

NCPE Assessment

Summary

Lecanemab (Leqembi®)

HTA ID: 24052

13 October 2026

Applicant: Eisai Limited

For the treatment of adult patients, with a clinical diagnosis of Early Alzheimer's disease (mild cognitive impairment or mild dementia due to Alzheimer's disease) who are apolipoprotein E ϵ 4 (APOE ϵ 4) non-carriers or heterozygotes with confirmed amyloid pathology.

The National Centre for Pharmacoeconomics (NCPE) has issued a recommendation regarding the cost-effectiveness of lecanemab (Leqembi®) for the treatment of adult patients, with a clinical diagnosis of Early Alzheimer's disease (mild cognitive impairment or mild dementia due to Alzheimer's disease), who are apolipoprotein E ε4 non-carriers or heterozygotes with confirmed amyloid pathology.

Following assessment of the Applicant's submission, the NCPE recommends that lecanemab (Leqembi®) not be considered for reimbursement*.

The Health Service Executive (HSE) asked the NCPE to carry out an evaluation of the Applicant's (Eisai Limited) Health Technology Assessment of lecanemab (Leqembi®). The NCPE uses a decision framework to systematically assess whether a technology is cost-effective. This includes comparative clinical effectiveness and health related quality of life benefits, which the new treatment may provide and whether the cost requested by the pharmaceutical company is justified.

Following the recommendation from the NCPE, the HSE examines all the evidence which may be relevant for the decision; the final decision on reimbursement is made by the HSE. In the case of cancer drugs the NCPE recommendation is also considered by the National Cancer Control Programme (NCCP) Technology Review Group.

About the National Centre for Pharmacoeconomics

The NCPE are a team of clinicians, pharmacists, pharmacologists and statisticians who evaluate the benefit and costs of medical technologies and provide advice to the HSE. We also obtain valuable support from clinicians with expertise in the specific clinical area under consideration. Our aim is to provide impartial advice to help decision makers provide the most effective, safe and value for money treatments for patients. Our advice is for consideration by anyone who has a responsibility for commissioning or providing healthcare, public health or social care services.

Summary

In January 2026, Eisai Limited submitted a dossier which investigated the comparative clinical effectiveness, cost-effectiveness and budget impact of lecanemab (Leqembi®) for the treatment of adult patients, with a clinical diagnosis of Early Alzheimer's disease (mild cognitive impairment (MCI) or mild dementia due to Alzheimer's disease (mild Alzheimer's disease)) who are apolipoprotein E ε4 (APOE ε4) non-carriers or heterozygotes with confirmed amyloid pathology. Eisai Limited is seeking hospital pricing approval for lecanemab.

Lecanemab is a humanised immunoglobulin G1 monoclonal antibody which binds with high selectivity to amyloid beta (Aβ) aggregate species, with preferential activity for soluble Aβ protofibrils. Once attached to the Aβ protofibrils, the antibody signals the brain's own immune cells to clear and dissolve harmful Aβ protofibrils accumulations. By reducing the amyloid burden, it is proposed that the underlying pathology of Alzheimer's disease is targeted. Lecanemab is administered via intravenous infusion at a weight-based dose of 10 mg/kg once every 14 days. Treatment with lecanemab should be discontinued once the patient progresses to moderate Alzheimer's disease and/or if the clinical course otherwise suggests that lecanemab has not demonstrated effectiveness in the patient. Lecanemab should be discontinued after the second occurrence of symptomatic or radiographically: moderate or severe ARIA with oedema or effusion (ARIA-E), or severe ARIA with hemosiderin deposition (ARIA-H). Treatment should be permanently discontinued after any intracerebral haemorrhage exceeding 1 cm in diameter. A subcutaneous formulation of lecanemab has been approved by the FDA for use in the US; it is not considered within this evaluation.

