CarePartners of Connecticut MEDICARE ADVANTAGE

Medical Necessity Guidelines
Medical Benefit Drugs

Aduhelm™ (aducanumab-avwa)

Effective: January 1, 2024

Guideline Type	☒ Prior Authorization ☐ Non-Formulary ☐ Step-Therapy ☐ Administrative

Applies to:

☒ CarePartners of Connecticut Medicare Advantage HMO plans, Fax 617-673-0956
☒ CarePartners of Connecticut Medicare Advantage PPO plans, Fax 617-673-0956

Note: While you may not be the provider responsible for obtaining prior authorization, as a condition of payment you will need to ensure that prior authorization has been obtained.

Overview

An estimated 6.7 million Americans aged 65 and older are living with Alzheimer's in 2023. Seventy-three percent are age 75 or older. Currently, Aduhelm is one of two disease-modifying agents (both amyloid-targeting monoclonal antibodies) approved by the FDA for early Alzheimer's Disease.

Aduhelm is indicated for the treatment of Alzheimer’s disease. Treatment with Aduhelm should be initiated in patients with mild cognitive impairment or mild dementia stage of disease, the population in which treatment was initiated in clinical trials. There are no safety or effectiveness data on initiating treatment at earlier or later stages of the disease than were studied.

Aduhlem is a human, immunoglobulin gamma 1 (IgG1) monoclonal antibody directed against aggregated soluble and insoluble forms of amyloid beta.

The approval was largely based on two Phase 3 clinical trials, EMERGE (Study 1) and ENGAGE (Study 2), in patients with early stages of AD (MCI and mild dementia) with confirmed presence of amyloid pathology. In these two studies, and a third Phase 1B study (PRIME), Aduhelm showed a dose- and time-dependent effect on the lowering of amyloid beta plaques: 59% in ENGAGE, 71% in EMERGE, and 61% in PRIME. There has been significant controversy over the trial data,
as EMERGE and ENGAGE have conflicting clinical results. In the EMERGE trial, patients treated with high-dose aducanumab showed less cognitive decline than patients receiving placebo. However, the identically designed ENGAGE trial failed to show a benefit to aducanumab versus placebo.

SIde effects and Safety: In both ENGAGE and EMERGE, around 35% of patients on high-dose aducanumab experienced a side effect known as amyloid-related imaging abnormalities-edema (ARIA-E), a type of brain swelling that can cause headache and nausea. Usually, these symptoms are mild, and the swelling diminishes on its own. ARIA-E was the most common adverse event (35%) followed by headache (20.5%). Discontinuation rates were not addressed in the label. The majority of patients who experienced ARIA-E (74%) did not experience symptoms during the ARIA-E episode. ARIA-E episodes generally resolved within 4–16 weeks, typically without long-term clinical sequelae. This brain swelling is a side effect likely to unnerve some doctors, especially initially after approval and for a drug that could be prescribed to many patients. Another type of ARIA, amyloid-related imaging abnormalities-hemorrhage (ARIA-H), was fairly common and
consistent across the trials, with around 18% of high-dose patients experiencing a microhemorrhage because of it. ARIA-H: Across the two trials, 18% (200/1095), 14% (159/1095), and 0.5% (6/1095) of the patients in the highdose cohort experienced ARIA-H–related microhemorrhage, superficial siderosis, and microhemorrhage, respectively. For comparison, 6% (69/1077), 2% (24/1077), and 0.3% (4/1077) of placebo patients experienced.

Food and Drug Administration (FDA) Approved Indications:

- Aduhelm™ (aducanumab-avwa) is an IgG1 human monoclonal anti-amyloid beta antibody indicated for the treatment of patients with Alzheimer disease (AD) exhibiting mild cognitive impairment or mild dementia. The rationale for the use of Aduhelm™ (Aducanumab-avwa) is based on the hypothesis that the accumulation of amyloid beta is a main driver of

AD. The deposition of amyloid beta plaques in the brain occurs before the onset of clinical symptoms and dementia. Aduhelm™ (aducanumab-avwa) has been shown to reduce the accumulation of amyloid beta, thus potentially slowing disease progression.

Nationally Covered Indication(s):
The Centers for Medicare & Medicaid Services (CMS) issued a National Coverage Determination (NCD for monoclonal antibodies directed against amyloid for the treatment of Alzheimer's disease (AD). The NCD utilizes a Coverage with Evidence Development (CED) to establish a dual coverage pathway for individuals with mild cognitive impairment (MCI) due to AD or mild AD dementia, both with confirmed presence of amyloid beta pathology consistent with AD to be covered according to their FDA approval pathway:

- If approved by the FDA based upon evidence of efficacy from a change in a surrogate endpoint (e.g., amyloid reduction) considered as reasonably likely to predict clinical benefit, the drug may be covered in a randomized controlled trial conducted under an investigational new drug (IND) application.
- If approved by the FDA based upon evidence of efficacy from a direct measure of clinical benefit, the drug may be covered in CMS approved prospective comparative studies.

