Clinical Policy: Aducanumab-avwa (Aduhelm)

Reference Number: CP.PHAR.468
Effective Date: 06.07.21
Last Review Date: 05.24
Line of Business: HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Aducanumab-avwa (Aduhelm™) is a monoclonal antibody targeting amyloid beta.

FDA Approved Indication(s)*

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 the disease, the population in which treatment was initiated in clinical trials.

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).

***Biogen, manufacturer of Aduhelm, announced that it will discontinue Aduhelm to reprioritize its resources; patients currently receiving Aduhelm will have access to the drug until November 1, 2024** (*see Appendix E*)

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Aduhelm may be medically necessary when the following criteria are met:

I. Initial Approval Criteria

A. Alzheimer's Disease (must meet all):

1. Diagnosis of mild cognitive impairment due to Alzheimer's disease or mild Alzheimer's disease dementia (see *Appendix D*);
2. Presence of beta-amyloid plaques verified by one of the following (a or b):
   a. Positron emission tomography scan;
   b. Cerebrospinal fluid testing;
3. Member meets one of the following (a or b):
   a. Member is enrolled in a randomized, controlled trial conducted under an investigational new drug application;
   b. Member is enrolled in a National Institute of Health-supported trial.

II. Continued Therapy

A. Alzheimer's Disease (must meet all):

1. Member meets one of the following (a or b):

a. Member is enrolled in a randomized, controlled trial conducted under an investigational new drug application;
b. Member is enrolled in a National Institute of Health-supported trial.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
CMS: Centers of Medicare and Medicaid Services
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s): none
- Boxed warning(s): amyloid related imaging abnormalities

Appendix D: Diagnosis of Alzheimer's disease
- Alzheimer's disease
  - Interference with ability to function at work or at usual activities
  - A decline from a previous level of functioning and performing
  - Not explained by delirium or major psychiatric disorder
  - Cognitive impairment established by history-taking from the patient and a knowledgeable informant; and objective bedside mental status examination or neuropsychological testing
  - Cognitive impairment involves a minimum of two of the following domains:
    - Impaired ability to acquire and remember new information
    - Impaired reasoning and handling of complex tasks, poor judgment
    - Impaired visuospatial abilities
    - Impaired language functions (speaking, reading, writing)
    - Changes in personality, behavior, or comportment
  - Insidious onset (gradual onset over months to years, not over hours to days)
  - Clear-cut history of worsening
  - Initial and most prominent cognitive deficits are one of the following:
    - Amnestic presentation (impairment in learning and recall of recently learned information)
    - Non-amnestic presentation in either a language presentation (prominently word-finding deficits), a visuospatial presentation with visual deficits, or executive dysfunction (prominently impaired reasoning, judgment and/or problem solving)
  - No evidence of substantial concomitant cerebrovascular disease, core features of dementia with DLB, prominent features of behavioral variant FTD or prominent

features of semantic or nonfluent/agrammatic variants of primary progressive aphasia (PPA), or evidence of another concurrent, active neurologic or non-neurologic disease or use of medication that could have a substantial effect on cognition

- Mild cognitive impairment due to Alzheimer's disease – core clinical criteria
  - Concern regarding change in cognition obtained from the patient, from an informant who knows the patient well, or from a skilled clinician observing the patient
  - Objective evidence of impairment in one or more cognitive domains that is not explained by age or education
  - Preservation of independence in functional abilities
  - Impairments do not meet criteria for dementia

Appendix E: Discontinuation of Aduhelm

- Aduhelm received accelerated approval from the FDA in June 2021. Biogen considered the time and investment required for the post-marketing confirmatory ENVISION study, a requirement of FDA accelerated approval, and the likely advancements in the field by the time of potential Aduhelm FDA traditional approval. Consequently, Biogen announced it will reprioritize its resources, continue to advance Leqembi® (lecanemab-irmb), and accelerate development of potential new treatment modalities. The company will discontinue the development and commercialization of Aduhelm and will terminate the ENVISION clinical study. This decision is not related to any safety or efficacy concerns. Patients currently receiving Aduhelm will have access to the drug via the commercial route until November 1, 2024.

