

## Leqembi™ (lecanemab-irmb) (Intravenous)

---

**Effective Date:** 11/01/2023

**Review Date:** 9/28/2023, 12/07/2023, 01/04/2024, 11/13/2024

**Scope:** Medicaid, Commercial, Medicare-Medicaid Plan (MMP)

### I. Length of Authorization

- Coverage will be provided for six (6) months and may be renewed.

### II. Dosing Limits

#### A. Quantity Limit (max daily dose) [NDC Unit]:

- Leqembi 200 mg/2 mL (100 mg/mL) solution in a single-dose vial: 2 vials every 14 days
- Leqembi 500 mg/5 mL (100 mg/mL) solution in a single-dose vial: 2 vials every 14 days

#### B. Max Units (per dose and over time) [HCPCS Unit]:

- 1200 billable units (1200 mg) every 14 days

### III. Summary of Evidence

Leqembi (lecanemab-irmb) is indicated for the treatment of Alzheimer's Disease (AD) in patients with mild cognitive impairment or mild dementia stage of disease with confirmed presence of amyloid beta pathology. The full approval of Leqembi was evaluated in the Clarity AD trial. The 1,795-participant phase three, double-blind, placebo-controlled trial randomized patients to Leqembi 10 mg/kg every two weeks or placebo. Participants had a median age of 72 years, were 52% women, and 77% white. The primary outcome of the study was change from baseline at 18 months on the Clinical Dementia Rating Scale - Sum of Boxes (CDR-SB). Leqembi statistically and clinically significantly met its primary outcome with an adjusted mean change from baseline on the CDR-SB scale at 18 months of 1.21 (difference from placebo -0.45,  $p < 0.0001$ ).

### IV. Initial Approval Criteria <sup>1,5,6,9</sup>

Coverage is provided in the following conditions:

MMP members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements

- Patient is at least 18 years of age; **AND**

- Physician has assessed baseline disease severity utilizing at least ONE objective measure/tool (i.e., Mini-Mental Status Exam [MMSE], Alzheimer's Disease Assessment Scale-Cognitive Subscale [ADAS-Cog-13], Alzheimer's Disease Cooperative Study-Activities of Daily Living Inventory-Mild Cognitive Impairment version [ADCS-ADL-MCI], Clinical Dementia Rating-Sum of Boxes [CDR-SB], Montreal Cognitive Assessment (MoCA), etc.); **AND**
- Patient does not have any of the following risk factors for intracerebral hemorrhage: prior cerebral hemorrhage > 1 cm in greatest diameter, > 4 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, or severe small vessel or white matter disease; **AND**
- Patients receiving antithrombotic medication (aspirin, other antiplatelets, or anticoagulants) prior to starting treatment with Leqembi have been on a stable dose for at least 4 weeks; **AND**
  - Patient has been tested prior to treatment to assess apolipoprotein E ε4 (ApoE ε4) status (e.g., homozygote, heterozygote, or noncarrier) and the prescriber has informed the patient that those who are homozygotes have a higher incidence of developing ARIA; **OR**
  - Genotype testing has not been performed and the prescriber has informed the patient that it cannot be determined if they are ApoE ε4 homozygotes and, therefore, if they are at higher risk for developing ARIA; **AND**

#### **Universal Criteria** <sup>1,5,6,9</sup>

- Must be prescribed by, or in consultation with, a specialist in neurology or gerontology; **AND**
- Patient has received a baseline brain magnetic resonance imaging (MRI) prior to initiating treatment (within one year prior – unless the patient has a more recent exacerbation, traumatic event [e.g., falls, etc.], or comorbidity necessitating an evaluation within one month preceding initiation) and periodically throughout therapy (*see prescribing information for schedule of MRI scans*); **AND**
- Patient has not had a stroke or transient ischemic attack (TIA) or seizures in the past 12 months; **AND**
- Patient does not have a clinically significant and unstable psychiatric illness in the past 6 months; **AND**
- Will not be used concurrently with other anti-amyloid immunotherapies (i.e., Kisunla (donanemab-azbt), etc.); **AND**
- Patient does not have a history of alcohol or substance abuse in the preceding year; **AND**
- Patient is included in the CMS approved Coverage with evidence development (CED) registry (only required for patients with Medicare [registry number, CED submission date, and submission number should be provided, if applicable]); **AND**

