DR.011.D IgG1 Monoclonal Antibodies for Alzheimer's

Original Implementation Date : 11/01/2021
Version [D] Date: 05/17/2024
Last Reviewed Date : 05/21/2025

PRODUCT VARIATIONS

This policy applies to all Jefferson Health Plans/Health Partners Plans lines of business unless noted below.

POLICY STATEMENT

We consider Aduhelm™ (aducanumab-avwa), Leqembi™ (lecanemab-irmb) and any newly approved drugs in this class medically necessary for its FDA approved indications when the prior authorization criteria listed in this policy are met.

OFF-LABEL USE

Authorization for off-labeled use of medication will be evaluated on an individual basis. Review of an off-labeled request by the Medical Staff will be predicated on the appropriateness of treatment and full consideration of medical necessity. For off-label use Medical Directors will review scientific literature and local practice patterns.

FDA APPROVED INDICATIONS

Leqembi™ and Aduhelm™ are humanized immunoglobulin gamma 1 monoclonal antibody directed against aggregated soluble and insoluble forms of amyloid beta indicated for the treatment of:

- Alzheimer's disease
    - This indication is approved under accelerated approval based on reduction in amyloid beta plaques observed in patients treated with ADUHELM™ or LEQEMBI™. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trial(s).

PRIOR AUTHORIZATION CRITERIA

INITIAL CRITERIA

Initial use of Leqembi™ and Aduhelm™ may be considered medically necessary when All of the following apply:

1. FDA approved age is 50 years old or older.
2. Must have documentation of a genetic mutation and/or documentation of Alzheimer's disease. *(Documentation must be attached).*
3. Must have documentation of a diagnosis of Alzheimer's disease of mild severity (a MMSE score between 24 and 20 or a CDR-SB score of 0.5 to 1).
4. Must have no contraindications to the requested drug or its components (no history of hypersensitivity to the requested drug)
5. Must have no medical or neurological condition that may be contributing to cognitive impairment.
6. Must have no history of a stroke, TIA, seizures, or unexplained loss of consciousness in the past year.
7. If requesting for Aduhelm™, must have no history of unstable angina, MI, advanced chronic HF, or clinically significant conduction abnormalities for $\geq$ 1 year.
8. Must have no history of brain hemorrhage, bleeding disorder, cerebrovascular abnormalities or on blood thinners other than prophylactic dose aspirin.
9. Must have recent (within the last year) PET scan showing presence of beta-amyloid plaque and/or CSF testing, showing presence of tau protein? (Attach results).
10. The medication is prescribed by or in consultation with a physician who is a psychiatrist, neurologist, geriatrician, or neuropsychiatrist.
11. Must confirm that all other causes of dementia are ruled out? (Vascular dementia, Lewy body dementia (DLB), Frontotemporal dementia (FTD), Parkinson's disease dementia)
12. The prescription is consistent with the FDA approved package labeling.
13. Must not be used in combination with any other amyloid beta-directed antibodies.
14. If the patient has a recent MRI scan (within one year to initiating treatment) with results attached, **approve for 6 months.**

RENEWAL CRITERIA

1. The patient continues to meet the diagnostic criteria after initial treatment with the requested drug for Alzheimer's.

2. The patient does not have unacceptable toxicity which precludes safe administration of the drug.
    a. (Examples of unacceptable toxicity include the following: ARIA-E (cerebral edema) excluding mild ARIA-E on MRI and asymptomatic or has mild clinical symptoms ARIA-H (hemosiderin deposition) excluding mild ARIA-H on MRI and asymptomatic).

3. The patient obtained an MRI after the 5th dose and will have an MRI prior to the 7th, 9th and 14th infusions.
    a. There are no observed ARIA, showing 10 or more new incident microhemorrhages or > 2 focal areas of superficial siderosis (radiographic severe ARIA-H) and/ or the MRI is showing radiographic stabilization (i.e., no increase in size or number of ARIA-H) with results attached.

4. If patient has been on treatment for less than 12 months, approve for the duration of 6 months.

5. If the patient has been on the treatment for greater than 12 months and the patient shows clinical benefit (stabilization) (Attach notes), approve for the duration of 6 months.

DOSAGE AND ADMINISTRATION

Single-use dose vial containing 170mg/1.7mL or 300mg/3mL of aducanumab-avwa as a solution and 500 mg/5 mL or 200 mg/2 mL (both 100mg/mL) solution in a single dose vial for lecanemab-irmb. Dilution in 100mL of 0.9% Sodium Chloride for aducanumab-avwa and dilution in 250mL of 09% Sodium Chloride for lecanemab-irmb. Infused through an IV line containing a sterile, low-protein binding, 0.2 or 0.22 micron in-line filter, is required.

