Leqembi (lecanemab-irmb) Medical Necessity Guideline

Medical Necessity Guideline (MNG) Title: Leqembi (lecanemab-irmb)		
Classification: Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease (AD)		
MNG #:	**☒ SCO ☒ One Care** **☒ MA Medicare Preferred** **☒ MA Medicare Value** **☒ RI Medicare Preferred** **☒ RI Medicare Value** **☒ RI Medicare Maximum**	**Prior Authorization Needed?** **☒ Yes (always required)** **☐ Yes (only in certain situations. See this MNG for details)** **☐ No**
Clinical: ☐	**Operational: ☐**	**Informational: ☐**
Benefit Type: **☒ Medicare** **☐ Medicaid**	**Approval Date: 9/14/23**	**Effective Date: 9/14/23**
Last Revised Date:	**Next Annual Review Date: 9/14/24**	**Retire Date:**

OVERVIEW: Alzheimer's disease (AD) is a currently irreversible brain disorder that progressively degrades memory, cognitive function, and ability to carry out tasks of daily living. AD is the number one cause of dementia in older Americans, contributing to 60-80% of cases. Over 6 million older Americans are believed to have AD. This prevalence is expected to rise to 14 million by 2060 barring effective interventions (such as lifestyle changes, treatment of risk factors, and possibly combinations of Alzheimer's drugs). AD is the sixth leading cause of death in the United States but may rank from fifth to as high as third (after heart disease and cancer) as a cause of death for older Americans. Women are more likely to have AD than men, although this is in part because women live longer. Most individuals with AD become symptomatic after age 65. Alzheimer's can be fatal anywhere between 2 and 20 years of symptom onset, but 8 years on average (in those with onset before age 75 years). However, pathophysiologic changes in the brain (including amyloid-beta [Aβ] plaques and neurofibrillary tangles of tau) may be evident up to decades before symptoms occur. AD is characteristically a disease of older age. The incidence and prevalence of AD increase exponentially with age, essentially doubling in prevalence every 5 years after the age of 65 years. Although less common, early-onset dementia occurs in patients < 65 years of age. These patients often present with symptoms somewhat atypical for this disease, such as language, visual, or mood-behavioral changes rather than predominant memory loss.

AD is characterized by deposition of Aβ plaques and neurofibrillary tangles (comprised of abnormal tau protein) in the brain, accompanied by synaptic dysfunction and neurodegeneration.3,4 The deposition of Aβ (as amyloid plaques) generally begins decades before any symptoms of AD are observed. More specifically, Aβ deposition is followed sequentially by markers of neurodegeneration, accumulation of tau pathology, and brain volume loss. This pre-symptomatic phase of AD will precede the emergence of AD symptoms 10 to 20 years prior.

Inherited forms of AD typically exhibit an autosomal-dominant inheritance pattern related to mutations in genes that alter Aβ protein production or metabolism, including amyloid precursor protein (APP), presenilin-1 (PSEN1), and presenilin-2 (PSEN2). Aging is an important risk factor for dementia. Nonmodifiable risk factors for AD include female

gender, Black race, Hispanic ethnicity, and genetic factors such as presence of the APOE gene. Modifiable risk factors for all-cause dementia include hypertension, diabetes, diet, and limited cognitive, physical, and social activities.

While the genetic basis for early-onset AD is much better understood, the genetic basis of late-onset AD is considered far more complex, with susceptibility conferred by a variety of more common but less penetrant genetic factors likely interacting with environmental and epigenetic influences. To date, the most firmly established genetic risk factor for late-onset disease is APOE. The APOE gene is located on chromosome 19 and exists in 3 alleles: epsilon 2, 3, and 4. Factors that may influence the impact of APOE ε4 on AD risk include female gender, African/African American race (although there are conflicting data), vascular risk factors (e.g., smoking, diabetes, hypertension, and hypercholesterolemia), and modifier genes/environment. Genetic testing is available for the known causative genes in early-onset AD but has not been widely adopted, likely in part because of the current lack of highly effective preventive or therapeutic strategies.

DEFINITIONS:

Alzheimer's Disease: Alzheimer's disease (AD): is the most common type of dementia characterized by deposition of Aβ plaques and neurofibrillary tangles (comprised of abnormal tau protein) in the brain, accompanied by synaptic dysfunction and neurodegeneration that progressively degrades memory, cognitive function, and ability to carry out tasks of daily living.

