lecanemab (Leqembi IQLIK®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO343

Description

Lecanemab (Leqembi, Leqembi IQLIK) is an amyloid beta-directed antibody available as an intravenously and a subcutaneously administered injection.

Length of Authorization

- Initial: Six months
- Renewal: Six months

Quantity Limits

Product Name	Indication	Dosage Form	Quantity Limit
lecanemab SC (Leqembi IQLIK)	Alzheimer's disease	360 mg/1.8mL autoinjector	7.2 mL (4 autoinjectors)/28 days
Provider Administered Agents*			
lecanemab IV (Leqembi)	Alzheimer's disease	200 mg/2mL vial 500 mg/5mL vial	Not applicable

**Medical drug that requires administration by a healthcare professional and is not available for self-administration by the member (considered one of the excluded classes under the prescription benefit).*

Initial Evaluation

I. **Lecanemab (Leqembi IQLIK)** may be considered medically necessary when the following criteria are met:
   A. Member has been established on lecanemab IV (Leqembi) therapy for at least 18 months; **AND**
   B. The request is for maintenance treatment with a subcutaneous formulation; **AND**
   C. Medication is not used in combination with another monoclonal antibody targeting Alzheimer's disease (e.g., donanemab [Kisunla]); **AND**
   D. A diagnosis of **mild cognitive impairment (MCI) due to Alzheimer's disease or mild Alzheimer's dementia** when the following are met:
      1. Positron Emission Tomography (PET) scan or cerebrospinal fluid (CSF) assessment confirming presence of amyloid pathology (e.g., hybrid ratios of Aβ 42/40, CSF p-tau 181/Aβ42, or CSF t-tau/Aβ42); **AND**
      2. Member has exhibited improvement or stability of cognitive and/or functional impairment following initial treatment as evidenced by objective scoring tools (e.g., MMSE, CDR-SB, MoCA, etc); **AND**
      3. Member has not progressed to moderate or severe Alzheimer's disease as evidenced by objective scoring tools (e.g., MMSE, CDR-SB, MoCA, etc); **AND**
      4. There is absence of unacceptable toxicity from the requested medication (e.g., ARIA-E, ARIA-H, intracerebral hemorrhage, severe hypersensitivity); **AND**

5. Provider attestation that member has not received any new medications that would increase risk for ARIA (e.g., tissue plasminogen activator use within time since last authorization, antiplatelets, anticoagulants); **AND**
6. There is a documented plan for safety monitoring (prescriber must document discussion of ARIA risk and plans for monitoring); **AND**
7. There is documentation confirming adherence to required MRI monitoring, and any ARIA-related imaging findings have been submitted; **AND**
8. Provider attestation that the member's cognitive impairment does not interfere with the ability to safely and reliably self-administer subcutaneous lecanemab (Leqembi-IQLIK), or member has a reliable, consistent caregiver who can administer the medication as scheduled

II. Lecanemab (Leqembi IQLIK) is considered investigational when used for all other conditions, including but not limited to:
   A. Other forms of dementia (e.g., vascular)
   B. Moderate-severe dementia associated with Alzheimer's disease

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Member has exhibited improvement or stability of cognitive and/or functional impairment on objective scoring tools (e.g., MMSE, CDR-SB, MoCA, etc); **AND**
IV. Member has not progressed to moderate or severe Alzheimer's disease as evidenced by objective scoring tools (e.g., MMSE, CDR-SB, MoCA, etc); **AND**
V. There is absence of unacceptable toxicity from the requested medication (e.g., ARIA-E, ARIA-H, intracerebral hemorrhage, severe hypersensitivity); **AND**
VI. Provider attestation that member has not received any new medications that would increase risk for ARIA (e.g., tissue plasminogen activator use within time since last authorization, antiplatelets, anticoagulants); **AND**
VII. There is a documented plan for safety monitoring (prescriber must document discussion of ARIA risk and plans for monitoring); **AND**
VIII. There is documentation confirming adherence to required MRI monitoring, and any ARIA-related imaging findings have been submitted; **AND**
IX. Provider attestation that the member's cognitive impairment does not interfere with the ability to safely and reliably self-administer subcutaneous lecanemab (Leqembi IQLIK), or member has a reliable, consistent caregiver who can administer the medication as scheduled.