The Centers for Medicare & Medicaid Services (CMS) proposes to cover FDA approved monoclonal antibodies directed against amyloid for the treatment of Alzheimer's disease (AD) under Coverage with Evidence Development (CED) in CMS approved randomized controlled trials that satisfy the coverage criteria specified below, and in trials supported by the National Institutes of Health (NIH). All trials must be conducted in a hospital-based outpatient setting.

For any CMS approved trials, or trials supported by the NIH, that include a beta amyloid positron emission tomography (PET) scan as part of the protocol, it has been determined that these trials also meet the CED requirements included in the Beta Amyloid Positron Emission Tomography in Dementia and Neurodegenerative Disease NCD (220.6.20), and one beta amyloid PET scan will be covered per patient, if the patient did not previously receive a beta amyloid PET scan.

Nationally Non-Covered Indication(s):
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 nationally non-covered.

See NCA - Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease (CAG-00460N) - Decision Memo (cms.gov) for additional information

Clinical Guideline Coverage Criteria

CMS may cover Aduhelm™ (aducanumab-avwa) when all the following clinical criteria is met:

Initial Authorization Criteria:

1. The Member is enrolled in a CMS-approved randomized controlled trial for Aduhelm™ (aducanumab-avwa) or a trial supported by the National Institutes of Health (NIH), ***and*** the trial is conducted in a hospital-based outpatient setting.

AND

2. The Member has documented clinical evidence of mild cognitive impairment (MCI) due to AD or mild AD dementia based on the National Institute on Aging and the Alzheimer's Association (NIA-AA) criteria[2,3]

AND

3. Aduhelm™ (aducanumab-avwa) is prescribed by a Neurologist who specializes in the treatment of Alzheimer's Disease

AND

4. The Member is between 50 and 85 years of age

AND

5. There is documented evidence of amyloid pathology consistent with AD as evidenced by **ONE** of the following tests:
    a. An Amyloid Positron Emission Tomography (PET) scan; ***or***
    b. Lumbar puncture confirming the presence of elevated phosphorylated tau (P-tau) protein and reduced beta amyloid-42 (AB42) ***or*** a low AB42/AB40 ratio as determined by the lab assay detected in cerebrospinal fluid (CSF)

AND

6. The Provider attests that the Member does **not** have:
    a. Any neurological or other medical condition (other than AD) that may significantly contribute to cognitive decline; ***or***
    b. Expected death from any cause during the duration of the study; ***or***

c. Any medical condition other than AD likely to increase significant adverse events

Reauthorization Criteria:

CMS may cover Aduhelm™ (aducanumab-avwa) when all the following clinical criteria is met:

1. The Member is enrolled in a CMS-approved randomized controlled trial for Aduhelm™ (aducanumab-avwa) or a trial supported by the National Institutes of Health (NIH), ***and*** the trial is conducted in a hospital-based outpatient setting.

AND

2. Member meets all **initial** criteria when starting Aduhelm™ (aducanumab-avwa) therapy

AND

3. Medical records confirm that the member has received scheduled MRIs (e.g., pre-7th infusion, pre-12th infusion, and every 12 months thereafter) for ARIA monitoring and there is no evidence of severe ARIA-H that would warrant discontinuation of treatment

AND

4. For members who have been receiving the medication for more than 12 months, documentation of change from baseline PET scan or CSF analysis confirming **ONE** of the following obtained at or around 18 months of treatment:
    a. Amyloid PET scan demonstrating a reduction in amyloid plaques from baseline noted by **both** of the following:
        i. Composite Standard Uptake Value Ratio (SUVR) reduction of at least 0.2 points; ***and***
        ii. Amyloid PET Centiloid reduction of at least 50%.

    OR

    b. CSF results demonstrating a reduction in tau pathophysiology and neurodegeneration from baseline as noted by **both** of the following:
        i. P-Tau reduction of at least 20 pg/mL; ***and***
        ii. T-Tau reduction of at least 110 pg/mL

AND

5. The Provider attests that the Member does not have any of the following:
    a. Any neurological or other medical condition (other than AD) that may significantly contribute to cognitive decline; ***or***
    b. Expected death from any cause during the duration of the study; ***or***
    c. Any medical condition other than AD likely to increase significant adverse events

Limitations

- Initial authorization of Aduhelm is limited to a total of 6 monthly dose if initial authorization criteria are met.
- Reauthorization for Aduhelm may be granted for a period of up to 6 monthly doses (per renewal) when reauthorization criteria are met.
- The plan will not cover:
    - Members who are not enrolled in a CMS-approved randomized controlled trial for Aduhelm™ (aducanumab-avwa) or a trial supported by the National Institutes of Health (NIH), and the trial is conducted in a hospital-based outpatient setting.
    - Members at increased risk for intracranial hemorrhage based on any of the following:
        - History of brain hemorrhage, bleeding disorders, cerebrovascular abnormalities, stroke or Transient Ischemic Attack (TIA)
        - Anticoagulant (e.g., apixaban, dabigatran, enoxaparin, heparin, rivaroxaban, warfarin) or antiplatelet (e.g., aspirin dosed > 325 mg/day, cilostazol, clopidogrel, dipyridamole, prasugrel, ticagrelor) medication use
    - Members with a brain MRI that shows evidence of acute or sub-acute hemorrhage or prior subarachnoid hemorrhage
    - Members with a brain MRI that shows evidence of severe ARIA-H
    - Members who are not maintained on a dose of 10 mg/kg
    - Members with a diagnosis of cerebral amyloid angiopathy[11]

