Neighborhood Health Plan OF RHODE ISLAND™
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Leqembi™ (lecanemab-irmb)
(Intravenous)

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

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 [1,5,6,9]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**
- Physician has assessed baseline disease severity utilizing an 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], 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**
- Documentation is provided of the applicable registry clinical trial identification number including attestation that it will be submitted on the claim
- MMP members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements

Universal Criteria [1,5,6,9]

- Must be prescribed by, or in consultation with, a specialist in neurology; **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 co-morbidity 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**
- Patient is not currently receiving any anticoagulants (e.g., Factor Xa inhibitors), or anti-thrombins (e.g., heparin) or anti-platelet agents with the exception of prophylactic aspirin or clopidogrel; **AND**
- Patient does not have a history of alcohol or substance abuse in the preceding year

Alzheimer's Disease (AD) † [1,2,5,6]

- Patient has mild cognitive impairment (MCI) due to AD or has mild Alzheimer's dementia (there is insufficient evidence in moderate or severe AD) as evidenced by all of the following:
    - Clinical Dementia Rating (CDR)-Global Score of 0.5-1.0
    - Memory Box Score of at least 0.5
    - Objective evidence of cognitive impairment at screening
    - MMSE score between 22-30, inclusive
    - Positron Emission Tomography (PET) scan or CSF assessment of Aß (1-42) is positive for amyloid beta plaque
- 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.)

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

V. Renewal Criteria [1,5,6]

Coverage may be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria identified in section III; **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, 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; ADCS-ADL-MCI; MMSE; CDR-SB, etc.; **AND**
- Patient has not progressed to moderate or severe AD; **AND**
- Patient has received a pre- 5th, 7th, AND 14th 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 [1]	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 [1]

Indication	Dose
Alzheimer's Disease (AD)	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.* – *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; Esai, Inc; July 2023. Accessed November 2023.
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-Aβ 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.

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
G30.9	Alzheimer's disease, unspecified
G31.84	Mild cognitive impairment, so stated

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

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 Determination (NCD), Local Coverage Articles (LCAs), and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered 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		
Jurisdictio	**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, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
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.