Reference number(s)
7213-A

Specialty Guideline Management
Leqembi IQLIK

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Leqembi IQLIK	lecanemab-irmb

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-approved Indications[1]

Leqembi is indicated for the treatment of Alzheimer's disease. 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.

All other indications are considered experimental/investigational and not medically necessary.

Documentation

Submission of the following information is necessary to initiate the prior authorization review:

Initial Requests

- Genetic testing results documenting a mutation in amyloid precursor protein (APP), presenilin-1 (PSEN1), or presenilin-2 (PSEN2), if applicable.

- Clinical documentation to support early onset Alzheimer's Disease, if applicable.
- Medical records (e.g., chart notes) documenting the following:
    - Diagnosis of Clinical Stage 3 or 4 Alzheimer's Disease.
    - Baseline and the most recent repeat (less than 1 month prior to request) assessments for any of the following assessment tools:
        - Clinical Dementia Rating-Global Score (CDR-GS)
        - Mini-Mental Status Examination (MMSE)
        - Montreal Cognitive Assessment (MoCA)
- Presence of amyloid pathology documented by either of the following:
    - Baseline positron emission tomography (PET) scan
    - Lumbar puncture results
- Recent (within one year) brain magnetic resonance imaging (MRI) prior to initiating treatment.

Continuation requests (where applicable)

- Medical records (e.g., chart notes) documenting the most recent (less than 1 month prior to continuation request) assessment tool for any of the following:
    - Clinical Dementia Rating-Global Score (CDR-GS)
    - Mini-Mental Status Exam (MMSE)
    - Montreal Cognitive Assessment (MoCA)

Prescriber Specialties

This medication must be prescribed by or in consultation with a geriatrician, neurologist, psychiatrist, or neuropsychiatrist.

Exclusions

- Coverage will not be provided for members with any of the following conditions:
    - Suspected neurodegenerative etiology of cognitive impairment other than Alzheimer's disease (AD), including but not limited to frontotemporal lobar degeneration (FTLD) or Lewy body disease (i.e., meeting consensus criteria for possible or probable dementia with Lewy bodies that lack AD biomarkers of a positive amyloid PET or CSF profile).
    - > 4 cerebral microbleeds, cortical superficial siderosis, or a major vascular contribution to cognitive impairment confirmed via MRI.
    - Cerebral contusion, encephalomalacia, brain aneurysm or other vascular malformation, central nervous system infection, or brain tumor.
    - History of transient ischemic attacks (TIA), stroke, uncontrolled hypertension, or seizures within the past 12 months.

  - Bleeding disorder that is not under adequate control (including a platelet count <50,000 or international normalized ratio [INR] >1.5).
  - Immunologic disorder requiring therapy with immunoglobulins, monoclonal antibodies, immunosuppressants, or plasmapheresis.
- Leqembi IQLIK will not be used in combination with any other amyloid beta-directed antibodies (e.g., aducanumab, donanemab).
- Leqembi IQLIK will not be used within the initial 18 months of therapy.

Coverage Criteria

Alzheimer's Disease[1,2,8-13,18-20]

Authorization of 12 months may be granted for treatment of Alzheimer's Disease (AD) when all of the following criteria are met:

- Member must meet one of the following criteria*.
  - Member is 50 years of age or older
  - If less than 50 years of age, member 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.
- Member must have Clinical Stage 3 (cognitive impairment with early functional impact) or Clinical Stage 4 (dementia with mild functional impact) AD (Appendix A)*.
- Member must have objective evidence of cognitive impairment at baseline*.
- Member must have one of the following scores at baseline on any of the following assessment tools*:
  - Clinical Dementia Rating-Global Score (CDR-GS) of 0.5 or 1 (Appendix B).
  - Mini-Mental Status Examination (MMSE) score of 21 – 30 (Appendix C).
  - Montreal Cognitive Assessment (MoCA) score of greater than or equal to 16 (Appendix D).
- Member must meet one of the following criteria*:
  - Have a positron emission tomography (PET) scan confirming the presence of amyloid pathology.
  - Have results from a lumbar puncture confirming at least one of the following detected in cerebrospinal fluid (CSF) as determined by the lab assay:
    - Low AB42/AB40 ratio
    - Elevated P-Tau/AB42 ratio
    - Elevated T-Tau/AB42 ratio
- Member must have a recent brain magnetic resonance imaging (MRI) within one year prior to initiating treatment to evaluate for pre-existing Amyloid Related Imaging Abnormalities (ARIA)*.