Amyloid-beta [Aβ] plaques: are one of the two lesions in the brain that define the neuropathological diagnosis of Alzheimer's disease. Plaques are highly diverse structures; many of them include massed, fibrillar polymers of the Aβ protein referred to as *A*β-*amyloid*, but some lack the defining features of amyloid. Cellular elements in 'classical' plaques include abnormal neuronal processes and reactive glial cells, but these are not present in all plaques. Plaques have been given various names since their discovery in 1892, including *senile plaques*, *amyloid plaques*, and *neuritic plaques*. However, with the identification in the 1980s of Aβ as the obligatory and universal component of plaques, the term 'Aβ plaques' has become a unifying term for these heterogeneous formations.

Food and Drug Administration (FDA) Approved Indications:

Leqembi (Lecanemab) is a human IgG1 monoclonal anti-A-β antibody, targeting amyloid aggregates indicated for the treatment of Alzheimer's disease. Treatment should be initiated in Alzheimer's patients who have mild cognitive impairment **OR** mild dementia stage of the disease. On January 6, 2023, the U.S. Food and Drug Administration approved Leqembi (lecanemab) for this indication under accelerated approval and traditional approval on July 6, 2023**,** based on reduction in amyloid beta plaques observed in patients treated with Leqembi. Binding of antibody is intended to lead to clearance of amyloid from the brain. Lecanemab is believed to reduce the number of amyloid plaques present in the brain, potentially slowing neurodegeneration and disease progression.

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Mild cognitive impairment (or mild dementia): Mild cognitive impairment (MCI) is an early stage of memory loss or other cognitive ability loss (such as language or visual/spatial perception) in individuals who maintain the ability to independently perform most activities of daily living. It causes cognitive changes that are serious enough to be noticed by the person affected and by family members and friends but do not affect the individual's ability to carry out everyday activities.

Mini Mental Status Exam: The Mini-Mental State Exam (MMSE) is a widely used performance-based test of global cognitive status. The MMSE is a measure of cognition that includes 11 tasks relating to topics of word recall, attention and calculation, language ability, and visuospatial function. The scale ranges from 0 to 30 with a lower score reflecting greater cognitive impairment. It has several known limitations impacting sensitivity to change, particularly in earlier disease stages: substantial ceiling effects, sensitivity to practice effects, scores are impacted by patients' educational achievement, and learning effects are observed. The minimal clinically important difference of the MMSE in AD is estimated to be 1-3 points, and in early AD to be 1-2 points

Montreal Cognitive Assessment (MoCA): is a widely used screening test specifically designed to detect more subtle cognitive deficits that characterize mild cognitive impairment. Like the MMSE, the MoCA is scored on a 30-point scale, with items that assess delayed word recall, visuospatial/executive function, language, attention/concentration, and orientation. Studies examining head-to-head performance of patients on the MMSE and MoCA have shown that the MoCA is more difficult; MoCA scores are consistently lower than those obtained on the MMSE. The MoCA appears to be more sensitive than the MMSE for detecting MCI, though perhaps slightly less specific. A minimum clinically important difference of the MoCA in AD has not been described.4

DECISION GUIDELINES:

Clinical Coverage Criteria:

Commonwealth Care Alliance (CCA) follows Medicare (Medicaid *when applicable*) regulations, uses InterQual Smart Sheets, when available, to review prior authorization requests for medical necessity. This Medical Necessity Guideline (MNG) applies to all CCA Products unless a more expansive and applicable CMS National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), or state-specific medical necessity guideline exists.

AUTHORIZATION GUIDELINES:

Commonwealth Care Alliance may authorize coverage of Leqembi (Lecanemab-irmb) when all the following criteria are met**.** Initial authorization of Leqembi is limited to a total of 6 months if initial authorization criteria are met.

Prescribing Specialty:

Leqembi must be prescribed by a qualified physician who specializes in the treatment of Alzheimer's Disease, such as a gerontologist, neurologist, psychiatrist, or neuropsychiatrist **AND** participates in a registry.

