

KEY FINDINGS

Intervention	Comparator	Evidence Rating	Annual WAC*	Annual Health-Benefit Price Benchmark	Change from Annual Price to Reach Threshold Price
Lecanemab (Leqembi, Eisai Co., Ltd)	Supportive care only	Promising but Inconclusive (P/I)	\$26,500	\$8,900-\$21,500	19%-66%

* Wholesale Acquisition Cost

“Individuals and families dread Alzheimer’s disease, and the first therapy that effectively halts or reverses dementia will warrant a very high price in the US health system. Current evidence strongly suggests that lecanemab mildly slows the loss of cognition in patients with early Alzheimer’s disease. However, given the risks of brain swelling and bleeding, particularly when lecanemab is used outside of clinical trials, our report concluded that significant uncertainties remain as to whether the average benefits of lecanemab will exceed its risks. A majority of the California Technology Assessment Forum was clearly unconvinced that the current evidence adequately demonstrates that lecanemab provides a net benefit to patients. In addition, using the best current data from the clinical trials, at its announced list price lecanemab exceeds typical thresholds for cost-effectiveness and, given the large number of patients with Alzheimer’s disease, it is particularly important that therapies for Alzheimer’s disease be priced in line with their value to patients.”

– ICER’s Chief Medical Officer, David Rind, MD

THEMES AND RECOMMENDATIONS

- All stakeholders have a responsibility and an important role to play in ensuring that new treatment options for patients with AD are introduced in a way that addresses the impact on health inequities. This includes, for example, fair pricing according to value assessments from independent analysts to avoid financial toxicity, coverage of PET scans and ApoE ε4 genotype testing, and increasing capacity for screening, diagnosis, and treatment, particularly in rural or underserved areas.
- Manufacturers of future treatments for Alzheimer’s disease should follow the example set by the manufacturer of lecanemab by sharing a transparent, explicit justification for their pricing. However, pricing should be based on independent – not industry-funded - assessments of the drug.
- Manufacturers should release all patient-level data in order to help patients, clinicians, researchers, and regulators to understand more about the link between amyloid reduction and cognitive outcomes. Failure to do so will impair scientific advances about the mechanisms underlying AD.

Clinical Analyses

KEY CLINICAL BENEFITS STUDIED IN CLINICAL TRIALS

Alzheimer's disease (AD) is a fatal neurodegenerative brain disease characterized by the progressive accumulation of beta-amyloid protein plaques and neurofibrillary tangles; these are hypothesized to damage neurons and lead to the loss of cognition and physical functioning. AD affects more than six million people in the United States (US), with more women than men affected and Black Americans at a higher risk of developing the disease. Symptoms of AD include impairment of memory, language, executive function, and visuospatial function that affects one's ability to care for themselves. People living with AD require a substantial amount of caregiving, and eventually may require around-the-clock in-home or institutional care. Caregivers, most often unpaid family members and friends, can suffer significant negative physical, financial, and emotional outcomes from the strain of caregiving.

Current treatment of AD is focused on supportive care, including treatment of dementia symptoms with medications that do not alter the course of the disease. Because of the devastating burden of AD, there is a great need for disease-modifying treatments (DMTs) that slow or stop progression of the disease. Although aducanumab (Aduhelm™, Biogen) was granted accelerated approval for the treatment of AD in June 2021, there remain substantial uncertainties about its benefits and harms. In this report, we focus on lecanemab (Leqembi™, Eisai Co., Ltd), an anti-amyloid monoclonal antibody approved by the FDA on January 6, 2023, also under an accelerated pathway based on removal of amyloid plaques. A prior version of this report included a review of donanemab. Due to the manufacturer receiving a Complete Response Letter from the FDA on January 19, 2023 for donanemab's accelerated approval biologics license application, we have removed donanemab from the report.

Lecanemab was evaluated in a Phase III randomized clinical trial, CLARITY AD. The trial randomized 1,795 participants with early AD (i.e., mild cognitive impairment [MCI] or mild dementia due to AD) to a biweekly 10 mg/kg intravenous infusion of lecanemab or placebo. The primary clinical outcome was change in mean score on the Clinical Dementia Rating Scale – Sum of Boxes (CDR-SB). At 18 months, the lecanemab-treated group showed a statistically significant 27% slowing of cognitive decline compared with placebo, representing an average difference of about 0.5 points on the 18-point CDR-SB scale. Analyses of secondary endpoints, including other cognitive measures and patient and caregiver quality of life consistently favored the lecanemab-treated group. Among participants treated with lecanemab, 21.5% experienced amyloid related imaging abnormalities with edema/effusion (ARIA-E), ARIA-hemorrhage or superficial siderosis (ARIA-H), or both compared with 9.5% in the placebo group, and 3.5% of patients in the lecanemab group experienced symptomatic ARIA-E or -H compared with 0.2% in the placebo group.