Dosing recommendations for Alzheimer's disease:

Leqembi™:

- Recommended dose for LEQEMBI™ is 10 mg/kg diluted then administered as an intravenous (IV) infusion over approximately one hour, once every two weeks for 18 months.
- After 18 months, 10mg/kg once every 2 weeks may be continued or transition to a maintenance dosing regimen of 10mg/kg once every 4 weeks.

Aduhelm:

- After an initial titration, the recommended dosage of ADUHELM™ is 10 mg/kg (see Table 1). ADUHELM™ is administered as an (IV) over approximately one hour every four weeks and at least 21 days apart.

IV Infusion (every 4 weeks)	ADUHELM™ Dosage (Administered over approximately one hour)
Infusion 1 and 2	1 mg/kg
Infusion 3 and 4	3 mg/kg
Infusion 5 and 6	6 mg/kg
Infusion 7 and beyond	10 mg/kg

RISK FACTORS/SIDE EFFECTS

- **Amyloid Related Imaging Abnormalities (ARIA)** Enhanced clinical vigilance for ARIA is recommended during the first 8 doses of treatment with ADUHELM™ and the first 14 weeks of treatment with LEQEMBI™, particularly during titration. If a patient experiences symptoms which could be suggestive of ARIA (e.g., headache, altered mental status, dizziness, visual disturbance, nausea), clinical evaluation should be performed, including MRI testing if indicated.

- **Hypersensitivity Reactions**: Angioedema and urticaria have occurred with ADHUELM and angioedema, bronchospasm, and anaphylaxis have occurred with LEQEMBI™. If a hypersensitivity reaction occurs, promptly discontinue the infusion of ADUHELM™and LEQEMBI™ and initiate appropriate therapy.

- **Infusion-Related Reactions: Infusion rate of Leqemb™i may be reduced or discontinued if infusion reaction occurs. Pre-medication of antihistamines, NSAIDs, or corticosteroids is considered .**

MONITORING

Efficacy

- Physical Findings
    - ADAS-Cog 13 (Alzheimer's disease Assessment Scale-Cognitive Subscale 13).
    - Aβ PET composite SUVR (Beta-amyloid positron emission tomography.
    - Baseline and periodic monitoring of MRI.
    - CDS-SB (Clinical Dementia Rating-Sum of Boxes).
    - MMSE score (Mini0Mental State Examination).
    - Standardized uptake value ratio.

Safety

- Look for signs and symptoms stated above in Risk Factors/Side Effects section to ensure safety.

BLACK BOX WARNING

Aduhelm and Leqembi™ : Amyloid Related Imaging Abnormalities (ARIA) can occur in early treatment and is typically asymptomatic. Patients who are apolipoprotein E ε4 (ApoE ε4) homozygotes have a higher incidence of ARIA. Testing for ApoE ε4 status should be performed prior to initiation of treatment to inform the risk of developing ARIA.

CLINICAL EVIDENCE

N/A

BACKGROUND

ALZHEIMER'S DISEASE

Alzheimer's disease is a neurodegenerative disorder resulting in progressive cognitive and behavioral decline. Alzheimer's disease is the leading cause of dementia, a general term for memory loss and cognitive decline, accounting for 60% to 80% of cases. Estimating to affect 5.8 million Americans, or 10% if people 65 years old or older, with 80% being older than 75 years old. Additionally, 200,000 Americans have early-onset Alzheimer's disease, defined as Alzheimer's disease affecting those younger than 65 years old. Due to the aging population, the estimated number of people aged 65 years and older with Alzheimer's disease is estimated to be 13.8 million in the United States in 2050, barring any developments in therapies. Alzheimer's disease is the sixth leading cause of death in the United States and the fifth leasing cause of death among those age 65 years and older. Almost two-thirds of Americans with Alzheimer's disease are women. African Americans and Latino Americans are twice as likely and one and half times as likely, respectively to have Alzheimer's disease as older White Americans. On average, patients survive approximately 4 to 8 years after diagnosis, with survival time affected by age at diagnosis and severity of other medical conditions.

The pathogenesis of Alzheimer's disease has been attributed to extracellular aggregates of beta-amyloid plaques and intracellular neurofibrillary tangles in the cortical and limbic areas of the human brain. Beta-

amyloid peptides are created through the proteolytic cleavage of the amyloid precursor protein; this process likely instigates the intraneuronal accumulation of phosphorylated tau, which is the primary component of the neurofibrillary tangles. It is estimated that beta-amyloid plaques begin to develop 10 years to 30 years before Alzheimer's disease onset, while neuronal degeneration, such as the presence of tau in the cerebrospinal fluid, may develop shortly before clinical symptoms first appear. Both biomarkers of Alzheimer's disease can be detected in the CSF and by positron emission computed tomography (PET).