In Ireland, the standard of care (SoC) for people living with MCI or mild Alzheimer's disease is dependent on the person's stage on the Alzheimer's disease continuum. There are currently no pharmacological treatments for MCI due to Alzheimer's disease used in clinical practice. For patients diagnosed with mild Alzheimer's disease, pharmacological treatment with acetylcholinesterase inhibitors may be initiated to manage symptoms. Memantine is licensed for use in moderate to severe Alzheimer's disease and is thus outside of the scope of SoC for the target population considered here.

1. Comparative effectiveness of lecanemab

The efficacy and safety of lecanemab was informed by the pivotal international, phase III Clarity AD study. Outcomes, relevant to the licensed indication, were derived from a post-hoc analysis. Specifically, this post-hoc analysis was undertaken in participants who were APOE ε4 non-carriers or heterozygotes only. This subpopulation accounted for approximately 85% of full population of Clarity AD. This subpopulation, of interest here, is herein referred to as the 'EU-licensed population'. The reliance on a post-hoc analysis in a subpopulation introduces a risk of bias and uncertainty.

Clarity AD included two phases; Core Clarity AD and the Clarity AD open-label extension (OLE). Core Clarity AD was an 18 month, double-blind, active-controlled study. Eligible participants were adults aged ≥ 50 to ≤ 90 years, with a clinical diagnosis of MCI or mild Alzheimer's disease, with a positive biomarker for brain amyloid pathology. Background symptomatic treatment use was permitted. However, the use of acetylcholinesterase inhibitors for MCI, and memantine for mild Alzheimer's disease did not align with SoC in Ireland. Furthermore, no stopping rule upon progression to moderate Alzheimer's disease, as is specified in the product license for lecanemab, was applied. These factors limit the generalisability of Clarity AD to clinical practice in Ireland.

In Core Clarity AD, participants were randomly assigned in a 1:1 ratio to receive intravenous lecanemab 10 mg/kg or placebo, once every 14 days. Baseline demographic and clinical characteristics were overall balanced across the trial arms. In the EU-licensed population, the mean age was 71.8 years, 51.5% were female, and 77.8% were White. The majority had MCI due to Alzheimer's disease (61.9%), and 38.1% had mild Alzheimer's disease. The primary efficacy outcome was the change from baseline at 18 months in the Clinical Dementia Rating – Sum of boxes (CDR-SB) score, which measures changes across both cognitive and functional domains. Secondary outcomes included the change from baseline in brain amyloid burden. This was measured using amyloid positron emission topography [PET]) in a subgroup of the EU-licensed population (herein referred to as the 'Amyloid PET sub study').

All outcomes and safety described in this report were derived from the EU-licensed population unless it is stated that these were derived from the Amyloid PET sub study.

At 18 months in Core Clarity AD, the mean difference in change from baseline in the CDR-SB score between the lecanemab and placebo arms was -0.58 (95% confidence interval [CI]: -0.811 to -0.347). While this was statistically significant, the size of observed effects in the full population of Core Clarity AD was considered small by the Committee for Medicinal Products for Human Use (CHMP). An exploratory “time-to-event” analysis was presented, which analysed time from randomisation to worsening of the Global Clinical Dementia Rating score at two consecutive visits. This represented progression to the next more severe stage of Alzheimer's disease (e.g. moving from MCI to mild Alzheimer's disease), which was considered clinically meaningful by the CHMP. At 18 months, the hazard ratio (HR) for progression to the next more severe stage was 0.656 (95% CI: 0.534 to 0.806). When measured using the CDR-SB, the HR was 0.698 (95% CI: 0.568 to 0.858). In an exploratory “time saved” slope analysis, cognition and function, measured using the CDR-SB, were preserved by approximately 6.1 months in participants treated with lecanemab, relative to placebo at 18 months. However, this analysis is uncertain, due to the assumption that decline remains linear over time. In the Amyloid PET sub study, 63.7% of participants on lecanemab achieved amyloid negativity compared with 0.7% of participants on placebo. The CHMP considered this to be supportive of a pharmacological rationale and biological plausibility for the mechanism of action of lecanemab. However, removal of amyloid is not a validated surrogate for clinical benefit.

