Aduhelm® (aducanumab-avwa)

Humana

Pharmacy Coverage Policy

Effective Date: December 15, 2021
Revision Date: January 24, 2024
Review Date: January 17, 2024
Line of Business: Medicaid - South Carolina, Medicaid - Ohio
Policy Type: Prior Authorization

Products Affected
Aduhelm intravenous solution

Listed Indications
Alzheimer's Disease

Alzheimer's Disease	
Does the member meet all of the following criteria?	
Criteria #1	Enrollment in an FDA-approved randomized controlled trial or a clinical trial supported by the NIH (National Institutes of Health) **OR** meets all of the following criteria:
Criteria #2	Member has a confirmed diagnosis of mild cognitive impairment (MCI) due to Alzheimer's disease (AD) or mild AD dementia
Criteria #3	Submitted documentation (must include assessment form and chart notes) that cognitive impairment has been established on neurological exam within the past 12 months with MMSE of 24-30, CDR-global score of 0.5, or MoCA 21-30
Criteria #4	Amyloid beta deposits consistent with a diagnosis of Alzheimer's disease are present as confirmed by one of the following (must submit a copy of medical imaging results or diagnostic immunoassay): • Amyloid positron emission tomography (PET) • Cerebrospinal fluid (CSF) (i.e. Aß42, Aß42/Aß40 ratio, tau/Aß42 ratio) assay with evidence of high concordance with amyloid PET scan to assess the presence of amyloid deposition
Criteria #5	Symptoms are not related to another neurological or psychiatric condition (e.g. Lewy body dementia, cerebrovascular disease, etc.)
Criteria #6	Prescribed by or in consultation with a neurologist or other specialist with experience treating AD
Criteria #7	Member has received in-person evaluation(s) related to diagnosis and eligibility for treatment with Aduhelm
Criteria #8	Provider attestation that monitoring for Amyloid Related Imaging Abnormalities (ARIA) will be conducted via MRI prior to initiation, prior to the 7th and 12th infusions of Aduhelm, and as clinically indicated if any symptoms suggestive of ARIA occur
Criteria #9	Member does NOT have any of the following on pre-treatment MRI within 1 year of treatment initiation (must submit copy of medical imaging results): • evidence of acute or subacute hemorrhage • macrohemorrhage • greater than 1 area of superficial siderosis • greater than 4 brain microhemorrhages • cortical infarction • lacunar infarction • diffuse white matter disease
Criteria #10	Member does NOT have history of cerebrovascular abnormalities or bleeding disorder that would present a risk for ARIA-related bleeding

Criteria #11	Member is NOT currently taking a blood thinner other than prophylactic aspirin that would present a risk for ARIA-related bleeding
Criteria #12	Provider attestation that member will be titrated to 10mg/kg dose of Aduhelm and will discontinue therapy if dosing is unable to be achieved
Criteria #13	Member will NOT receive Aduhelm via home infusion during initial titration phase (i.e., must be established on maintenance 10mg/kg dosing prior to transition to home infusion)
For continuation of therapy requests, does the member meet all of the following renewal criteria?	
Renewal Criteria #1	Enrollment in an FDA-approved randomized controlled trial or a clinical trial supported by the NIH (National Institutes of Health) **OR** meets all of the following criteria:
Renewal Criteria #2	Member has a confirmed diagnosis of mild cognitive impairment (MCI) due to Alzheimer's disease (AD) or mild AD dementia
Renewal Criteria #3	Submitted documentation (must include assessment form and chart notes) that cognitive impairment has been re-evaluated on neurological exam within the past 12 months with MMSE of 24-30, CDR-global score of 0.5, or MoCA 21-30
Renewal Criteria #4	Member has received in-person evaluation(s) related to continuation of Aduhelm
Renewal Criteria #5	Symptoms are not related to another neurological or psychiatric condition (e.g. Lewy body dementia, cerebrovascular disease, etc)
Renewal Criteria #6	Prescribed by or in consultation with a neurologist or other specialist with experience treating AD
Renewal Criteria #7	Provider attestation that monitoring for Amyloid Related Imaging Abnormalities (ARIA) will be conducted via MRI prior to the 7th and 12th infusions of Aduhelm and as clinically indicated if any symptoms suggestive of ARIA occur

Renewal Criteria #8	One of the following applies:
	• Member does NOT have any of the following on most recent MRI (must submit a copy of medical imaging results):
	  ◦ Symptomatic ARIA-E or ARIA-H
	  ◦ 5 or more new incident microhemorrhages
	  ◦ Greater than or equal to 2 focal areas of superficial siderosis (radiographic moderate to severe ARIA-H)
	  ◦ FLAIR hypersensitivity greater than or equal to 5 cm or more than 1 site of involvement (radiographic moderate to severe ARIA-E); **OR**
	• If one or more of the above ARIA findings are present, clinical evaluation and follow-up MRI demonstrate radiographic stabilization of ARIA-H (i.e. no increase in size or number) and resolution of ARIA-E

