Leqembi™ (lecanemab-irmb)
(Intravenous)

Document Number: EOCCO-0694

Last Review Date: 08/08/2023
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Dates Reviewed: 02/2023, 06/2023, 08/2023

I. Length of Authorization

- Coverage will be provided for 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]:

a. 1200 billable units (1200 mg) every 14 days

III. 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: findings suggestive of cerebral amyloid angiopathy (prior cerebral hemorrhage > 1 cm in greatest diameter, > 4 microhemorrhages, superficial siderosis, vasogenic edema) or other lesions (aneurysm, vascular malformation) that could potentially increase the risk of intracerebral hemorrhage; **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 [1,5,6,9]

- 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 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 does not have a history of alcohol or substance abuse in the preceding year; **AND**

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, etc.)

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

IV. 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

V. 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, once 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.*	

VI. Billing Code/Availability Information

HCPCS Code:

- J3590 – Unclassified biologicals *(Discontinue on 07/06/2023)*
- C9399 – Unclassified drugs or biologicals *(Hospital Outpatient Use Only) (Discontinue on 07/06/2023)*
- J0174 – Injection, lecanemab-irmb, 1mg; 1 billable unit = 1 mg *(Effective 07/06/2023)*

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

VII. References

1. Leqembi [package insert]. Nutley, NJ; Esai, Inc; January 2023. Accessed May 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		
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, 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