- Member will not use the requested medication in combination with anticoagulants including warfarin, heparin, and direct oral anticoagulants (e.g., dabigatran, rivaroxaban, edoxavan, apiximab, betrixaban).
- If there is concurrent use of antiplatelet agents (e.g., aspirin up to 325 mg/day, clopidogrel, prasugrel, ticagrelor), member will use antiplatelet agent as monotherapy at a standard therapeutic dose (i.e., not using as dual agent anti-platelet therapy).
- Member has undergone genotype testing to determine apolipoprotein E ε4 (ApoE ε4) status prior to initiation of the requested medication to inform member of the risk of developing ARIA*.
- Member and/or provider must currently be participating in a provider-enrolled patient registry that collects information on treatments for Alzheimer's disease (e.g., Alzheimer's Network for Treatment and Diagnostics (ALZ-NET)).
- Member has received 18 months of intravenous lecanemab therapy and has had a positive clinical response as evidenced by stabilization or slowing of disease progression as documented by any of the following (Note: repeat assessment tool (s) must be the same tool that was completed at baseline):
    - CDR-Global Score (i.e., score of 0.5 or 1)
    - MMSE (i.e., decline of 3 points or less per year)
    - MoCA (i.e., score of greater than or equal to 16)

Note: Continuation requests for members with assessment scores outside of the provided ranges (i.e. mild dementia) or who have progressed greater than the provided rate of decline may be reviewed on a case-by-case basis.

*must be met at time of initial start of lecanemab intravenous therapy

Continuation of Therapy

Authorization of 12 months may be granted for members requesting continuation of therapy after receiving 12 months of Leqembi IQLIK when all of the following criteria are met:

- Member has met all requirements in the coverage criteria at the time of initial approval.
- Member has a positive clinical response as evidenced by stabilization or slowing of disease progression as documented by any of the following (Note: repeat assessment tool(s) must be the same tool that was submitted upon initial request):
    - CDR-Global Score (i.e., score of 0.5 or 1)
    - MMSE (i.e., decline of 3 points or less per year)
    - MoCA (i.e., score of greater than or equal to 16)

Note: Continuation requests for members with assessment scores outside of the provided ranges (i.e. mild dementia) or who have progressed greater than the provided rate of decline may be reviewed on a case-by-case basis.

- Member and/or provider continues to participate in a provider-enrolled patient registry that collects information on treatments for Alzheimer's disease (e.g., Alzheimer's Network for Treatment and Diagnostics (ALZ-NET)).

Appendix

Appendix A: Diagnostic criteria for mild cognitive impairment (MCI) and dementia with mild functional impact[14,19-20]

- Mild cognitive impairment (MCI)/Clinical Stage 3:
  - Cognitive concerns by the patient, knowledgeable informant, or the physician
  - Objective impairment in one or more cognitive domains including memory, executive function, attention, language, or visuospatial skills
  - Generally preserved activities of daily living (ADL)
  - No dementia
- Dementia with mild functional impairment/Clinical Stage 4:
  - Congitive concerns by the patient, knowledgeable informant, or the physician
  - Performance in the impaired/abnormal range on objective cognitive tests
  - Evidence of decline from baseline, documented by the individual's report or by observer (e.g., study partner) report or by change on longitudinal cognitive testing or neurobehavioral assessments
  - Progressive cognitive and mild functional impairment on instrumental ADL with independence in basic ADL

Appendix B: Clinical Dementia Rating (CDR) Scale[3-5]

The CDR is obtained through semi-structured interviews of patients and informants with cognitive functioning rated on a 5-point scale in the following domains: memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care. The score relates to the member's level of dementia:

- 0 = Normal
- 0.5 = Very Mild Dementia
- 1 = Mild Dementia
- 2 = Moderate Dementia
- 3 = Severe Dementia

Appendix C: Mini-Mental Status Exam (MMSE)[6]

The MMSE is scored on a 30-point scale, with items that assess orientation (temporal and spatial; 10 points), memory (registration and recall; 6 points), attention/concentration (5 points), language (verbal

and written, 8 points), and visuospatial function (1 point). The score relates to the member's level of dementia:

- 25 – 30 suggests normal cognition
- 20 – 24 suggests mild dementia
- 13 – 20 suggests moderate dementia
- Less than 12 suggests severe dementia

Appendix D: Montreal Cognitive Assessment (MoCA)[7,8]

Per MoCA assessment, average scores for the following ranges are:

- Mild Cognitive Impairment: 19 – 25
- Mild Dementia: 11 – 21
- Normal: 26 and above

Appendix E: ARIA MRI Classification Criteria[1]

ARIA Type	**Radiographic Severity Mild**	**Radiographic Severity Moderate**	**Radiographic Severity Severe**
ARIA-E	FLAIR hyperintensity confined to sulcus and or cortex/subcortical white matter in one location < 5 cm	FLAIR hyperintensity 5 to 10 cm, or more than 1 site of involvement, each measuring < 10 cm	FLAIR hyperintensity measuring > 10 cm with associated gyral swelling and sulcal effacement. One or more separate/independent sites of involvement may be noted.
ARIA-H microhemorrhage	≤ 4 new incident microhemorrhages	5 to 9 new incident microhemorrhages	10 or more new incident microhemorrhages
ARIA-H superficial siderosis	1 focal area of superficial siderosis	2 focal areas of superficial siderosis	> 2 areas of superficial siderosis

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