Renewal Criteria #9	Member does NOT have history of cerebrovascular abnormalities or bleeding disorder that would present a risk for ARIA-related bleeding
Renewal Criteria #10	Member is NOT currently taking a blood thinner other than prophylactic aspirin that would present a risk for ARIA-related bleeding
Renewal Criteria #11	Member is not experiencing limitations related to ARIA and is tolerating titration to 10mg/kg if prior to 7th dose, or has reached 10mg/kg dosing if 7th dose or later
Renewal Criteria #12	Member will NOT receive Aduhelm via home infusion during initial titration phase (i.e., must be established on maintenance 10mg/kg dosing prior to transition to home infusion)
Renewal Criteria #13	Provider attestation that potential benefits of continued Aduhelm therapy exceed risks associated with therapy

Approval Duration	
Initial	6 months
Renewal	6 months

Back to top

Background

This is a prior authorization policy about Aduhelm (aducanumab-avwa). Please refer to the package insert for complete prescribing information.

Aducanumab is an anti-amyloid beta monoclonal antibody directed against aggregated soluble and insoluble forms of amyloid beta. The accumulation of amyloid beta plaques in the brain is a defining pathophysiological feature of Alzheimer's disease. Aduhelm reduces amyloid beta plaques in the brain, which is theorized to slow disease progression.

Alzheimer's disease is an irreversible, progressive, neurodegenerative disease primarily in patients older than 65 years of age that slowly affects memory, cognition, and function. It is categorized broadly into preclinical disease where symptoms are not yet apparent but imaging shows disease activity, mild cognitive impairment (MCI) due to AD which is associated with mild cognitive decline, and dementia due to AD where normal activities of daily living are impaired and cognition worsens. Hallmarks of disease pathology include amyloid beta deposits and tau tangles in the brain that lead to the irreversible destruction of neurons and resulting symptoms.

Identically designed phase 3 trials (ENGAGE, EMERGE) evaluating patients with mild cognitive impairment due to AD or mild Alzheimer's disease dementia with positive amyloid plaque were stopped early in March 2019 due to a futility analysis predicting no difference compared to placebo. In August 2020, the FDA accepted the BLA for aducanumab based on new analysis showing potentially positive results in one trial. In November 2020, an FDA Advisory Committee voted against approval. According to the FDA, the June 2021 approval of Aduhelm was based on the reduction of amyloid beta plaques demonstrated in clinical trials as a surrogate for clinical benefit.

ENGAGE did not meet statistical significance for primary or secondary endpoints evaluating cognition and function. A subset of patients were evaluated at week 78 regarding their biomarker status and demonstrated a statistically significant reduction from baseline in amyloid beta as determined by PET, compared to placebo. The high dose (10mg/kg) group of EMERGE demonstrated a statistically significant difference from placebo in the primary endpoint, change in Clinical Dementia Rating Scale-Sum of Boxes (CDR-SB) with a decline versus placebo of 22% (-0.39 vs 1.74). A clinically meaningful difference in CDR-SB has not been established, however, the scale ranges from 0 to 18, with higher scores indicating worse cognitive status. Secondary endpoints evaluating cognition and function with other scales (e.g. MMSE, ADAS-Cog 13) met statistical significance in the high dose group. The low dose group did not meet statistical significance. The 10mg/kg group in EMERGE also demonstrated a statistically significant reduction from baseline in amyloid beta.

The most common adverse events in the 10mg/kg group included ARIA-E, headache, ARIA-H, falls, and diarrhea. Amyloid-Related Imaging Abnormalities (ARIA) are thought to be due to drug-induced amyloid clearance from blood vessels, which become leaky and cause amyloid deposits occur throughout small arteries in brain.

Aduhelm (aducanumab) 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. This indication is approved under accelerated approval based on reduction in amyloid beta plaques observed in patients treated with Aduhelm. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trial(s).

Aducanumab is available as Aduhelm in 170 mg/1.7 mL and 300 mg/3 mL single-dose vials for intravenous use.