#### **Alzheimer's Disease (AD) †** <sup>1,2,5,6</sup>

- Patient has a diagnosis of mild cognitive impairment (MCI) due to AD or has mild Alzheimer's dementia (there is insufficient evidence in moderate or severe AD) **AND** both of the following:
  - Positron Emission Tomography (PET) scan positive for amyloid beta plaque or CSF assessment positive for hybrid ratios of Aβ 42/40, CSF p-tau 181/Aβ 42, or CSF t-tau/Aβ 42; **AND**

- One of the following\*:
  - Clinical Dementia Rating (CDR)-Global Score of 0.5-1.0 with Memory Box Score of at least 0.5; **OR**
  - MMSE score between 20-28, inclusive; **OR**
  - Montreal Cognitive Assessment (MoCA) score 18-25, inclusive; **AND**
- Other conditions mimicking, but of non-Alzheimer’s Dementia etiology, have been ruled out (e.g., vascular dementia, dementia with Lewy bodies [DLB], frontotemporal dementia [FTD], normal pressure hydrocephalus, non-Alzheimer’s related psychiatric illness [i.e., depression], etc.)

*\* Note: the aforementioned cognitive tests are typically the most commonly used but do NOT represent an exhaustive list. Use of alternative cognitive assessment tests not listed will be reviewed on a case-by-case basis.*

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); ☉ Orphan Drug

## V. Renewal Criteria <sup>1,5,6</sup>

Coverage may be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria identified in section IV; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: amyloid related imaging abnormalities-edema (ARIA-E) and -hemosiderin deposition (ARIA-H), intracerebral hemorrhage, severe hypersensitivity reactions including anaphylaxis, etc.; **AND**
- Patient has responded to therapy compared to pretreatment baseline as evidenced by improvement, stability, or slowing in cognitive and/or functional impairment in one or more of the following (not all-inclusive): ADAS-Cog 13/14; ADCS-ADL-MCI; MMSE; CDR-SB, MoCA etc.; **AND**
- Patient has not progressed to moderate or severe AD; **AND**
- Patient has received a pre- 5<sup>th</sup>, 7<sup>th</sup>, AND 14<sup>th</sup> infusion MRI for monitoring of Amyloid Related Imaging Abnormalities-edema (ARIA-E) and Amyloid Related Imaging Abnormalities-hemosiderin (ARIA-H) microhemorrhages; **AND**

### ARIA-E §

- Patient is asymptomatic or mildly symptomatic\* with mild radiographic severity\*\* on MRI; **OR**
- Patient is asymptomatic or mildly symptomatic\* with moderate to severe radiographic severity\*\* on MRI AND administration will be suspended until MRI demonstrates radiographic resolution and symptoms, if present, resolve; **OR**

- Patient has moderate to severe symptoms\* with mild to severe radiographic severity\*\* on MRI AND administration will be suspended until MRI demonstrates radiographic resolution and symptoms, if present, resolve

### ARIA-H §

- Patient is asymptomatic with mild radiographic severity\*\* on MRI; **OR**
- Patient is asymptomatic with moderate radiographic severity\*\* on MRI AND administration will be suspended until MRI demonstrates radiographic stabilization and symptoms, if present, resolve; **OR**
- Patient is symptomatic with mild to moderate radiographic severity\*\* on MRI AND administration will be suspended until MRI demonstrates radiographic stabilization and symptoms, if present, resolve; **OR**
- Patient has severe radiographic severity\*\* on MRI AND administration will be suspended until MRI demonstrates radiographic stabilization and symptoms, if present, resolve

