Clinical Policy: Aducanumab-avwa (Aduhelm)

Reference Number: PA.CP.PHAR.468
Effective Date: 06/2021
Last Review Date: 04/2025

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, has discontinued Aduhelm to reprioritize its resources** (*see Appendix G*)

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 PA Health & Wellness® that Aduhelm is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria*

**The manufacturer has discontinued Aduhelm (see Appendix G).*

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

1. Diagnosis of Alzheimer's disease (*see Appendix E*);
2. Prescribed by a neurologist or geriatric psychiatrist;
3. Age ≥ 50 years;
4. Presence of beta-amyloid plaques verified by positron emission tomography (PET) scan;
5. Documentation of recent (within the last year) brain magnetic resonance imaging (MRI) demonstrating all of the following (a, b, and c):
   a. No localized superficial siderosis;
   b. Less than 10 brain microhemorrhages;
   c. No brain hemorrhage > 1 cm within the past year;
6. Objective evidence of cognitive impairment at screening (*see Appendix F*);
7. Clinical Dementia Rating-Global Score (CDR-GS) of 0.5;
8. Mini-Mental State Exam (MMSE) score ≥ 24;
9. Member is currently not taking any blood thinners, except aspirin ≤ 81 mg;
10. Member has not had any brain hemorrhage, bleeding disorder, or cerebrovascular abnormalities in the last 6 months;
11. All of the following causes of dementia have been ruled out:
    a. Vascular dementia;

b. Lewy body dementia (DLB);
c. Frontotemporal dementia (FTD);
d. Parkinson's disease dementia;

12. Member does not have poorly controlled diabetes mellitus;
13. Dose does not exceed the following (must meet all):
    a. Infusion 1 and 2: 1 mg/kg per 4 weeks;
    b. Infusion 3 and 4: 3 mg/kg per 4 weeks;
    c. Infusion 5 and 6: 6 mg/kg per 4 weeks.

Approval duration: 6 months (6 doses of infusion only)

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy*

**The manufacturer has discontinued Aduhelm (see Appendix G)*

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy as evidenced by slowed decline in cognition as evidenced by improvement in the following (a and b):
    a. Mini-Mental State Exam (MMSE);
    b. Clinical Dementia Rating-Global Score (CDR-GS);
3. Prescribed by a neurologist or geriatric psychiatrist;
4. Member was monitored and assessed every 3 months by prescribing specialist;
5. Member will continue to be monitored and assessed every 3 months by prescribing specialist;
6. Member has not had a history of stroke or TIA or unexplained loss of consciousness in the past year;
7. Member does not have poorly controlled diabetes mellitus;
8. Member is currently not taking any blood thinners, except aspirin ≤ 81 mg;
9. Prior to the 7th and 12th infusion, documentation of recent (within the last month) brain MRI showing one of the following (a or b):
    a. Less than 10 new incident microhemorrhages and less than 2 focal areas of superficial siderosis;
    b. Radiographic stabilization since baseline (i.e., no increase in size or number of ARIA-H);
10. If request is for a dose increase, new dose does not exceed 10 mg/kg once every 4 weeks.

Approval duration:

- **Members with < 7 total infusions: up to the 6th total infusion**
- **Members with < 12 total infusions but > 7 total infusions: up to the 11th total infusion**
- **Members with > 12 total infusions: 6 infusions per PA approval**

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

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 – PA.CP.PMN.53

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
CDR-GS: Clinical Dementia Rating – global score
CMS: Centers of Medicare and Medicaid Services
CSF: cerebrospinal fluid
DLB: Lewy body dementia
FTD: frontotemporal dementia
MMSE: Mini-Mental State Exam
MRI: magnetic resonance imaging
PET: positron emission tomography

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none
- Boxed warning(s): amyloid related imaging abnormalities

Appendix D: Dementia Rating Scales

- CDR-GS is useful for characterizing and tracking a patient's level of impairment/ dementia:
  - 0 = normal
  - 0.5 = very mild dementia
  - 1 = mild dementia
  - 2 = moderate dementia
  - 3 = severe dementia
- Clinical Dementia Rating Sum of Boxes (CDR-SB) assessment is a 5-point scale used to characterize six domains of cognitive and functional performance applicable to Alzheimer disease and related dementias: Memory, Orientation, Judgment & Problem Solving, Community Affairs, Home & Hobbies, and Personal Care. The information is obtained through an interview of the patient and a reliable informant (e.g., family member). This score is useful for characterizing and tracking a patient's level of impairment/dementia.
  - 0 suggests normal
  - 0.5 to 4 suggests questionable cognitive impairment
  - 0.5 to 2.5 suggests questionable impairment
  - 3.0 to 4.0 suggests very mild dementia
  - 4.5 to 9.0 suggests mild dementia

  - 9.5 to 15.5 suggests moderate dementia
  - 16.0 to 18.0 suggests severe dementia
- MMSE is a series of questions asked by a health professional designed to test a range of everyday mental skills. The maximum score is 30 points where the following levels of dementia are indicated and a score of:
  - 25 to 30 suggest normal cognition,
  - 20 to 24 suggests mild dementia,
  - 13 to 20 suggests moderate dementia, and
  - less than 12 indicates severe dementia.
  - On average, the MMSE score of a person with Alzheimer's declines about two to four points each year.
- The Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS-Cog 13) is the standard cognitive scale used to measure neuropsychological changes in Alzheimer's disease clinical trials. A 4-point change is generally considered as indicating a clinically meaningful difference.

Appendix E: 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)
    - Nonamnestic 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 F: Objective Evidence of Cognitive Impairment

- Cognitive impairment is established by history-taking from the patient and a knowledgeable informant, along with validated cognitive assessment instruments:
  - Evidence of memory impairment
  - Evidence of impairment in one or more cognitive domains that is not explained by age or education
  - Evidence of language presentation, with prominent word-finding deficits; a visuospatial presentation, with visual cognitive deficits; or a dysexecutive presentation, with prominent impairment of reasoning, judgment, and/or problem solving
  - AD Assessment Scale-Cognitive Subscale (13 items) [ADAS-Cog 13]
  - AD Cooperative Study-Activities of Daily Living Inventory (Mild Cognitive Impairment version) [ADCS-ADL-MCI]

Appendix G: 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</td><td>10 mg/kg every 21 days</td></tr>
</table>

Indication	Dosing Regimen	Maximum Dose
	approximately one hour every four weeks, and at least 21 days apart.	

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 June 10, 2021.
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
Policy created	06/2021
2Q 2022 annual review: updated to more closely align with DPS policy	04/2022

Reviews, Revisions, and Approvals	Date
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.	04/2023
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.	04/2024
2Q 2025 annual review: no significant changes; retained policy since Medispan obsolete date is 11/12/2026 and added discontinuation statement to initial and continued criteria.	04/2025