Aside from increasing age, which is the greatest risk factor for Alzheimer's disease, the two other major risk factors are family history and genetics (risk genes and deterministic genes, the latter being genes that cause the disease rather than genes that increase the risk for disease development). Familial Alzheimer's disease has mainly been associated with mutation in APP and presenilin genes PSEN1 and PSEN2/ Comparatively, non-familial or sporadic-onset Alzheimer's disease has a complex etiology, involving genetic, environmental, metabolic, viral, and other factors. The E4 variant of apolipoprotein E is the main susceptibility gene for Alzheimer's disease, while the E2 variant of APOE is considered a protective factor that reduces the incidence of Alzheimer's disease and beta-amyloid accumulation and delays the age of Alzheimer's disease onset. Acquired risk factors include but are not limited to head trauma, hypertension, cerebrovascular disease, hypercholesteremia, and environment risk factors (lead, pesticides). Conversely, higher education and socioeconomic status have been associated with lower age-adjusted incidence of Alzheimer's disease diagnosis.

Alzheimer's disease is characterized by memory loss and progressive neurocognitive dysfunction. Signs and symptoms include memory loss that disrupts daily life; challenges in planning or problem-solving; difficulty completing familiar tasks at home, work, or at leisure; confusion with orientation to time or place; difficulty with visual images and spatial relationships; difficulties with speaking or writing; decreased or poor judgment; withdrawal from work or social activities; and changes in mood and personality/ Individuals may present with one or more of these symptoms and in varying degree of severity, as listed below.

1. Clinical Dementia Rating (CDR)-Global Score
    a. 0 = Normal
    b. 0.5 = Very Mild Dementia
    c. 1 = Mild Dementia
    d. 2 = Moderate Dementia
    e. 3 = Severe Dementia

2. Mini-Mental Examination Status (MMSE)
    a. 25 - 30 suggest normal cognition
    b. 20 – 24 suggests mild dementia
    c. 13 – 20 suggests moderate dementia
    d. Less than 12 suggests severe dementia.

3. Montreal Cognitive Assessment (MoCA)
    a. Mild Cognitive Impairment: 19 – 25
    b. Mild Alzheimer's Disease: 11 – 21
    c. Normal: 26 and above

CODING

Note: The Current Procedural Terminology (CPT®), Healthcare Common Procedure Coding System (HCPCS), and the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) codes that *may* be listed in this policy are for reference purposes only. Listing of a code in this policy does not imply that the service is covered and is not a guarantee of payment. Other policies and coverage guidelines may apply. When reporting services, providers/facilities should code to the highest level of specificity using the code that was in effect on the date the service was rendered. This list may not be all inclusive.

CPT Code	Description
99483	Cognition-focused evaluation including a pertinent history and examination

HCPCS Code	Description
J0172	Injection, aducanumab-avwa, 2 mg
J0174	Legembi (lecanemab-irmb 1mg)
G0336	PET imaging brain Alzheimer's

ICD-10 Codes	Description
G30	Alzheimer's disease
G30.0	Alzheimer's disease with early onset
G30.1	Alzheimer's disease with late onset

DISCLAIMER

Approval or denial of payment does not constitute medical advice and is neither intended to guide nor influence medical decision making. Policy Bulletins are developed to assist in administering plan benefits and constitute neither offers of coverage nor medical advice. This Policy Bulletin may be updated and therefore is subject to change. For Health Partners Plans Medicaid and Health Partners Plans Chip products: Any requests for services that do not meet criteria set in PARP will be evaluated on a case-by-case basis.

POLICY HISTORY

This section provides a high-level summary of changes to the policy since the previous version.

Summary	Version	Version Date
2025 Annual Review. Revisions to Dosage, Risk Factors and Side Effects, and Black Box Warning. References updated accordingly.	D	05/17/2024
2024 Annual review. Prior authorization and renewal criteria were updated.	D	05/17/2024
July 2023 Ad-hoc code update. J0174 was added to the coding table for the drug Legembi (lecanemab-irmb, 1 mg) J3590 was removed.	C	07/01/2023
2023 Annual review. Title of policy changed from: Aduhelm™ (aducanumab-avwa) to IgG1 Monoclonal Antibodies for Alzheimer's. Revisions made to include the drug Legembi (lecanemab-irmb). Prior authorization and renewal criteria were revised. Code J0172 was added to the coding table. References were updated accordingly.	C	05/24/2023
2022 Annual review. Renewal criteria and disclaimer sections were updated.	B	09/01/2022
This is a new drug policy.	A	11/01/2021

REFERENCES

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6. UpToDate : Treatment of Alzheimer Disease Authors: Daniel Press, MD; Stephanie S Buss, MD-last update September, 30, 2021, Literature review February, 2024 https://www.uptodate.com/contents/treatment-of-alzheimer-disease?search=alzheimer%20treatment&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1#H3053641237

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