

**Clinical Policy: Lecanemab-irmb (Leqembi)**

Reference Number: CP.PHAR.596

Effective Date: 01.06.23

Last Review Date: 11.23

Line of Business: Commercial, HIM, Medicaid

[Coding Implications](#)[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

**Description**

Lecanemab-irmb (Leqembi™) is a monoclonal antibody targeting amyloid beta.

**FDA Approved Indication(s)**

Leqembi is indicated for the treatment of Alzheimer's disease (AD). Treatment with Leqembi should be initiated in patients with mild cognitive impairment (MCI) or mild dementia stage of disease, the population in which treatment was initiated in clinical trials.

**Policy/Criteria**

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of health plans affiliated with Centene Corporation® that Leqembi is **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria****A. Alzheimer's Disease** (must meet all):

1. Diagnosis of MCI or mild AD dementia (see *Appendix E*);
2. Prescribed by or in consultation with a geriatrician or neurologist;
3. Age  $\geq 50$  and  $\leq 90$  years;
4. Documentation of the presence of beta-amyloid plaques as verified by one of the following (a or b):
  - a. Positron emission tomography scan;
  - b. Cerebrospinal fluid testing;
5. Documentation of one of the following baseline cognitive tests (a or b; see *Appendix D*):
  - a. Mini-Mental State Examination (MMSE) score  $\geq 22$ ;
  - b. Montreal Cognitive Assessment (MoCA) score  $\geq 16$ ;
6. Documentation of one of the following baseline functional tests and the resulting score (a, b, or c):
  - a. Functional Assessment Questionnaire (FAQ) score  $\leq 9$ ;
  - b. Functional Assessment Staging Test (FAST) score of 3-4;
  - c. Clinical Dementia Rating-Sum of Boxes (CDR-SB) of 0.5-9;
7. Documentation of recent (within the last year) brain magnetic resonance imaging (MRI) demonstrating all of the following (a-d):
  - a. Fewer than 4 microhemorrhages (defined as  $\leq 10$  mm at the greatest diameter);
  - b. Absence of any macrohemorrhages  $> 10$  mm at greatest diameter;

- c. Absence of superficial siderosis;
- d. Absence of vasogenic edema, cerebral contusion, encephalomalacia, aneurysms, or vascular malformations;
- 8. Member has no history of transient ischemic attacks (TIA), stroke, or seizures within the past 12 months;
- 9. Member is not currently taking concomitant anticoagulant or antiplatelet therapy;
- 10. Prescriber attestation that the prescriber has discussed with the member the potentially increased risk of amyloid-related imaging abnormalities (ARIA) in those who are ApoE4 genetic homozygotes;
- 11. Dose does not exceed 10 mg/kg every 2 weeks.

**Approval duration: 3 months (6 doses of infusion only)**

**B. Other diagnoses/indications (must meet 1 or 2):**

- 1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
  - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
  - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace and CP.PMN.16 for Medicaid; or
- 2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**II. Continued Therapy**

**A. Alzheimer's Disease (must meet all):**

- 1. Member meets one of the following (a or b):
  - a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
  - b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
- 2. Member is responding positively to therapy as evidenced by slowed decline in cognition;
- 3. Documentation of one of the following baseline cognitive tests (a or b; *see Appendix D*):
  - a. Mini-Mental State Examination (MMSE) score  $\geq 22$ ;
  - b. Montreal Cognitive Assessment (MoCA) score  $\geq 16$ ;

4. Documentation of one of the following baseline functional tests and the resulting score (a, b, or c):
  - a. Functional Assessment Questionnaire (FAQ) score  $\leq$  9;
  - b. Functional Assessment Staging Test (FAST) score of 3-4;
  - c. Clinical Dementia Rating-Sum of Boxes (CDR-SB) of 0.5-9;
5. Prior to the 7<sup>th</sup> and 14<sup>th</sup> infusions, documentation of a recent (within the last month) brain MRI showing all of the following (a, b, and c):
  - a. Absence of any macrohemorrhage (>10 mm at greatest diameter; symptomatic or not);
  - b. Fewer than 10 cerebral microhemorrhages cumulatively (symptomatic or not);
  - c. Absence of symptomatic cerebral microhemorrhages or symptomatic superficial siderosis;
6. Member is not currently taking concomitant anticoagulant or antiplatelet therapy;
7. If request is for a dose increase, new dose does not exceed 10 mg/kg once every 2 weeks.