Participants who completed Core Clarity AD could enrol to the Clarity AD OLE. Participants initially randomised to lecanemab continued lecanemab treatment. Those initially randomised to placebo crossed over to lecanemab treatment. There was no placebo arm in the Clarity AD OLE. Relative effect estimates, during the OLE period, were derived based on matching to an external longitudinal cohort. Due to methodological limitations, namely a lack of randomisation or adequate control for potential confounders, results from Clarity OLE were not considered sufficient to estimate long-term relative treatment effects, nor to support claims of disease modification. These results are therefore not reported here.

Health Related Quality of Life (HRQoL) measurements included the EQ-5D-5L, which was measured directly from participants and from their carers (as both a proxy for participants and to self-report utility for themselves). In Core Clarity AD, the difference in participant-reported EQ-5D-5L visual analogue scale (VAS) scores between the lecanemab and placebo arms was statistically significant at 18 months (1.824 [95% CI: 0.310 to 3.337]); participants treated with lecanemab showed 49% less decline in VAS score compared to those treated with placebo. No significant difference was observed when measured by proxy.

2. Safety of lecanemab

Safety was analysed in the EU-licensed population of Clarity AD. In Core Clarity AD, treatment-emergent adverse events (TEAEs) at 18 months were similar across both arms; most were mild to moderate in severity. TEAEs leading to dose interruption (21.9% versus 10.1%) and treatment-related TEAEs (41.5% versus 19.2%), were more common with lecanemab than placebo. TEAEs of special interest (AESIs) were more common in with lecanemab than placebo (39% versus 15%). These included: infusion related reactions (25.8% and 7.1%), hypersensitivity reactions (1.5% versus 0.8%) and amyloid-related imaging abnormalities (ARIA). The CHMP acknowledged the potential for functional unblinding, due to the relatively large proportion of infusion related reactions in the lecanemab arm.

Monoclonal antibodies which target A β , such as lecanemab, are associated with ARIA, which are a recognised and potential safety concern. ARIA-E (8.9% versus 1.3%), isolated ARIA-H (8.1% versus 5.9%), and concurrent ARIA-H (4.8% versus 0.8%) were more frequent in the lecanemab arm, relative to the placebo arm. Of those who experienced ARIA-H or ARIA-E, a higher proportion in the lecanemab arm experienced severe ARIA. The incidence of symptomatic ARIA-E were low, observed in 1.6% of participants on lecanemab and in no participants on placebo. Symptomatic ARIA-H were reported in 0.8% and 0.1% of the lecanemab and placebo arms respectively. Data from the OLE showed that the incidence of ARIAs increased from that reported at 18 months to 36 months (i.e. ARIA-E 8.9% to 10.7%; ARIA-H 12.9% to 19.3%).

Risk minimisation measures specified in the Summary of Product Characteristics (SmPC) include magnetic resonance imaging (MRI) monitoring requirements, at baseline and prior to the third, fifth, seventh and fourteenth dose of lecanemab. Additional MRI scans are

required where patients present with symptoms suggestive of ARIA. Therefore, both planned and responsive access to MRI would be required to facilitate treatment with lecanemab.

3. Cost effectiveness of lecanemab

Methods

The incremental cost-effectiveness of lecanemab, compared to SoC, was assessed, from the perspective of the HSE, using a Markov state transition model. The model uses a cohort-level state transition approach which characterises disease progression in Alzheimer's disease using four distinct health states based on disease severity; MCI due to Alzheimer's disease, mild Alzheimer's disease, moderate Alzheimer's disease, and severe Alzheimer's disease. Each state is replicated in both community and institutional care settings, and an additional state for death is included. Disease severity is based on the CDR-SB with health states defined according to O'Bryant et al 2008. The modelled population was based on Core Clarity AD study participants, however the distribution of disease severity (i.e. proportion of patients living with MCI or mild Alzheimer's disease) was informed by clinical opinion from clinicians based in Ireland, as obtained by the Applicant.

