Aduhelm (aducanumab-avwa)

Humana

Pharmacy Coverage Policy

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Line of Business: Medicaid - Humana, Medicaid - Ohio
Policy Type: Prior Authorization

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.

Description

Aduhelm (aducanumab) is an anti-amyloid beta monoclonal antibody.

Aduhelm (aducanumab) is 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.

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 as 170 mg/1.7 mL and 300 mg/3 mL (100 mg/mL) solutions in a single-dose vial.

Coverage Determination

Please note the following regarding medically accepted indications:

All reasonable efforts have been made to ensure consideration of medically accepted indications in this policy. Medically accepted indications are defined by CMS as those uses of a covered Part D drug that are approved under the federal Food, Drug and Cosmetic Act, or the use of which is supported by one or more citations included or approved for inclusion in any of the compendia described in section 1927(g)(1)(B)(i) of the Act. These compendia guide review of off-label and off-evidence prescribing and are subject to minimum evidence standards for each compendium. Currently, this review includes the following references when applicable and may be subject to change per CMS:

- American Hospital Formulary Service-Drug Information (AHFS-DI)
- National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
- Truven Health Analytics Micromedex DrugDEX
- Elsevier/Gold Standard Clinical Pharmacology
- Wolters Kluwer Lexi-Drugs

Aduhelm (aducanumab) will require prior authorization. This agent may be considered medically necessary when the following criteria are met:

Alzheimer's Disease - Initial Criteria

- 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
- Member has a confirmed diagnosis of mild cognitive impairment (MCI) due to Alzheimer’s disease (AD) or mild AD dementia **AND**
- 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 **AND**
- 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. Aβ42, Aβ42/Aβ40 ratio, tau/Aβ42 ratio) assay with evidence of high concordance with amyloid PET scan to assess the presence of amyloid deposition **AND**
- Symptoms are not related to another neurological or psychiatric condition (e.g. Lewy body dementia, cerebrovascular disease, etc) **AND**
- Prescribed by or in consultation with a neurologist or other specialist with experience treating AD **AND**
- Member has received in-person evaluation(s) related to diagnosis and eligibility for treatment with Aduhelm **AND**
- 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 **AND**
- Member does NOT have any of the following on pre-treatment MRI within 1 year of treatment initiation (must submit a 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 **AND**
- Member does NOT have history of cerebrovascular abnormalities or bleeding disorder that would present a risk for ARIA-related bleeding **AND**
- Member is NOT currently taking a blood thinner other than prophylactic aspirin that would present a risk for ARIA-related bleeding **AND**
- Provider attestation that member will be titrated to 10mg/kg dose of Aduhelm and will discontinue therapy if dosing is unable to be achieved **AND**
- 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)

Alzheimer's Disease - Continuation Criteria

- 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
- Member has a confirmed diagnosis of mild cognitive impairment (MCI) due to Alzheimer's disease (AD) or mild AD dementia **AND**
- 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 **AND**
- Member has received in-person evaluation(s) related to continuation of Aduhelm **AND**
- Symptoms are not related to another neurological or psychiatric condition (e.g. Lewy body dementia, cerebrovascular disease, etc) **AND**
- Prescribed by or in consultation with a neurologist or other specialist with experience treating AD **AND**
- 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 **AND**
- 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 **AND**
- Member does NOT have history of cerebrovascular abnormalities or bleeding disorder that would present a risk for ARIA-related bleeding **AND**
- Member is NOT currently taking a blood thinner other than prophylactic aspirin that would present a risk for ARIA-related bleeding **AND**
- 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 **AND**

- 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) **AND**
- Provider attestation that potential benefits of continued Aduhelm therapy exceed risks associated with therapy

Aduhelm (aducanumab) will be approved in six month durations or as determined through clinical review.

Coverage Limitations

Aduhelm (aducanumab) therapy is not considered medically necessary for members with the following concomitant conditions:

- Experimental/Investigational Use – Indications not supported by CMS recognized compendia or acceptable peer reviewed literature.

Background

This is a prior authorization policy about Aduhelm (aducanumab).

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. Other approved therapies for Alzheimer’s disease include cholinesterase inhibitors (donepezil, rivastigmine, galantamine) and NMDA receptor antagonists (memantine). Aduhelm is the first drug approved to include treatment of MCI due to AD and it is the first with a potentially disease modifying mechanism of action.

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. Clinical significance of changes in biomarkers is unknown at this time.

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. Labeling outlines MRI monitoring timelines prior to initiation, the 7th dose, and the 12th dose, and as clinically indicated. Based on MRI results, treatment may be continued, temporarily suspended, or discontinued.

Warnings and 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. 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.

Refer to package labeling for complete details.

Provider Claims 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; intravenous; Alzheimer's disease; pharmacy

References

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