Supporting Evidence

I. Lecanemab (Leqembi) has not been evaluated in combination with other anti-amyloid therapies. The safety and efficacy of combination treatment is unestablished.

II. Lecanemab (Leqembi) has been evaluated in patients with early Alzheimer's disease (AD). Specifically, in clinical trials patients were required to carry a diagnosis of mild cognitive impairment (MCI) due to AD or mild dementia due to AD. The diagnosis of AD is established through a clinical exam including comprehensive history, cognitive and functional assessments, along brain MRI to rule out alternative causes of cognitive decline and establish baseline risk for amyloid-related imaging abnormalities (ARIA). Biomarker testing, such as amyloid positron emission tomography (PET) or cerebrospinal fluid (CSF) Aβ/tau, may be used when additional confirmation is needed, and is required when evaluating eligibility for anti-amyloid therapies. Mild cognitive impairment is characterized by measurable cognitive decline without loss of independence while mild Alzheimer's dementia is associated with more prominent memory and functional impairments. Moderate-to-severe stages are marked by substantial cognitive and behavioral symptoms requiring full-time care.

III. Confirmation of amyloid pathology is required prior to administration of lecanemab (Leqembi) as clinical trials demonstrated safety and efficacy only in amyloid-positive early AD. Additionally, FDA labeling explicitly requires confirmation of amyloid pathology prior to initiating treatment ensuring that only patients with this AD subtype receive therapy. Lastly, lecanemab (Leqembi) is a monoclonal antibody specifically designed to bind to and clear aggregated amyloid-β from the brain. Its therapeutic effect depends on the presence of these plaques; therefore, treating individuals without amyloid pathology would provide no biologically plausible benefit.

IV. Amyloid-β (Aβ) positron emission tomography (PET) imaging and cerebrospinal fluid (CSF) biomarkers are well-established tools for the evaluation of Alzheimer's disease (AD). Aβ-PET imaging uses radiolabeled tracers that selectively bind to fibrillar Aβ, enabling direct visualization and quantification of amyloid deposits in the brain. This minimally invasive technique provides a regional assessment of cerebral Aβ burden. Cerebrospinal fluid biomarkers provide an indirect assessment of AD pathology by reflecting underlying biochemical changes associated with amyloid plaque formation and neuronal injury. Key CSF biomarkers used to detect Aβ pathology include the Aβ42/Aβ40 ratio and composite ratios that combine Aβ42 with tau measures, such as p-tau181/Aβ42 and t-tau/Aβ42. A reduced CSF Aβ42/Aβ40 ratio, together with elevated total tau and phosphorylated tau levels, represents the characteristic CSF biomarker profile of Alzheimer's disease.

V. Members are required to be established on lecanemab (Leqembi) IV and to experience observable cognitive or functional benefit without toxicities prior to switching to subcutaneous maintenance treatment. Members can switch to the SC formulation after being established on IV formulation for 18 months or more as that's when patients were allowed to transition in the open-label extension clinical trial. Safety and efficacy of transitioning to the SC formulation earlier in time has not been established. This transition should be initiated at one week following the last maintenance dose of the intravenous dosing regimen.