The treatment effects captured in the cost-effectiveness model (CEM) consist of treatment-specific transition probabilities between Alzheimer's disease severity states, which lead indirectly to treatment effects on the outcomes of HRQoL, institutionalisation, and death. Transition probabilities between MCI, mild Alzheimer's disease, and moderate Alzheimer's disease, up to month 48 were estimated by fitting parametric multistate survival models to patient-level transition data from Core Clarity AD and the Clarity AD OLE. External data sources were used to estimate other transition probabilities in the CEM including transitions to severe Alzheimer's disease, transitions occurring after month 48, and health state-specific probabilities of institutionalisation and death. The Review Group noted a substantial difference between the resulting predictions of health state occupancy and observed health state occupancy in Core Clarity AD and the Clarity AD OLE. Despite extensive investigations, a clear rationale for the discrepancy could not be determined. The magnitude of these differences cast doubt upon the suitability of the submitted CEM for decision-making. Due to

this major limitation, the cost-effectiveness analysis presented under NCPE preferred assumptions is regarded as exploratory only.

Adverse events considered the proportion of participants experiencing an AESI; specifically, infusion related reactions, ARIA-E, and ARIA-H, in Core Clarity AD. This underestimated the incidence of ARIA-E and ARIA-H, given that these had also been reported in Clarity AD OLE.

HRQoL was captured in the model using health state-specific utility values, with additional disutilities applied to capture the impact of adverse events and institutionalisation. Utility and disutility values were derived from Clarity AD and the literature. Disutility due to TEAEs may be underestimated due to limitations associated with modelling of AESIs. Costs and resources included were drug acquisition and administration costs, monitoring, direct medical and non-medical costs, diagnosis, and genetic testing, and management of TEAEs.

The Review Group identified a number of limitations in the Applicant's base case analysis. Some of these were addressed in the NCPE exploratory base case: the methods used to calculate certain transition probabilities in the CEM, the assumptions regarding the persistence of treatment effect following lecanemab discontinuation, the estimation of utility values, and the source of the intravenous administration cost for lecanemab. Despite these changes, considerable uncertainty remains due to the discrepancy between modelled and observed health state occupancy, which could not be resolved.

Results

Deterministic incremental cost-effectiveness ratios (ICERs) for lecanemab versus SoC generated under Applicant base case and NCPE exploratory base case assumptions, are presented in Table 1 and Table 2, respectively.

Table 1: Applicant base case incremental cost-effectiveness results ^{a,b}

Treatments	Total costs (€)	Total QALYs	Incremental costs (€)	Incremental QALYs	ICER (€/QALY)
SoC	23,053	4.31	-	-	-
Lecanemab	96,710	4.84	73,656	0.53	139,566

ICER: Incremental cost-effectiveness ratio; **QALYs:** Quality Adjusted Life Years; **SoC:** Standard of care.

^a Corresponding probabilistic ICER using 1,000 iterations =€140,528/QALY. Figures in the table are rounded, and so calculations may not be directly replicable. Discount rate of 4% applied to costs and outcomes.

Table 2: NCPE exploratory base case incremental cost-effectiveness results^a

Treatments	Total costs (€)	Total QALYs	Incremental costs (€)	Incremental QALYs	ICER (€/QALY)
SoC	23,184	4.36	-	-	-
Lecanemab	112,631	4.75	89,447	0.39	231,128

ICER: Incremental cost-effectiveness ratio; **QALYs:** Quality Adjusted Life Years; **SoC:** Standard of care.

^a Corresponding probabilistic ICER using 1,000 iterations =€228,726/QALY. Figures in the table are rounded, and so calculations may not be directly replicable. Discount rate of 4% applied to costs and outcomes.

Sensitivity analysis

The most influential change in the NCPE exploratory base case was the source used for administration costs. The CEM was sensitive to the choice of utility values (i.e. values obtained from the trial participant or from their proxy [carer]), the baseline proportions of patients with MCI and mild Alzheimer's disease, the methods used to calculate transition probabilities, and the assumptions regarding the persistence of treatment effect following lecanemab discontinuation.

