

Cost-Effectiveness of Lecanemab for Individuals With Early-Stage Alzheimer Disease

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Study Question

Is lecanemab cost-effective compared with the current standard of care for individuals with early-stage Alzheimer disease (AD)?

What Is Known and What This Paper Adds?

Lecanemab (Leqembi) was approved by the US Food and Drug Administration for the treatment of mild cognitive impairment or mild dementia due to AD, but its adverse effects, together with its modest clinical impact, have heightened interest and scrutiny of its cost and cost-effectiveness. Previous studies of cost-effectiveness of lecanemab assumed optimistic long-term benefits and failed to address the attendant costs of diagnostic testing (including PET, CSF or plasma assays) for early detection of AD that is required for lecanemab to work. Furthermore, it is unknown how restricting lecanemab treatment to *APOE* ϵ 4 noncarriers or heterozygous patients (“targeted treatment”), rather than offering treatment to individuals regardless of *APOE* ϵ 4 status, may affect lecanemab’s cost-effectiveness. This study’s results showed that neither targeted lecanemab treatment nor treatment unrestricted by *APOE* ϵ 4 genotype is cost-effective vs standard of care alone, regardless of the test used to diagnose patients with early-stage AD. They also showed, however, that a CSF assay followed by targeted treatment would become cost-effective if lecanemab is priced below \$5,100 per year.

Methods

This Markov modelling study compared 7 alternative test-treat-target strategies defined by combinations of testing approaches (PET, CSF, or plasma assays), treatment strategies (standard of care [SoC] alone or lecanemab in addition to SoC), and treatment targeting (targeted to patients with *APOE* ϵ 4 non-carrier or heterozygous status or unrestricted by *APOE* ϵ 4 genotype) for patients with characteristics largely mirroring the CLARITY AD trial. Specifically, strategy 1 reflected the SoC. Based on the CLARITY AD trial, we assumed that 53% of individuals in SoC with mild cognitive impairment or mild dementia received cholinesterase inhibitors (donepezil). Over time, patients with AD progressed to moderate dementia and received donepezil and a glutamate receptor antagonist (memantine) while those who progressed to severe dementia received memantine alone. Strategies 2–4 (“PET/CSF/Plasma + lecanemab to all,” hereafter) involved testing for AD using PET, CSF, or plasma (+ confirmatory PET if plasma test is positive) assays. In these strategies, all patients with a positive

AD diagnosis underwent treatment with lecanemab (intravenously at a dose of 10 mg/kg biweekly) in addition to SoC. Strategies 5–7 (“PET/CSF/Plasma + targeted lecanemab,” hereafter) were similar to strategies 2–4 except that among patients with a positive AD diagnosis, only patients with non-carrier or heterozygote *APOE* ϵ 4 genotype status received lecanemab in addition to SoC.

Data on accuracy of the 3 tests were obtained from previous studies while efficacy of lecanemab (measured by changes in CDR-SB scores) and risk of amyloid-related imaging abnormalities was based on the CLARITY AD trial. As drug efficacy data were available only for the 18-month trial duration, in the base case analysis, we extrapolated the drug’s effects beyond 18 months based on trends observed during months 12–18 in the CLARITY AD trial. Except for the SoC, each strategy involved the cost of AD testing and cost of treatment with lecanemab. Costs were estimated from the third-party payer perspective and were obtained from published sources. Effectiveness was measured in Quality Adjusted Life Years (QALYs). We estimated the total costs and QALYs of each strategy. A strategy was considered cost-effective relative to another if its incremental cost-effectiveness ratio (ICER) was below the conventional willingness-to-pay (WTP) threshold of \$100,000 per QALY. A strategy was dominated if it cost more and was less effective than another strategy (i.e., strongly dominated) or a combination of other strategies (weakly dominated).

Results and Study Limitations

Among the 7 strategies considered, SoC was the most cost-effective (Table). Strategies involving lecanemab treatment to all individuals with AD were dominated by strategies involving targeted lecanemab treatment. The targeted treatment not only cost \$6,870–\$8,780 less than treating all individuals with AD but also offered 0.03–0.05 additional QALYs. In addition, strategies involving AD testing with the plasma assay before lecanemab treatment were dominated. Among the 3 remaining undominated strategies (SoC, “CSF + targeted lecanemab” and “PET + targeted lecanemab”), SoC was the least costly but also the least effective. “CSF + targeted lecanemab” cost \$76,770 more than SoC but yielded only 0.27 additional QALYs, resulting in an ICER of \$287,280/QALY. Meanwhile, “PET + targeted lecanemab” cost \$5,540 more than “CSF + targeted lecanemab” and yielded 0.01 additional QALYs, leading to an ICER of

Table Base Case Cost-Effectiveness Results

Strategy	Cost (US\$)	Incremental cost (US\$)	Effectiveness (QALYs)	Incremental effectiveness (QALYs)	ICER (US\$/QALY)
SoC	190,123		5.58		
Plasma + targeted lecanemab	253,629	63,506	5.80	0.21	Weakly dominated
Plasma + lecanemab to all	260,509	6,880	5.77	-0.03	Strongly dominated
CSF + targeted lecanemab	266,896	76,773	5.85	0.27	287,284
PET + targeted lecanemab	272,433	5,537	5.86	0.01	475,336
CSF + lecanemab to all	275,467	3,034	5.81	-0.05	Strongly dominated
PET + lecanemab to all	281,214	8,781	5.82	-0.04	Strongly dominated

Abbreviation: ICER = incremental cost-effectiveness ratio; QALYs = Quality Adjusted Life Years; SoC = standard of care.

\$475,340/QALY. These ICERs exceeded the WTP threshold of \$100,000 per QALY gained. Our results were robust to several sensitivity analyses including accounting for caregiver costs and disutilities, using alternative disease progression rates and assumptions on long-term efficacy of lecanemab, and accounting for risk of death from lecanemab.

Our study has some limitations. First, the data on AD progression rates for SoC and lecanemab groups and the efficacy and risk of adverse events with lecanemab were only available for an 18-month period. However, extensive sensitivity analyses using alternative data on AD progression rates and alternative scenarios for long-term efficacy of lecanemab yielded very similar results. Second, our study relied on data from the CLARITY AD trial that studied a relatively younger, predominantly White population than that seen in real-world

clinical settings in the United States and other countries. It will be worthwhile to revisit the cost-effectiveness of lecanemab in other clinical contexts as more real-world data become available. Finally, our findings are intended to inform decision-making at the population health level and do not necessarily reflect the clinical benefits and economic value that individual patients may derive from lecanemab. As efficacy of lecanemab varies across patients, patients may choose lecanemab treatment based on faith that they too will receive tangible benefits similar to those observed in the clinical trial. Such faith-based expectations, though very powerful, could not be quantified and captured within our analyses.

Study Funding and Competing Interests

This study received no targeted funding. Some authors report competing interests. Go to [Neurology.org/N](https://www.neurology.org/N) for full disclosures.