negative recommendations	Positive recommendations
England and Scotland: Neither donanemab nor lecanemab are recommended for use following appraisals conducted between May and July 2025. Both are due for appeal with NICE in October 2025.[7] Reasons cited by NICE and SMC for the negative recommendations included limited evidence to demonstrate long-term effects, uncertain cost-effectiveness, and minimal benefits relative to the high costs associated with infusions and monitoring for adverse events.[7,8] The SMC specifically queried whether the benefit with donanemab was clinically meaningful.[8]	**Germany:** Lecanemab received funding as the first monoclonal antibody available for early AD treatment in Germany because it offers a new DMT option in this indication. However, the scope has been restricted due to safety risks and high diagnostic/monitoring demands. Therefore, use is restricted to selected patients under specialist supervision, with mandatory checks every 6 months and controlled access programme registration to monitor patient progress.[12]
France: HAS rejected the request for early-access use of lecanemab for AD. The decision cited a modest level of efficacy deemed not clinically meaningful, a concerning safety profile, the need for frequent MRI monitoring, and a lack of a robust QoL assessment.[9]	**US:** ICER did not assess donanemab because it received accelerated FDA approval.[11] Both lecanemab and donanemab are reimbursed by Medicare.[5,13]
Australia: PBAC rejected the PBS application of donanemab, noting a high burden for patients and the health system, substantial risks, modest clinical impact, uncertainty that trial results would translate into meaningful improvements, and the requirement for frequent infusions and monitoring.[10]	
US: ICER determined that currently available evidence is insufficient to demonstrate a net benefit of lecanemab over BSC. It concluded that the safety risks and high list price of lecanemab may outweigh its efficacy benefits.[11]	

Abbreviations: AD = Alzheimer's disease; BSC = best supportive care; DMT = disease modifying treatment; HAS = Haute Autorité de Santé; HTA = health technology assessment; ICER = Institute for Clinical and Economic Review; NICE = National Institute for Health and Care Excellence; PBAC = Pharmaceutical Benefits Advisory Committee; PBS = Pharmaceutical Benefits Scheme; QoL = quality of life; SMC = Scottish Medicines Consortium

Considerations for the future

- DMTs present unique challenges to HTA due to uncertainties related to long-term effectiveness, cost-effectiveness, and clinically meaningful patient benefit. The majority of HTA assessments for donanemab and lecanemab have resulted in negative recommendations.
- As of October 2025, NICE is the only HTA body that has published a review of challenges and considerations in the evaluation of DMTs. There are currently three DMT appraisals in development (hydromethylthionine mesylate) or awaiting development (gantenerumab and blarcamesine) for NICE, which may provide additional insights once published. However, there is a need for additional guidance that captures the HTA requirements and priorities across different markets.

Conclusions

- **Our findings highlight a potential disconnect between HTA evidence requirements for DMTs in AD and the available evidence provided in appraisals. This is particularly relevant given that three additional appraisals for DMTs in AD are awaiting development at NICE at the time of writing and more appraisals are expected in the future. Findings from our research may also be applicable to other DMTs for neurodegenerative diseases, such as pridopidine for treating Huntington's disease.**

References

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Disclosures

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