Appendix:

ARIA MRI Classification Criteria

ARIA Type	Radiographic Severity		
	Mild	**Moderate**	**Severe**
ARIA-E	FLAIR hyperintensity	FLAIR hyperintensity 5	FLAIR hyperintensity measuring > 10 cm, often

	confined to sulcus and or cortex/subcortical white matter in one location < 5 cm	to 10 cm, or more than 1 site of involvement, each measuring < 10 cm	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

Codes

The following code(s) require prior authorization:

Table 1: HCPCS Codes

HCPCS Codes	Description
J0172	Injection, aducanumab-avwa, 2mg

References

1. Aduhelm Prescribing Information. Accessed November 9, 2023. https://www.biogencdn.com/us/aduhelm-pi.pdf.
2. Clinical Guidelines Clinical Diagnosis of Alzheimer's Disease, Lancet Neurol, 2021 . Accessed November 9. 2023. https://www.thelancet.com/journals/laneur/article/PIIS1474-4422(21)00066-1/fulltext.
3. American Academy of Neurology Practice Guideline Update Summary: Mild Cognitive Impairment, Neurology, 2018. Accessed November 9, 2023. https://www.aan.com/Guidelines/home/GuidelineDetail/881.
2. McKhann GM, Knopman DS, Chertkow 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):263-269.
3. 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. Alzheimers Dement. 2011;7(3):270-279.
4. ClinicalTrials.gov: https://clinicaltrials.gov/ct2/show/NCT02477800. Accessed June 1, 2020.
5. ClinicalTrials.gov: https://clinicaltrials.gov/ct2/show/NCT02484547. Accessed June 1, 2020.
6. CMS Finalizes Medicare Coverage Policy for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease. Centers for Medicare & Medicaid Services. Published April 7, 2022. Accessed online May 6, 2022 at CMS Finalizes Medicare Coverage Policy for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease | CMS
7. Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease. National Coverage Analysis. Centers for Medicare & Medicaid Services. Published April 7, 2022. Accessed online May 6, 2022 at NCA - Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease (CAG-00460N) - Decision Memo (cms.gov)
8. O'Bryant SE, Waring SC, Cullum CM, et al. Staging Dementia Using Clinical Dementia Rating Scale Sum of Boxes Scores: A Texas Alzheimer's Research Consortium Study. Arch Neurol. 2008;65(8):1091–1095.
9. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975;12(3):189-198.
10. CDR Dementia Staging Instrument. Knight Alzheimer Disease Research Center. https://knightadrc.wustl.edu/cdr/cdr.htm. Accessed: June 17, 2021.
11. Mendez MF, Mental status scales to evaluate cognition. UpToDate, updated April 16, 2019. http.uptodate.com. Accessed June 17, 2021.
12. Wolk DA, Dickerson BC. Clinical features and diagnosis of Alzheimer disease. UpToDate, updated December 11, 2020. http://www.uptodate.com. Accessed June 10, 2021.
13. Greenberg, Steven M. et al. Off Label Use of Aducanumab for Cerebral Amyloid Angiopathy. Lancet, Neurology. July 5, 2021. https://doi.org/10.1016/S1474-4422(21)00213-1.

Approval And Revision History

September 13, 2022: Reviewed by Pharmacy and Therapeutics Committee (P&T)

September 21, 2022: Reviewed by the Medical Policy Approval Committee (MPAC)

December 12, 2023: Removed Dosing Schedule in Appendix. Administrative Update in support of calendar year 2024 Medicare Advantage and PDP Final Rule.

Background, Product and Disclaimer Information

Point32Health prior authorization criteria to be applied to Medicare Advantage plan members is based on guidance from Medicare laws, National Coverage Determinations (NCDs) or Local Coverage Determinations (LCDs). When no guidance is provided, Point32Health uses clinical practice guidance published by relevant medical societies, relevant medical literature, Food and Drug Administration (FDA)-approved package labeling, and drug compendia to develop prior authorization criteria to apply to Medicare Advantage plan members. Medications that require prior authorization generally meet one or more of the following criteria: Drug product has the potential to be used for cosmetic purposes; drug product is not considered as first-line treatment by medically accepted practice guidelines, evidence to support the safety and efficacy of a drug product is poor, or drug product has the potential to be used for indications outside of the indications approved by the FDA. Prior authorization and use of the coverage criteria within this Medical Necessity Guideline will ensure drug therapy is medically necessary, clinically appropriate, and aligns with evidence-based guidelines. We revise and update Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests revisions.

Treating providers are solely responsible for the medical advice and treatment of Members. The use of this guideline is not a guarantee of payment or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to eligibility and benefits on the date of service, coordination of benefits, referral/authorization, utilization management guidelines when applicable, and adherence to plan policies, plan procedures, and claims editing logic.