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Section:	Prescription Drugs	**Effective Date:**	April 1, 2023
Subsection:	Central Nervous System Drugs	**Original Policy Date:**	January 27, 2023
Subject:	Leqembi	**Page:**	1 of 5

Last Review Date: March 10, 2023

Leqembi

Description

Leqembi (lecanemab-irmb)

Background
Leqembi (lecanemab-irmb) is a humanized immunoglobulin gamma 1 (IgG1) monoclonal antibody directed against aggregated soluble and insoluble forms of amyloid beta. The accumulation of amyloid beta plaques in the brain is a defining pathophysiological feature of Alzheimer's disease (AD). Leqembi reduces amyloid beta plaques (1).

Regulatory Status
FDA-approved indication: Leqembi is an amyloid beta-directed antibody indicated for the treatment of Alzheimer's disease (1).

Leqembi has warnings regarding amyloid related imaging abnormalities (ARIA) and infusion-related reactions. A baseline brain magnetic resonance imaging (MRI) should be obtained prior to initiating treatment. An MRI should be obtained prior to the 5th, 7th, and 14th infusions (1).

In Study 1 (NCT 01767311), the age of patients ranged from 50 to 90 years (1). Clinically, AD can be categorized into two phenotypes based on the ages of onset: early-onset AD (EOAD; <65 years) and late-onset AD (LOAD; >65 years), of which LOAD is the more common form worldwide. The proportion of EOAD in all AD cases is between 5% and 10%. Presenilin 1 (*PSEN1*), presenilin 2 (*PSEN2*), and amyloid precursor protein (*APP*) are mostly associated with autosomal dominant forms of EOAD. Apart from genetic factors, mutations are environmentally related. Genetic–environmental interactions may be caused by variation in the age of onset,

neuropathological patterns, and disease duration. To date, more than 200 mutations have been described in *PSEN1* throughout the world, but mutations in *PSEN2* are extremely rare (2).

The safety and effectiveness of Leqembi in pediatric patients have not been established (1).

Related policies
Aduhelm

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Leqembi may be considered **medically necessary** in patients 50 years of age or older with Alzheimer's disease (AD), or less than 50 years of age with early onset AD; and if the conditions indicated below are met.

Leqembi may be considered **investigational** for patients less than 50 years of age and for all other indications.

Prior-Approval Requirements

Diagnosis

Patient must have the following:

Alzheimer's disease (mild cognitive impairment or mild dementia stage of disease)

AND ALL of the following:

1. 50 years of age or older **OR** if less than 50 years of age, patient has a genetic mutation in amyloid precursor protein (APP), presenilin-1 (PSEN1), or presenilin-2 (PSEN2), or other clinical documentation to support early onset AD
2. Positive amyloid Positron Emission Tomography (PET) scan, confirming the presence of amyloid pathology
3. Other causes of dementia (e.g., Lewy body dementia) have been ruled out
4. Patient has mild cognitive impairment as confirmed by **ONE** of the following:
    a. Clinical Dementia Rating (CDR)-Global score of 0.5 or 1.0

(e.g., *https://www.aafp.org/dam/AAFP/documents/patient_care/cognitive_care_kit/cdr-chart.pdf*)

b. Mini-Mental State Examination (MMSE) score of 22 to 30
(e.g., https://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/cogimp-smmse.pdf)

5. A recent (within one year) brain MRI has been obtained or will be obtained prior to initiating treatment with Leqembi
6. Prescriber agrees to monitor for signs and symptoms of amyloid related imaging abnormalities (ARIA) using MRI as clinically appropriate
7. **NO** neurological or other medical condition, other than AD, that may significantly contribute to cognitive decline
8. **NO** medical conditions, other than AD, likely to increase significant adverse events

Prior – Approval *Renewal* Requirements

Diagnosis

Patient must have the following:

Alzheimer's disease (mild cognitive impairment or mild dementia stage of disease)

AND ALL of the following:

1. 50 years of age or older **OR** if less than 50 years of age, patient has a genetic mutation in amyloid precursor protein (APP), presenilin-1 (PSEN1), or presenilin-2 (PSEN2), or other clinical documentation to support early onset AD
2. Reduction in brain amyloid beta plaque as confirmed by PET scan
3. Patient continues to have mild cognitive impairment as confirmed by stabilization in score in **ONE** of the following:
   a. Clinical Dementia Rating (CDR)-Global score of 0.5 or 1.0
   (e.g., *https://www.aafp.org/dam/AAFP/documents/patient_care/cognitive_care_kit/cdr-chart.pdf*)
   b. Mini-Mental State Examination (MMSE) score of 22 to 30
   (e.g., https://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/cogimp-smmse.pdf)
4. Prescriber agrees to continue monitoring for signs and symptoms of ARIA using MRI as clinically appropriate
5. **NO** neurological or other medical condition, other than AD, that may significantly contribute to cognitive decline

6. **NO** medical conditions, other than AD, likely to increase significant adverse events

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Leqembi (lecanemab-irmb) is a humanized immunoglobulin gamma 1 (IgG1) monoclonal antibody that reduces amyloid beta plaques in Alzheimer's disease. Patients should have a baseline MRI done prior to initiating therapy with Leqembi and prior to the 5th, 7th, and 14th infusions. The safety and effectiveness of Leqembi in pediatric patients have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Leqembi while maintaining optimal therapeutic outcomes.

References

1. Leqembi [package Insert]. Nutley, NJ: Eisai Inc.; January 2023.
2. Cai, Y., An, S. S., & Kim, S. (2015). Mutations in presenilin 2 and its implications in Alzheimer's disease and other dementia-associated disorders. *Clinical interventions in aging*, *10*, 1163–1172. https://doi.org/10.2147/CIA.S85808

Policy History

Date	Action
January 2023	Addition to PA

March 2023	Annual review. Per SME, clarified diagnosis to indicate Alzheimer's disease must be in the mild cognitive impairment or mild dementia stage of disease

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 10, 2023 and is effective on April 1, 2023.