Effective Date **1/15/2024**
Coverage Policy Number **IP0547**

Neurology – Leqembi (lecanemab-irmb)

Table of Contents

Related Coverage Resources

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Overview

This policy addresses the usage of lecanemab (Leqembi™).

Conditions Not Covered

The use of lecanemab-irmb (Leqembi) intravenous infusion is considered to be experimental, investigational, or unproven due to insufficient data establishing safety, efficacy, and improved health outcomes for any condition.

- **Alzheimer's Disease.** 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 traditional FDA on July 6, 2023. 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.

Coding Information

1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Experimental/Investigational/Unproven:

HCPCS Codes	Description
J0174	Injection, lecanemab-irmb, 1 mg

Background

OVERVIEW

Leqembi, an amyloid beta-directed antibody, is indicated for the treatment of Alzheimer's disease.[1] Treatment with Leqembi should be initiated in patients with mild cognitive impairment or mild dementia stage of disease, the population in which treatment was initiated in clinical trials.

Disease Overview

An estimated 6.7 million Americans ≥ 65 years of age are living with Alzheimer's dementia in 2023, 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 to 7 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 15% develop dementia after 2 years. 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.

Dosing/Administration
The recommended dose of Leqembi is 10 mg/kg administered as an intravenous (IV) infusion every 2 weeks.

References

1. Leqembi® intravenous infusion [prescribing information]. Nutley, NJ: Eisai; July 2023.
2. Alzheimer's Association. Alzheimer's disease facts and figures-2023. Available at: https://www.alz.org/media/Documents/alzheimers-facts-and-figures.pdf. Accessed on January 22, 2024.
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

Revision History

Type of Revision	Summary of Changes	Approval Date
New		11/28/2023
Selected Revision	Coding updated	1/15/2024