PRIOR AUTHORIZATION POLICY

POLICY: Neurology – Leqembi Prior Authorization Policy
- Leqembi™ (lecanemab-irmb intravenous infusion – Eisai/Biogen)

REVIEW DATE: 01/25/2023

OVERVIEW

Leqembi, an amyloid beta-directed antibody, is indicated for the **treatment of Alzheimer's disease**.[1]

This indication is approved under accelerated approval based on reduction in amyloid beta plaques observed in patients treated with Leqembi.[1] Continued approval for this indication may be contingent upon verification of clinical benefit in a confirmatory trial.

Disease Overview

An estimated 6.5 million Americans ≥ 65 years of age are living with Alzheimer's dementia in 2022, with 73% of these people ≥ 75 years of age.[2] The number and proportion of older adults who have mild cognitive impairment due to Alzheimer's disease is difficult to estimate; however, a rough approximation suggests that 5 million older Americans may have mild cognitive impairment due to Alzheimer's disease. People with mild cognitive impairment due to Alzheimer's disease have biomarker evidence of brain changes due to the disease in addition to subtle problems with memory and thinking. Biomarker evidence includes abnormal levels of amyloid beta as evidenced on positron emission tomography (PET) scans and in analysis of cerebrospinal fluid, and decreased metabolism of glucose as shown on PET scans. These cognitive problems may be noticeable to the individual family members and friends, but not to others, and they do not interfere with the person's ability to carry out everyday activities. The mild changes in cognitive abilities occur when the brain can no longer compensate for the damage and death of nerve cells due to Alzheimer's disease. Among those with mild cognitive impairment, about 10% to 15% develop dementia each year. Approximately one-third of people with mild cognitive impairment develop Alzheimer's dementia within 5 years.

Clinical Efficacy

The current Leqembi efficacy information is insufficient to determine if the medication demonstrates any clinically meaningful benefits. In the absence of additional clinical trials, there is not enough information to support approval.

POLICY STATEMENT

Due to safety concerns and the lack of clinically significant efficacy data, **approval is not recommended** for Leqembi. The current Leqembi efficacy information is insufficient to determine if the medication demonstrates any clinically meaningful benefits; whereas, safety concerns have been demonstrated in clinical trials. In the absence of additional clinical trials, there is not enough information to support approval.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA
None.

CONDITIONS NOT RECOMMENDED FOR APPROVAL
Coverage of Leqembi is not recommended in the following situations:

1. **Alzheimer's Disease.** Due to the lack of clinically significant efficacy data, approval is not recommended for Leqembi. The prescribing information for Leqembi states that it was approved under accelerated approval based on reduction in amyloid beta plaques observed in patients treated with Leqembi.[1]

   The efficacy of Leqembi for accelerated approval was evaluated in one Phase IIb randomized, double-blind, placebo-controlled, multicenter, pivotal study in patients with mild cognitive impairment due to Alzheimer's disease and mild Alzheimer's disease dementia (n = 854).[3] In the Phase IIb study, the primary endpoint, change from baseline at 12 months on Alzheimer's Disease Composite Score (ADCOMS), reached a 64% probability of being better than placebo with 25% less decline at 12 months, missing the pre-specified 80% probability threshold. However, the secondary endpoint of least squares mean change from baseline in amyloid PET Standard Uptake Value ratio (SUVr) at 18 months was significantly reduced for all dosage regimens, including Leqembi 10 mg/kg once every 2 weeks ($P < 0.001$ for all doses).

   Additionally, one Phase III, randomized, double-blind, placebo-controlled, multicenter study (CLARITY AD) was conducted in patients with mild cognitive impairment due to Alzheimer's disease and mild Alzheimer's disease dementia (n = 1,795).[4] CLARITY AD provided the basis for a supplemental Biologics License Application to the FDA for potential approval under the traditional pathway. In CLARITY AD, the adjusted mean change from baseline at Week 78 in the Clinical Dementia Rating-Sum of Boxes (CDR-SB) score demonstrated slowing of clinical progression for Leqembi vs. placebo (treatment difference -0.45; $P < 0.001$ [scores range from 0 to 18, with higher scores indicating greater disease severity]). However, this slowing of progression did not achieve clinical significance.[5]

   Leqembi can cause amyloid related imaging abnormalities-edema (ARIA-E) and amyloid related imaging abnormalities-hemosiderin deposition (ARIA-H), which includes microhemorrhage and superficial siderosis, which can be observed on magnetic resonance imaging (MRI).[1] A recent (within 1 year) MRI of the brain should be obtained prior to initiating treatment with Leqembi. The safety of Leqembi has not been evaluated in patients with prior cerebral hemorrhage > 1 cm in greatest diameter, more than four microhemorrhages, superficial siderosis, evidence of vasogenic edema, evidence of cerebral contusion, aneurysm, vascular malformation, infective lesions, multiple lacunar infarcts or stroke involving a major vascular territory, and severe small vessel or white matter disease. Enhanced clinical vigilance for asymptomatic amyloid related imaging abnormalities (ARIA) is recommended during the first seven doses of treatment with Leqembi, particularly during titration, because the majority of ARIA was observed during this time. MRIs of the brain should be obtained prior to the fifth infusion, seventh, and 14th infusion of Leqembi to evaluate for the presence of asymptomatic ARIA. There is no experience in patients who continued dosing through symptomatic ARIA-E or through asymptomatic, but radiographically severe, ARIA-E. There is limited experience in patients who continued dosing through asymptomatic but radiographically mild to moderate ARIA-E. There are limited data in dosing patients who experienced recurrent ARIA-E.

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Leqembi™ intravenous infusion [prescribing information]. Nutley, NJ: Eisai; January 2023.
2. Alzheimer's Association. Alzheimer's disease facts and figures-2022. Available at: https://www.alz.org/media/Documents/alzheimers-facts-and-figures.pdf. Accessed on January 16, 2023.
3. Swanson CJ, Zhang Y, Dhadda S, et al. A randomized, double-blind, phase 2b proof-of-concept clinical trial in early Alzheimer's disease with lecanemab, an anti-Aβ protofibril antibody. *Alzheimers Res Ther*. 2021;13(1):80.
4. van Dyck CH, Swanson CJ, Aisen P, et al. Lecanemab in early Alzheimer's disease. *N Engl J Med*. 2023;388(1):9-21.
5. Andrews JS, Desai U, Kirson NY, et al. Disease severity and minimal clinically important differences in clinical outcome assessments for Alzheimer's disease clinical trials. *Alzheimers Dement*. 2019;5:354-363.