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1. **INITIAL AUTHORIZATION CRITERIA:**

Initial 6 months of treatment

a. Member is 50 years or older **OR** if less than 50 years of age; the member has a genetic mutation in amyloid precursor protein (APP), presenilin-1 (PSEN1), or presenilin-2 (PSEN2), or other clinical documentation supporting early onset AD, and
b. Documentation is submitted that confirms the diagnosis of mild cognitive impairment (MCI) or early dementia caused by Alzheimer's disease as noted by one of the following:
    i. Cognitive concern reflecting a change in cognition reported by patient or informant or clinician (i.e., historical or observed evidence of decline over time)
    ii. Objective evidence of impairment in one or more cognitive domains, typically including memory (i.e., formal, or bedside testing to establish level of cognitive function in multiple domains)
    iii. Preservation of independence in functional abilities
    iv. Not demented, and
c. Member has one of the following scores at baseline on any of the following assessment tools:
    i. Clinical Dementia Rating-Global Score (CDR-GS) of 0.5 or 1; **or**
    ii. Mini-Mental Status Examination (MMSE) score of 21 - 30; **or**
    iii. Montreal Cognitive Assessment (MoCA) score of greater than or equal to 16, and
d. Confirmation that the member has presence of amyloid beta pathology consistent with AD prior to initiating treatment, and
e. Member has obtained a recent brain MRI (within one year) prior to initiating treatment to evaluate for pre-existing Amyloid Related Imaging Abnormalities (ARIA), and
f. Provider attests that the Member does not have any neurological or other medical condition (other than AD) that may significantly contribute to cognitive decline.

2. **REAUTHORIZATION CRITERIA:** CCA may re-authorize coverage of Leqembi for members continuing therapy when all the following criteria are met:

Re-authorized for an additional 12 months beyond the initial 6-month authorization

a. Member has met all initial authorization criteria at the time of initial approval,
b. Member has been evaluated for evidence of amyloid-related imaging abnormalities (ARIA) on MRI prior to the 5th dose, 7th dose, and 14th dose, and
c. Member with radiographic evidence of amyloid related imaging abnormalities-edema (ARIA-E), dosing may continue based on clinical judgement, and radiographic severity of ARIA type if member has mild ARIA-E on MRI and is asymptomatic or has mild clinical symptoms (see appendix)

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Re-authorized for an additional 12 months beyond the initial 18-month authorization

a. Member has met all initial authorization criteria at the time of initial approval
b. Member meets ***one*** of the following criteria:
    i. Member has a positive clinical response as evidenced by stabilization in score in any of the following measures:
        a) CDR-Global Score (i.e., score of 0.5 or 1); ***OR***
        b) MMSE (i.e., score of 21 - 30); ***OR***
        c) MoCA (i.e., score greater than or equal to 16).

LIMITATIONS/EXCLUSIONS: CCA will not cover

1. Leqembi for an early or late-stage Alzheimer's Disease that does not meet the criteria outlined above. All other indications will be considered experimental and investigational.
2. Monoclonal antibodies directed against amyloid for the treatment of AD provided outside of the CMS approved randomized controlled trials and trials supported by the NIH or a CMS-approved study, as appropriate based on the FDA-approval type, are non-covered and are considered experimental and investigational.
3. Leqembi for suspected or confirmed neurodegenerative diseases 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).
4. Leqembi for members who are at increased risk for intracranial hemorrhage based on any of the following, including but not limited to:
    a. Requirement for therapeutic anticoagulation (e.g., anticoagulants, antiplatelets), except for aspirin at a prophylaxis dose or less (no more than 325mg daily).
    b. History of brain hemorrhage, bleeding disorders, cerebrovascular abnormalities, stroke, or Transient Ischemic Attack (TIA), or seizures within the past 12 months.
    c. Bleeding disorder that is not under adequate control (including a platelet count less than 50,000 or international normalized ratio [INR] greater than 1.5).
    d. Members with a brain MRI that shows evidence of acute or sub-acute hemorrhage or prior subarachnoid hemorrhage.
5. Leqembi will not be used in combination with any other amyloid beta-directed antibodies (e.g., aducanumab).

The following list(s) of codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this guideline does not signify that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. This Medical Necessity Guideline is subject to all applicable Plan Policies and Guidelines, including requirements for prior authorization and other requirements in Provider's agreement with the Plan (including complying with Plan's Provider Manual specifications).