We remain uncertain that amyloid removal is an appropriate surrogate outcome for clinical benefit and instead look to the clinical outcomes found in randomized trials. However, there is disagreement among experts about the clinical meaningfulness of the magnitude of change in CDR-SB in the lecanemab trial. We also remain concerned that real world ARIA occurrences and consequences may be more severe if, as expected, monitoring MRIs are not as frequent as in the clinical trial, the patient population treated differs from the trial population, and clinicians are less expert than those who participated in the randomized trial.

Clinical Analyses

In aggregate, the net health benefits of lecanemab in patients with early AD may be small or even substantial, but there remains a possibility of net harm from ARIA. We rate treatment with lecanemab in MCI

due to AD or mild AD as “Promising but Inconclusive” (P/I).

LONG-TERM COST EFFECTIVENESS

We estimated the lifetime cost effectiveness of lecanemab in addition to supportive care as compared to supportive care alone from a health care sector perspective (i.e., focusing on the direct medical care costs and health outcomes of the patient) and a modified societal perspective (i.e., including patient productivity impacts, caregiver time spent caregiving, caregiver quality of life, and caregiver direct medical costs). From both perspectives, lecanemab’s annual

price of \$26,500 exceeded commonly used cost-effectiveness thresholds. ICER’s Health Benefit Price Benchmark (HBPB) for lecanemab is \$8,900 to \$21,500, requiring a 66% to 19% discount from lecanemab’s wholesale acquisition cost (WAC).

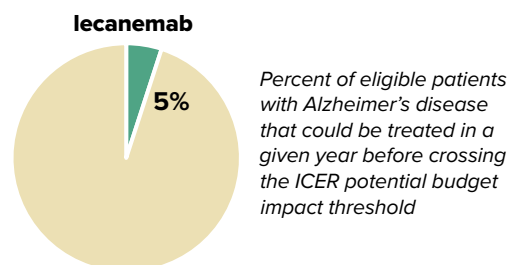
Economic Analyses

POTENTIAL BUDGET IMPACT

Assuming lecanemab’s current wholesale acquisition cost, approximately 5% of the roughly 1.4 million US patients eligible for AD treatment that targets beta-amyloid could be treated within five years without crossing the Institute for Clinical and Economic Review potential budget impact threshold of \$777 million per year.

Therefore, at current pricing and projected uptake that is likely to exceed 5% of the eligible population, lecanemab’s short-term potential budget impact exceeds our threshold. Additional efforts at achieving affordability and access must be considered, thus we are issuing an access and affordability alert.

The purpose of an ICER access and affordability alert is to signal to stakeholders and policy makers that the amount of added health care costs associated with a new service may be difficult for the health system to absorb over the short term without displacing other needed services, creating pressure on payers to sharply restrict access, or causing rapid growth in health care insurance costs that would threaten sustainable access to high-value care for all patients.



Public Meeting Deliberations

VOTING RESULTS

For adults with early Alzheimer's disease (i.e., Mild Cognitive Impairment due to Alzheimer's disease and mild Alzheimer's dementia):

- A majority of panelists (12-3) found that current evidence is **not adequate** to demonstrate a net health benefit of lecanemab when compared to supportive care alone.

During their deliberations, panel members also weighed lecanemab's potential benefits and disadvantages beyond its direct health effects, and broader contextual considerations. Voting highlighted the following as particularly important for payers and other policymakers to note:

- The acuity of need for treatment of individual patients based on short-term risk of death or progression to permanent disability;
- The magnitude of the lifetime impact of Alzheimer's disease on individual patients is substantial;
- Patients' ability to achieve major life goals related to education, work, or family life;

- Caregivers' quality of life and/or ability to achieve major life goals related to education, work, or family life.

Lecanemab has been approved by the FDA and has a list price of \$26,500 per year. ICER has calculated a health-benefit price benchmark (HBPB) for lecanemab to be between \$8,900 – \$21,500 per year.

After reviewing the clinical evidence and considering the treatments' other potential benefits, disadvantages, and contextual considerations noted above, the CTAF evaluated the long-term value of lecanemab at its current pricing:

- A majority (15-0) of panelists found that that lecanemab at its current pricing represents **"low"** long-term value for money.

About ICER

The Institute for Clinical and Economic Review ([ICER](#)) is an independent nonprofit research institute that produces reports analyzing the evidence on the effectiveness and value of drugs and other medical services. ICER's reports include evidence-based calculations of prices for new drugs that accurately reflect the degree of improvement expected in long-term patient outcomes, while also highlighting price levels that might contribute to unaffordable short-term cost growth for the overall health care system.

ICER's reports incorporate extensive input from all stakeholders and are the subject of public

hearings through three core programs: the California Technology Assessment Forum ([CTAF](#)), the Midwest Comparative Effectiveness Public Advisory Council ([Midwest CEPAC](#)) and the New England Comparative Effectiveness Public Advisory Council ([New England CEPAC](#)). These independent panels review ICER's reports at public meetings to deliberate on the evidence and develop recommendations for how patients, clinicians, insurers, and policymakers can improve the quality and value of health care.

For more information about ICER, please visit ICER's website (www.icer.org).