**Approval duration:**

- **Members with < 7 total infusions: up to the 6<sup>th</sup> total infusion**
- **Members with < 14 total infusions but > 7 total infusions: up to the 13<sup>th</sup> total infusion**
- **Members with  $\geq$  14 total infusions: 12 infusions per PA approval**

**B. Other diagnoses/indications (must meet 1 or 2):**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
  - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
  - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 2 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**III. Diagnoses/Indications for which coverage is NOT authorized:**

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

#### IV. Appendices/General Information

##### *Appendix A: Abbreviation/Acronym Key*

AD: Alzheimer's disease

ARIA: amyloid-related imaging abnormalities

CDR-SB: Clinical Dementia Rating-Sum of Boxes

FAQ: Functional Assessment Questionnaire

FAST: Functional Assessment Staging Test

FDA: Food and Drug Administration

IADL: instrumental activity of daily living

MCI: mild cognitive impairment

MMSE: Mini-Mental State Examination

MoCA: Montreal Cognitive Assessment

MRI: magnetic resonance imaging

TIA: transient ischemic attack

##### *Appendix B: Therapeutic Alternatives*

Not applicable

##### *Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s): serious hypersensitivity to lecanemab-irmb or to any of the excipients of Leqembi
- Boxed Warning(s): increased risk of ARIA

##### *Appendix D: Dementia Rating Scales*

- MoCA is a highly sensitive tool for early detection of MCI and has been widely adopted in clinical settings. The maximum score is 30 points. The following ranges may be used to grade severity: 18-25 = mild cognitive impairment, 10-17 = moderate cognitive impairment and < 10 = severe cognitive impairment. However, research for these severity ranges has not been established yet. The average MoCA score for MCI is 22 (range 19-25) and the average MoCA score for Mild AD is 16 (range 11-21).
- MMSE is a series of questions asked by a health professional designed to test a range of everyday mental skills. The maximum score is 30 points where the following levels of dementia are indicated with a score of:
  - 25 to 30 suggests normal cognition,
  - 21 to 24 suggests mild dementia,
  - 13 to 20 suggests moderate dementia, and
  - less than 12 indicates severe dementia.
  - On average, the MMSE score of a person with Alzheimer's declines about two to four points each year.
- The FAQ measures instrumental activities of daily living (IADLs), such as preparing balanced meals and managing personal finances. Since functional changes are noted earlier in the dementia process with IADLs that require a higher cognitive ability compared to basic activities of daily living, this tool is useful to monitor these functional changes over time. The score range is 0-30. A cut-point of 9 (dependent in 3 or more activities) is recommended to indicate impaired function and possible cognitive impairment.

- FAST is a measure commonly used to assess functional status in patients with dementia. It provides a comprehensive evaluation of functional ability and the potential for a functional decline over time, including physical functional abilities (dressing and grooming), functional language abilities (memory and recognition), and functional activities such as mobility or self-feeding. The FAST score ranges from 1 to 7, categorizing the stages of AD into one of the below:
  - 1: normal aging
  - 2: possible mild cognitive impairment
  - 3: mild cognitive impairment
  - 4: mild dementia
  - 5: moderate dementia
  - 6: moderately severe dementia
  - 7: severe dementia
- CDR-SB assessment is a 5-point scale used to characterize six domains of cognitive and functional performance applicable to Alzheimer’s disease and related dementias: memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care. The information is obtained through an interview of the patient and a reliable informant (e.g., family member). This score is useful for characterizing and tracking a patient's level of impairment/dementia.
  - 0 suggests normal
  - 0.5 to 4 suggests questionable cognitive impairment
  - 0.5 to 2.5 suggests questionable impairment
  - 3.0 to 4.0 suggests very mild dementia
  - 4.5 to 9.0 suggests mild dementia
  - 9.5 to 15.5 suggests moderate dementia
  - 16.0 to 18.0 suggests severe dementia

*Appendix E: Diagnosis of Alzheimer’s Disease*

- AD
  - Interference with ability to function at work or at usual activities
  - A decline from a previous level of functioning and performing
  - Not explained by delirium or major psychiatric disorder
  - Cognitive impairment established by history-taking from the patient and a knowledgeable informant; and objective bedside mental status examination or neuropsychological testing
  - Cognitive impairment involves a minimum of two of the following domains:
    - Impaired ability to acquire and remember new information
    - Impaired reasoning and handling of complex tasks, poor judgment
    - Impaired visuospatial abilities
    - Impaired language functions (speaking, reading, writing)
    - Changes in personality, behavior, or comporment
  - Insidious onset (gradual onset over months to years, not over hours to days)
  - Clear-cut history of worsening
  - Initial and most prominent cognitive deficits are one of the following:
    - Amnesic presentation (impairment in learning and recall of recently learned information)