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Drug	CPT/HCPCS Code	Description
Leqembi	J0174	Injection, lecanemab-irmb, 1mg

REGULATORY NOTES:

Medical Necessity Guidelines are published to provide a better understanding of the basis upon which coverage decisions are made. CCA makes coverage decisions on a case-by-case basis by considering the individual member's health care needs. If at any time an applicable CMS LCD or NCD or state-specific MNG is more expansive than the criteria set forth herein, the NCD, LCD, or state-specific MNG criteria shall supersede these criteria.

Disclaimer

This Medical Necessity Guideline is not a rigid rule. As with all CCA's criteria, the fact that a member does not meet these criteria does not, in and of itself, indicate that no coverage can be issued for these services. Providers are advised, however, that if they request services for any member who they know does not meet our criteria, the request should be accompanied by clear and convincing documentation of medical necessity. The preferred type of documentation is the letter of medical necessity, indicating that a request should be covered either because there is supporting science indicating medical necessity (supporting literature (full text preferred) should be attached to the request), or describing the member's unique clinical circumstances, and describing why this service or supply will be more effective and/or less costly than another service which would otherwise be covered. Note that both supporting scientific evidence and a description of the member's unique clinical circumstances will generally be required.

APPENDIX:

ARIA MRI Classification Criteria

ARIA Type	Radiographic Severity		
	Mild	Moderate	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, often with significant subcortical white matter and/or sulcal involvement. One or more separate sites of involvement may be noted.
ARIA-H microhemorrhage	≤ 4 new incidents microhemorrhages	5 to 9 new incidents microhemorrhages	10 or more new incidents microhemorrhages
ARIA-H superficial siderosis	1 focal area of superficial siderosis	2 focal areas of superficial siderosis	> 2 focal areas of superficial siderosis

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Source: Eisai, 2023

RELATED REFERENCES:

1. CMS Press Release: CMS announces plan to ensure availability of new Alzheimer's drugs, June 1, 2023:
2. National Coverage Determination (NCD), Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease (AD), 200.3, 12/12/2022: https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?ncdid=375&ncdver=1
3. CMS.GOV Coverage with Evidence Development, Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease (AD), 7/11/2023: https://www.cms.gov/medicare/coverage-evidence-development/monoclonal-antibodies-directed-against-amyloid-treatment-alzheimers-disease-ad
4. Prospective Study on Anti-Amyloid-β Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease Coverage of Evidence Development (The Anti-Aβ mAb CED Study), Clinicaltrials.gov number: NCT05925621, CMS Approval Date 07/11/23: https://www.cms.gov/files/document/ced-study-description.pdf
5. Mental status scales to evaluate cognition Mario F Mendez, MD, PhD, Apr 14, 2023: https://www.uptodate.com/contents/mental-status-scales-to-evaluate-cognition?search=Mental%20status%20scales%20to%20evaluate%20cognition&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1
6. Albert MS, DeKosky ST, Dickson D, et al. The diagnosis of mild cognitive impairment due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimer's Dement. 2011;7(3):270-279.
7. Alzheimer's Association Report on Mild Cognitive Impairment: https://www.alz.org/alzheimers-dementia/what-is-dementia/related_conditions/mild-cognitive-impairment#:~:text=Mild%20cognitive%20impairment%20(MCI)%20is,most%20activities%20of%20daily%20living.
8. AA 2021, NIA 2021, CDC 2021, Rajan 2021, Brookmeyer 2018, 2019.
9. Sherva R, Kowall NW. Genetics of Alzheimer disease. UpToDate Web site. Updated July 23, 2020. http://www.uptodate.com. Accessed January 10, 2021
10. Albert MS, DeKosky ST, Dickson D, et al. The diagnosis of mild cognitive impairment due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimer's Dement. 2011;7(3):270-279.

REVISION LOG:

REVISION DATE	DESCRIPTION

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APPROVALS:

Debra Poskanzer, MD	Senior Medical Director, Medical Policy
CCA Senior Clinical Lead [Print]	**Title [Print]**
	9/14/23
Signature	**Date**
Click here to enter text.	
CCA Senior Operational Lead [Print]	**Title [Print]**
Signature	**Date**
Nazlim Hagmann, MD	Chief Medical Officer
CCA CMO or Designee [Print]	**Title [Print]**
	9/14/23
Signature	**Date**