§ Clinical judgment will be used in considering whether to continue treatment or permanently discontinue. In patients who develop intracerebral hemorrhage greater than 1 cm in diameter during treatment from Leqembi, suspend dosing until MRI demonstrates radiographic stabilization and symptoms, if present, resolve. Consider a follow-up MRI to assess for resolution 2 to 4 months after initial identification.

| Clinical Symptom Severity *                                    |   |  |
|--|---|--|
| Mild   | Moderate  | Severe   |
| Discomfort noticed, but no disruption of normal daily activity | Discomfort sufficient to reduce or affect normal daily activity | Incapacitating, with inability to work or to perform normal daily activity |

| ARIA Type <sup>1</sup>       | Radiographic Severity**   |  |  |
|------------------------------|---|--|--|
|                              | Mild  | Moderate   | Severe   |
| ARIA-E                       | FLAIR hyperintensity confined to sulcus and/or cortex/subcortex white matter in one location < 5 cm | FLAIR hyperintensity 5 to 10 cm in single greatest dimension, 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 focal areas of superficial siderosis   |

## VI. Dosage/Administration <sup>1</sup>

| Indication   | Dose  |
|--|---|
| <b>Alzheimer's Disease (AD)</b>  | The recommended dosage of Leqembi is 10 mg/kg and administered as an intravenous (IV) infusion over approximately one hour every two weeks. |
| – Obtain an MRI prior to the 5th, 7th, and 14th infusions. If radiographically observed ARIA occurs, treatment recommendations are based on type, severity, and presence of symptoms.<br>– If an infusion is missed, resume administration at the same dose as soon as possible. |   |

## VII. Billing Code/Availability Information

### HCPCS Code:

- J0174 – Injection, lecanemab-irmb, 1mg; 1 billable unit = 1 mg

### NDC:

- Leqembi 200 mg/2 mL (100 mg/mL) solution in a single-dose vial: 62856-0212-xx
- Leqembi 500 mg/5 mL (100 mg/mL) solution in a single-dose vial: 62856-0215-xx

## VIII. References

1. Leqembi [package insert]. Nutley, NJ; Eisai, Inc; July 2023. Accessed November 2024.
2. McKhann GM, Knopman DS, Chertklow H, et al. The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimers Dement.* 2011;7(3):263. Epub 2011 Apr 21.
3. Sperling RA, Aisen PS, Beckett LA, et al. Toward defining the preclinical stages of Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimers Dement.* 2011;7(3):280. Epub 2011 Apr 21.
4. van Dyck CH, Swanson CJ, Aisen P, et al. Lecanemab in Early Alzheimer's Disease. *N Engl J Med* 2022 November 29. DOI: 10.1056/NEJMoa2212948.
5. 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. *Alzheimer's Research and Therapy* 2021;13:80. DOI: 10.1186/s13195-021-00813-8.
6. Reish NJ, Jamshidi P, Stamm B, et al. Multiple Cerebral Hemorrhages in a Patient Receiving Lecanemab and Treated with t-PA for Stroke. *N Engl J Med* 2023 January 4. DOI: 10.1056/NEJMc2215148.
7. O'Bryant SE, Lacritz LH, Hall J, et al. Validation of the new interpretive guidelines for the clinical dementia rating scale sum of boxes score in the national Alzheimer's coordinating center. *Arch Neurol.* 2010 Jun;67(6):746-9. doi: 10.1001/archneurol.2010.115.
8. Skinner J, Carvalho, JO, Potter GG, et al. The Alzheimer's Disease Assessment Scale-Cognitive-Plus (ADAS-Cog-Plus): an expansion of the ADAS-Cog to improve responsiveness in MCI. *Brain Imaging Behav.* 2012 Dec;6(4):489-501. doi: 10.1007/s11682-012-9166-3.
9. Lin GA, Whittington MD, Synnott PG, et al. Aducanumab for Alzheimer's Disease: Effectiveness and Value; Final Evidence Report and Meeting Summary. Institute for Clinical and Economic Review, August 5, 2021. <https://icer.org/assessment/alzheimers-disease-2021/>.
10. Lin GA, Whittington MD, Wright A, et al. Beta-Amyloid Antibodies for Early Alzheimer's Disease: Effectiveness and Value; Draft Evidence Report. Institute for Clinical and Economic Review, December 22, 2022. <https://icer.org/assessment/alzheimers-disease-2022/#timeline>.
11. Jack CR, Andrews JS, Beach TG, et al. Revised criteria for diagnosis and staging of Alzheimer's disease: Alzheimer's Association Workgroup. *Alzheimer's Dement.* 2024; 20: 5143–5169. <https://doi.org/10.1002/alz.13859>.
12. Ramanan VK, Armstrong MJ, Choudhury P, et al. Anti-amyloid Monoclonal Antibody Therapy for Alzheimer Disease: Emerging Issues in Neurology. *Neurology.* 2023 Nov 7;101(19):842-852. doi: 10.1212/WNL.0000000000207757. Epub 2023 Jul 26. PMID: 37495380; PMCID: PMC10663011