- Nonamnestic presentation in either a language presentation (prominently word-finding deficits), a visuospatial presentation with visual deficits, or executive dysfunction (prominently impaired reasoning, judgment and/or problem solving)
  - No evidence of substantial concomitant cerebrovascular disease, core features of dementia with Lewy bodies (DLB), prominent features of behavioral variant frontotemporal dementia (FTD) or prominent features of semantic or nonfluent/agrammatic variants of primary progressive aphasia (PPA), or evidence of another concurrent, active neurologic or non-neurologic disease or use of medication that could have a substantial effect on cognition
- MCI due to AD – core clinical criteria
  - Concern regarding change in cognition obtained from the patient, from an informant who knows the patient well, or from a skilled clinician observing the patient
  - Objective evidence of impairment in one or more cognitive domains that is not explained by age or education
  - Preservation of independence in functional abilities
  - Not demented

**V. Dosage and Administration**

Indication	Dosing Regimen	Maximum Dose
AD	10 mg/kg IV every 2 weeks	10 mg/kg every 2 weeks

**VI. Product Availability**

Vials for injection (single-dose): 200 mg/2 mL, 500 mg/5 mL

**VII. References**

1. Leqembi Prescribing Information. Nutley, NJ: Eisai Inc.; July 2023. Available at: <https://www.leqembi.com/-/media/Files/Leqembi/Prescribing-Information.pdf?hash=3d7bf1a2-5db2-4990-8388-81086f415676>. Accessed July 12, 2023.
2. Van Dyck CH, Swanson CJ, Aisen P, et al. Lecanemab in early Alzheimer’s disease. *NEJM* 2023 Jan 5;388(1):9-21.
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-A $\beta$  protofibril antibody. *Alz Res Therapy* 2021;13(80):1-14.
4. Centers for Medicare & Medicaid Services. Monoclonal antibodies directed against amyloid for the treatment of Alzheimer’s disease. Medicare Coverage Database. CAG099469N; 2022. Available at: <https://www.cms.gov/medicare-coverage-database/view/nccal-decision-memo.aspx?proposed=Y&NCAId=305>. Accessed July 12, 2023.
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. *Alzheimer’s & Dementia* 2019 Aug;5:354-63.
6. Trzepacz PT, Hochstetler H, Wang S, et al. Relationship between the Montreal Cognitive Assessment and Mini-Mental State Examination for assessment of mild cognitive impairment in older adults. *BMC Geriatrics* 2015;15:107. <https://doi.org/10.1186/s12877-015-0103-3>.



**Coding Implications**

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J0174	Lecanemab-irmb, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	10.04.22	11.22
Drug is now FDA approved - criteria updated per FDA labeling: added specialist requirement, added attestation that the prescriber has discussed the potentially increased risk of ARIA in ApoE4 homozygotes and with concomitant anticoagulants/antithrombotics, separated Commercial LOB into a separate policy (see CP.CPA.358); references reviewed and updated.	01.10.23	02.23
Previously granted accelerated approval is now converted to full (traditional) FDA approval – criteria updated per FDA labeling and CMS patient registry requirements: for Initial Approval Criteria, removed the requirement for enrollment in an NIH-sponsored trial; added requirements around cognitive testing (MoCA or MMSE) and functional testing (FAQ, FAST, or CDR-SB) to align with required elements of the CMS-sponsored patient registry; added a requirement for baseline MRI and history of stroke, TIA, and seizures to identify patients at increased risk for ARIA; added an exclusion for use with concomitant anticoagulant or antiplatelet therapy; for Continued Therapy, removed the requirement for enrollment in an NIH-sponsored trial; added a requirement for follow-up MRI results to identify new-onset ARIA; added requirement for cognitive and functional testing results to confirm that the member has not progressed beyond the mild stage of AD; added an exclusion for use with concomitant anticoagulant or antiplatelet therapy; added max dosing limits and Approval Durations; updated Boxed Warnings to include the new warning re: ARIA; combined Commercial policy (CP.CPA.358) with this policy since the coverage criteria across all LOBs is now the same, Commercial policy will be retired; new Jcode added; references reviewed and updated.	07.12.23	08.23
4Q 2023 annual review: no significant changes; recent full review completed at 3Q 2023 P&T after conversion of Leqembi’s accelerated approval to full approval.	08.08.23	11.23

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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**Note:**

**For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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