V. Dosage and Administration

<table>
<tr><th>Indication</th><th>Dosing Regimen</th><th>Maximum Dose</th></tr>
<tr><td>Alzheimer's disease</td><td>Initial dose should be titrated up as shown below:
<table>
<tr><th>IV infusion (every 4 weeks)</th><th>Aduhelm dosage (administered over approximately one hour)</th></tr>
<tr><td>Infusion 1 and 2</td><td>1 mg/kg</td></tr>
<tr><td>Infusion 3 and 4</td><td>3 mg/kg</td></tr>
<tr><td>Infusion 5 and 6</td><td>6 mg/kg</td></tr>
<tr><td>Infusion 7 and beyond</td><td>10 mg/kg</td></tr>
</table>
After an initial titration, the recommended maintenance dose is 10 mg/kg intravenously over approximately one hour every four weeks, and at least 21 days apart.</td><td>10 mg/kg every 21 days</td></tr>
</table>

VI. Product Availability

Vial for injection (single-dose): 170 mg/1.7 mL, 300 mg/3 mL

VII. References

1. Aduhelm Prescribing Information. Cambridge, MA: Biogen, Inc.; August 2023. Available at: https://www.biogencdn.com/us/aduhelm-pi.pdf. Accessed January 11, 2024.

2. Centers for Medicare & Medicaid Services. Monoclonal antibodies directed against amyloid for the treatment of Alzheimer's disease. Medicare Coverage Database. CAG-00460N; 2022. Available at: https://www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=N&ncaid=305. Accessed February 6, 2024.
3. ClinicalTrials.gov. 221AD301 Phase 3 Study of Aducanumab (BIIB037) in Early Alzheimer's Disease (ENGAGE). Available at: https://clinicaltrials.gov/ct2/show/NCT02477800. Accessed February 6, 2024.
4. ClinicalTrials.gov. 221AD302 Phase 3 Study of Aducanumab (BIIB037) in Early Alzheimer's Disease (EMERGE). Last updated May 6, 2021. Available at: https://clinicaltrials.gov/ct2/show/NCT02484547. Accessed February 6, 2024.
5. Peripheral and Central Nervous System (PCNS) Drugs Advisory Committee Meeting. Combined FDA and Applicant PCNS Drugs Advisory Committee Briefing Document. November 6, 2020. Available at: https://www.fda.gov/advisory-committees/advisory-committee-calendar/november-6-2020-meeting-peripheral-and-central-nervous-system-drugs-advisory-committee-meeting#event-materials. Accessed February 16, 2022
6. Institute for Clinical and Economic Review: Final Evidence Report and Meeting Summary - Aducanumab for Alzheimer's disease: Effectiveness and Value. August 5, 2021. Available at: https://icer.org/wp-content/uploads/2020/10/ICER_ALZ_Final_Report_080521.pdf. Accessed February 16, 2022.
7. Biogen press release. Biogen to realign resources for Alzheimer's disease franchise. Available at: https://investors.biogen.com/news-releases/news-release-details/biogen-realign-resources-alzheimers-disease-franchise. Accessed February 6, 2024.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

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

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created preemptively.	02.25.20	05.20
2Q 2021 annual review: added requirement for beta-amyloid plaque verification via diagnostic method as aducanumab has only shown efficacy in patients diagnosed with beta amyloid plaques; modified prescriber restriction to remove "in consultation with" and specify "geriatric" psychiatrist; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	02.16.21	05.21
RT1: drug is now FDA-approved – criteria updated per FDA labeling; added MRI requirements prior to initial, 7th, and 12th doses, added initial titration dosing requirement; divided continued therapy approval durations to allow verification of MRI scans prior to the 7th	06.22.21	08.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
and 12 doses, increased the minimum age to 50 years old, added exclusion criteria related to current use of blood thinners or recent brain hemorrhage, bleeding disorder, and cerebrovascular abnormalities in the last 6 months; references reviewed and updated.		
Updated FDA Approved Indication per updated PI to reflect that Aduhelm should be initiated in the patient population that was studied the in the clinical trials; allowed up to 325 mg of ASA.	07.12.21	
Removed Commercial line of business (separate Commercial policy created; see CP.CPA.356); revised policy to state Aduhelm can be obtained under coverage with evidence development.	04.19.22	05.22
2Q 2023 annual review: no significant changes; references reviewed and updated.	02.03.23	05.23
2Q 2024 annual review: added reference to the planned market withdrawal by November 1, 2024, and accompanying information in Appendix E; updated Appendix C with boxed warning; references reviewed and updated.	01.11.24	05.24

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan

retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.