13. Lin GA, Whittington MD, Wright A, et al. Lecanemab for Early Alzheimer's Disease: Final Evidence Report. Institute for Clinical and Economic Review, April 17, 2023. [https://icer.org/wp-content/uploads/2023/04/ICER\\_Alzheimers-Disease\\_Final-Report\\_For-Publication\\_04172023.pdf](https://icer.org/wp-content/uploads/2023/04/ICER_Alzheimers-Disease_Final-Report_For-Publication_04172023.pdf)
14. Nasreddine ZS, Phillips NA, Bédirian V, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. J Am Geriatr Soc. 2005 Apr;53(4):695-9. doi: 10.1111/j.1532-5415.2005.53221.x.

## Appendix 1 – Covered Diagnosis Codes

| ICD-10 | ICD-10 Description                   |
|--------|--------------------------------------|
| G30.0  | Alzheimer's disease with early onset |
| G30.1  | Alzheimer's disease with late onset  |
| G30.8  | Other Alzheimer's disease            |
| G30.9  | Alzheimer's disease, unspecified     |
| G31.84 | Mild cognitive impairment, so stated |

## Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: <https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCA/LCD): N/A

| Medicare Part B Administrative Contractor (MAC) Jurisdictions |  |   |
|---|--|---|
| Jurisdiction  | Applicable State/US Territory          | Contractor  |
| E (1)   | CA, HI, NV, AS, GU, CNMI               | Noridian Healthcare Solutions, LLC                |
| F (2 & 3)   | AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ | Noridian Healthcare Solutions, LLC                |
| 5   | KS, NE, IA, MO                         | Wisconsin Physicians Service Insurance Corp (WPS) |
| 6   | MN, WI, IL                             | National Government Services, Inc. (NGS)          |
| H (4 & 7)   | LA, AR, MS, TX, OK, CO, NM             | Novitas Solutions, Inc.                           |
| 8   | MI, IN                                 | Wisconsin Physicians Service Insurance Corp (WPS) |
| N (9)   | FL, PR, VI                             | First Coast Service Options, Inc.                 |
| J (10)  | TN, GA, AL                             | Palmetto GBA                                      |
| M (11)  | NC, SC, WV, VA (excluding below)       | Palmetto GBA                                      |

| Medicare Part B Administrative Contractor (MAC) Jurisdictions |   |  |
|---|---|--|
| Jurisdiction  | Applicable State/US Territory   | Contractor                               |
| L (12)  | DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA) | Novitas Solutions, Inc.                  |
| K (13 & 14)   | NY, CT, MA, RI, VT, ME, NH  | National Government Services, Inc. (NGS) |
| 15  | KY, OH  | CGS Administrators, LLC                  |

**Policy Rationale:**

Leqembi was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Leqembi according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For INTEGRITY (Medicare-Medicaid Plan) members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.