Under both the Applicant and NCPE adjusted base case assumptions, the probability of cost-effectiveness of lecanemab, versus SoC, at the willingness-to-pay thresholds of €45,000 per QALY and €20,000 per QALY was 0%. The Review Group conducted a Price-ICER analysis under the NCPE exploratory base case. Cost-effectiveness could not be achieved even under the assumption of a 100% discount on the price to wholesaler.

A scenario analysis was conducted which considered the carers' self-reported utilities, in addition to the patients' utilities, productivity loss, and unpaid carer costs. In these scenarios, the ICER still exceeded the €20,000 per QALY and €45,000 per QALY thresholds.

4. Budget impact of lecanemab

The price to wholesaler of one vial of lecanemab 200mg or 500mg (pack size: 1) is €310 and €615, respectively. The cost per patient per year is estimated to be €25,764 (including VAT) when a 93.65% compliance rate (from Clarity AD OLE), is considered. Where 100% compliance is assumed, the cost per patient per year is estimated to be €27,511 (including VAT). In the budget impact analysis, it was assumed that 12.88% of patients discontinue lecanemab each year, as informed by the Clarity AD OLE.

The Applicant predicted the eligible population as 2,905 patients in Year One, increasing to 3,353 in Year Five. The drug budget impact of lecanemab presented is constrained by capacity for treatment, assumed as 1% in Year One, increasing to 10% in Year Five of the eligible population. Thus, it was estimated that 29 patients would be treated with lecanemab in Year One, rising to 109 patients in Year Five. The resulting cumulative five-year net drug budget impact of lecanemab was estimated to be €18.6 million (including VAT).

A scenario increased capacity to 2% in Year One, increasing to 20% in Year Five. The resulting cumulative five-year net drug budget impact was €41.0 million (including VAT).

The Applicant did not consider any wider healthcare costs in their budget impact analysis. The Review Group acknowledge that treatment with lecanemab will incur additional costs for testing, administration, monitoring, and additional healthcare professional care costs, relative to the current SoC. Consideration should be given to the potential impact of lecanemab on demand for existing testing, administration and MRI facilities and the requirement for specialist care.

5. Patient Organisation Submission

A patient organisation submission was received from the Alzheimer Society of Ireland. This submission will form part of the information that the HSE considers when making their drug funding decision.

6. Conclusion

The NCPE recommends that lecanemab for the treatment of adult patients, with a clinical diagnosis of Early Alzheimer's disease (mild cognitive impairment or mild dementia due to Alzheimer's disease), who are APOE ε4 non-carriers or heterozygotes with confirmed amyloid pathology, not be considered for reimbursement.

The generalisability of Clarity AD, to clinical practice in Ireland, is limited. The short-term clinical evidence, for this indication, is derived from post hoc analysis and exploratory analysis from Core Clarity AD. Also, the long-term comparative evidence is derived from

matching single arm trial data to an external cohort. Subgroup analysis, from Clarity AD, indicated that lecanemab is more effective than placebo at reducing amyloid burden. However, a reduction in amyloid burden is not a validated surrogate for clinical benefit. In Clarity AD, ARIA occurred more frequently and with greater severity, in the participants who were on lecanemab. There were a number of limitations in the Applicant CEM that could not be addressed in the NCPE exploratory base case.

Lecanemab is not cost effective, for this indication at any price to wholesaler. At the time of this report, the Review Group note that seven out of eight national HTA bodies, that have assessed lecanemab, have recommended that lecanemab not be reimbursed for this indication.

*Next steps: The NCPE Assessment Report and recommendation and Patient Organisation submission, will be considered by the HSE when making their decision on reimbursement, while also having regard to the criteria specified in the Health (Pricing and Supply of Medical Goods) Act 2013.

Further information on this process may be found [here](#).