X. Lecanemab (Leqembi) was studied in one Phase 3, double-blind, placebo-controlled, 18-month study (CLARITY-AD) with a four-year open label extension (OLE) phase. The IV formulation was studied throughout the four-year period, while the SC formulation was studied as part of the OLE. The study included 1,795 patients randomized 1:1 to IV lecanemab (Leqembi) 10mg/kg or placebo once every 2 weeks. Patients were included if they were aged 50-90 years, had MCI due to AD with a global clinical dementia rating (CDR) score of 0.5 or mild AD with a global CDR score of 0.5 to 1, a CDR memory box score of ≥0.5, were amyloid positive as determined by Positron Emission Tomography (PET) or cerebrospinal fluid (CSF) measurement of t-tau/Aβ [1-42], and had an mini-mental state examination (MMSE) score ≥22 and ≤30. Patients were excluded if they had any major abnormal finding on the screening brain magnetic resonance imaging (MRI). The median age of patients was 72 years, 52% were women, 77% were White, 69% were ApoE ε4 carriers, 62% had MCI due to AD and 38% had mild dementia with 52% using medications for symptoms of AD. The primary endpoint was change from baseline at 18 months in the CDR-SB which was 1.21 vs 1.66 for lecanemab (Leqembi) vs placebo with a treatment difference of -0.45 $p<0.0001$. Key secondary endpoints included change from baseline at 18 months for amyloid PET and cognitive and functional assessments which also demonstrated statistically significant results. Efficacy data from the 48-month OLE demonstrates continued efficacy over time with mean change in CDR-SB in lecanemab (Leqembi) vs the Alzheimer's Disease Neuroimaging Initiative (ADNI) observational cohort of 1.74 and reducing the risk of progression to the next stage of disease by 34% (HR 0.661 [0.56, 0.78] $p<0.0001$). The data to support the SC formulation as maintenance treatment is available from PK/PD modeling studies that establish bioequivalence with IV as well as a human factor study which demonstrates that transitioning to the 360 mg SC weekly regimen is similar to continuing the IV 10 mg/kg biweekly dose in maintaining efficacy and biomarker response and is safe and effective for intended users.

XI. The most common reactions (≥5%) in the safety data of the double-blind, placebo-controlled period for IV lecanemab (Leqembi) vs placebo, were infusion-related reactions (26% vs 7%), amyloid-related imaging abnormalities with hemorrhage (ARIA-H) (14% vs 8%), amyloid-related imaging abnormalities with edema (ARIA-E) (13% vs 2%), headache (11% vs 8%), superficial siderosis of central nervous system (6% vs 3%), rash (6% vs 4%), nausea/vomiting (6% vs 4%). Severe adverse events occurred more frequently with lecanemab (Leqembi) than in placebo (14% vs 11%), with most common being infusion-related reactions (1.2% vs 0), ARIA-E (0.8% vs 0), atrial fibrillation (0.7% vs 0.3%), syncope (0.7% vs 0.1%), and angina pectoris (0.7% vs 0). Death was more commonly reported in placebo (0.8% vs 0.7%). The majority of ARIA-E events with lecanemab (Leqembi) were mild-moderate (91%), asymptomatic (78%), occurring in the first 3 months (71%), and resolving within 4 months after detection (81%). Symptomatic ARIA-E occurred in 2.8% of patients in the lecanemab (Leqembi) group. Commonly reported symptoms were headache, visual disturbance, and confusion. The incidence of isolated ARIA-H was 8.9% in lecanemab (Leqembi) vs 7.8% in placebo. The incidence of symptomatic ARIA-H in lecanemab (Leqembi) vs placebo was 0.7% vs 0.2%. The most common symptom was dizziness. Macrohemorrhage occurred in 5 of 898 patients (0.6%) and 1 patient of 897 (0.1%) in placebo. Isolated ARIA-H occurred throughout the trial. ARIA-H and ARIA-E were less common among ApoE noncarriers, with higher frequency among ApoE ε4 homozygotes than among ApoE ε4

heterozygotes. During the OLE period, there were 9 additional deaths with 3 occurring concurrently with ARIA or intracerebral hemorrhage. The overall rates for ARIA-E (14.7%) and ARIA-H (13.1%) increased with longer duration; however, rate of these adverse events over a standardized time (EAR) did not increase relative to placebo. The safety of the SC formulation was found to be similar to IV among the 49 patients that received it. Patients experienced mild-moderate localized and systemic injection-related reactions (e.g., erythema, swelling, rash, headache, fatigue, fever). Lecanemab (Leqembi) carries a black box warning for amyloid related imaging abnormalities including a higher risk among ApoE ε4 homozygotes. Contraindications include hypersensitivity and warnings and precautions include enhanced vigilance for ARIA during the first 14 weeks of treatment and in those with pretreatment microhemorrhages and/or superficial siderosis and infusion-related reactions.