Black Box Warning: AMYLOID RELATED IMAGING ABNORMALITIES

- Monoclonal antibodies directed against aggregated forms of beta amyloid, including ADUHELM, can cause amyloid related imaging abnormalities (ARIA), characterized as ARIA with edema (ARIA-E) and ARIA with hemosiderin deposition (ARIA-H). ARIA is usually asymptomatic, although rarely serious and life-threatening events can occur. Serious intracerebral hemorrhage greater than 1 cm have occurred in patients treated with this class of medications.
- ApoE ε4 Homozygotes: Patients treated with this class of medications, including ADUHELM, who are ApoE ε4 homozygotes have a higher incidence of ARIA, including symptomatic and serious ARIA, compared to heterozygotes and noncarriers. Testing for ApoE ε4 status should be performed prior to initiation of treatment to inform the risk of developing ARIA. Prior to testing, prescribers should discuss with patients the risk of ARIA across genotypes and the implications of genetic testing results.
- Consider the benefit of ADUHELM for the treatment of Alzheimer's disease and potential risk of serious adverse events associated with ARIA when deciding to initiate treatment with ADUHELM.

Warnings & Precautions:

- Amyloid Related Imaging Abnormalities (ARIA): Enhanced clinical vigilance for ARIA is recommended during the first 8 doses of treatment with ADUHELM, particularly during titration. Risk of ARIA, including symptomatic ARIA, was increased in apolipoprotein E ε4 (ApoE4) homozygotes compared to heterozygotes and non-carriers. If a patient experiences symptoms which could be suggestive of ARIA, clinical evaluation should be performed, including MRI testing if indicated
- Hypersensitivity Reactions: Angioedema and urticaria have occurred. If a hypersensitivity reaction occurs, promptly discontinue the infusion of Aduhelm and initiate appropriate therapy.

Monitoring:

- Obtain a recent brain magnetic resonance imaging (MRI) prior to initiating treatment with ADUHELM.
- Obtain MRIs prior to the 5th infusion (first dose of 6 mg/kg), 7th infusion (first dose of 10 mg/kg), 9th infusion (third dose of 10 mg/kg), and 12th infusion (sixth dose of 10 mg/kg). If a patient experiences symptoms suggestive of ARIA, clinical evaluation should be performed, including an MRI if indicated.
- Recommended dosing interruptions for patients with ARIA are provided in the product's package insert.

Provider Claim Codes

For medically billed requests, please visit www.humana.com/PAL. Select applicable Preauthorization and Notification List(s) for medical and procedural coding information.

Medical Terms

Aduhelm; aducanumab; aducanumab-avwa; Alzheimer's disease; AD; mild cognitive impairment; MCI; mild dementia; amyloid; intravenous

References

1. Aduhelm [package insert]. Cambridge, MA: Biogen, Inc.; Aug 2023.
2. 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):270-79.
3. Budd Haeberlein S, et al. Two Randomized Phase 3 Studies of Aducanumab in Early Alzheimer's Disease. J Prev Alzheimers Dis. 2022;9(2):197-210

4. Clinical Pharmacology [database online]. Phladelphia, PA: Elsevier, Inc.; URL: https://www.clinicalkey.com/pharmacology/. Updated periodically.
5. IBM Micromedex DRUGDEX® [database online]. Cambridge, MA: IBM Corporation; URL: http://www.micromedexsolutions.com. Updated periodically.
6. Institute for Clinical and Economic Review. Aducanumab for Alzheimer's Disease: Effectiveness and Value. Available at: https://icer.org/wp-content/uploads/2020/10/ICER_ALZ_Final_Report_080521-1.pdf. Published August 5, 2021.
7. Mayo Clinic Clinical Trials: 221AD301 Phase 3 Study of Aducanumab (BIIB037) in Early Alzheimer's Disease. Accessed June 2021. Available at: https://www.mayo.edu/research/clinical-trials/cls-20179704.
8. 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):263-69.
9. Unapproved Product Formulary Submission Dossier: Aducanumab in Mild Cognitive Impairment due to Alzheimer's Disease and Alzheimer's Disease Dementia. [dossier]. Cambridge, MA: Biogen and Eisai; 2021.

Disclaimer	State and federal law, as well as contract language, including definitions and specific inclusions/exclusions, take precedence over clinical policy and must be considered first in determining eligibility for coverage. Coverage may also differ for our Medicare and/or Medicaid members based on any applicable Centers for Medicare & Medicaid Services (CMS) coverage statements including National Coverage Determinations (NCD), Local Medical Review Policies (LMRP) and/or Local Coverage Determinations. See the CMS website at http://www.cms.hhs.gov/. The member's health plan benefits in effect on the date services are rendered must be used. Clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Clinical technology is constantly evolving, and we reserve the right to review and update this policy periodically. No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any shape or form or by any means, electronic, mechanical, photocopying or otherwise without permission from Humana.