VI. Lecanemab (Leqembi) has not been adequately studied in patients with moderate to severe Alzheimer's disease. Once patients progress to these stages, there is no clinical evidence to support continued treatment with lecanemab (Leqembi), and therapy should be discontinued. Moderate to severe Alzheimer's disease is generally defined as: MMSE: < 20–22, CDR SB: 9.5–18 MoCA: < 17.

VII. The most common reactions (≥5%) in the safety data of the double-blind, placebo-controlled period for IV lecanemab (Leqembi) vs placebo, were infusion-related reactions (26% vs 7%), amyloid-related imaging abnormalities with hemorrhage (ARIA-H) (14% vs 8%), amyloid-related imaging abnormalities with edema (ARIA-E) (13% vs 2%), headache (11% vs 8%), superficial siderosis of central nervous system (6% vs 3%), rash (6% vs 4%), nausea/vomiting (6% vs 4%). Severe adverse events occurred more frequently with lecanemab (Leqembi) than in placebo (14% vs 11%), with most common being infusion-related reactions (1.2% vs 0), ARIA-E (0.8% vs 0), atrial fibrillation (0.7% vs 0.3%), syncope (0.7% vs 0.1%), and angina pectoris (0.7% vs 0). Death was more commonly reported in placebo (0.8% vs 0.7%). The majority of ARIA-E events with lecanemab (Leqembi) were mild-moderate (91%), asymptomatic (78%), occurring in the first 3 months (71%), and resolving within 4 months after detection (81%). Symptomatic ARIA-E occurred in 2.8% of patients in the lecanemab (Leqembi) group. Commonly reported symptoms were headache, visual disturbance, and confusion. The incidence of isolated ARIA-H was 8.9% in lecanemab (Leqembi) vs 7.8% in placebo. The incidence of symptomatic ARIA-H in lecanemab (Leqembi) vs placebo was 0.7% vs 0.2%. The most common symptom was dizziness. Macrohemorrhage occurred in 5 of 898 patients (0.6%) and 1 patient of 897 (0.1%) in placebo. Isolated ARIA-H occurred throughout the trial. ARIA-H and ARIA-E were less common among ApoE noncarriers, with higher frequency among ApoE ε4 homozygotes than among ApoE ε4 heterozygotes. During the OLE period, there were 9 additional deaths with 3 occurring concurrently with ARIA or intracerebral hemorrhage. The overall rates for ARIA-E (14.7%) and ARIA-H (13.1%) increased with longer duration, however, rate of these adverse events over a standardized time (EAR) did not increase relative to placebo. The safety of the SC formulation was found to be similar to IV among the 49 patients that received it. Patients experienced mild-moderate localized and systemic injection-related reactions (e.g., erythema, swelling, rash, headache, fatigue, fever). Lecanemab (Leqembi) carries a black box warning for amyloid related imaging abnormalities including a higher risk among ApoE ε4 homozygotes. Contraindications

include hypersensitivity and warnings and precautions include enhanced vigilance for ARIA during the first 14 weeks of treatment and in those with pretreatment microhemorrhages and/or superficial siderosis and infusion-related reactions.

Investigational or Not Medically Necessary Uses

I. Lecanemab (Leqembi IQLIK) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   A. Other forms of dementia (e.g., vascular)
   B. Moderate-severe dementia associated with Alzheimer's disease

References

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Related Policies

Currently there are no related policies.

Policy Implementation/Update:

Action and Summary of Changes	Date
Policy created	05/2026