Clinical Policy: Aducanumab-avwa (Aduhelm)

Reference Number: CP.CPA.356
Effective Date: 06.01.22
Last Review Date: 05.24
Line of Business: Commercial

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 D*)

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 is **not medically necessary** for its FDA-approved indication:

I. Aduhelm is not medically necessary for the treatment of Alzheimer's disease in patients with mild cognitive impairment or mild dementia stage of the disease for the following reasons:

A. Aduhelm does not have proven efficacy in the treatment of Alzheimer's Disease.

1. Phase 3 clinical trials have shown discordant results. In its second phase 3 study (Study 2), no statistically significant differences were observed between the Aduhelm-treated arm and the placebo arm on the primary efficacy endpoint of change from baseline in the clinical dementia rating scale-sum of boxes (CDR-SB) score at Week 78.
2. Phase 3 studies were terminated due to a declaration of futility. Both Study 1 and Study 2 were terminated in March 2019 following an interim analysis by independent monitors which concluded that the drug was unlikely to benefit patients.
3. Post-hoc analysis results do not show clinically meaningful results. The analysis showed a small treatment difference of 0.39 points in CDR-SB and 0.6 points in MMSE, which is not considered clinically meaningful. Furthermore, post-hoc analyses are not appropriate for concluding causality of benefit.

4. The Centers of Medicare and Medicaid Services (CMS) National Coverage Analysis for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease concluded that current evidence is insufficient to determine that use of Aduhelm is reasonable and necessary for the treatment of Alzheimer's disease. CMS still recognizes the importance and current unmet need for a safe and effective treatment for Alzheimer's disease, and has proposed Coverage with Evidence Development, allowing Medicare coverage in either CMS-approved randomized controlled trials or trials supported by the National Institute of Health.

B. Aduhelm does not have proven safety in the treatment of Alzheimer's Disease.

1. In the clinical trials, a significantly higher number of amyloid-related imaging abnormality related to edema/effusion, microhemorrhages, hemosiderin deposits, and superficial siderosis of the central nervous system was observed in the treatment arm compared to the placebo arm. There is insufficient evidence to support that clinical benefits outweigh these potential harms of Aduhelm treatment.

II. 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: 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 and continue to advance Leqembi® (lecanemab-irmb) and will 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.

III. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Alzheimer's disease	Initial dose should be titrated up as shown below:	10 mg/kg every 21 days

Indication	Dosing Regimen		Maximum Dose
	IV infusion (every 4 weeks)	**Aduhelm dosage (administered over approximately one hour)**	
	Infusion 1 and 2	1 mg/kg	
	Infusion 3 and 4	3 mg/kg	
	Infusion 5 and 6	6 mg/kg	
	Infusion 7 and beyond	10 mg/kg	
	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.		

IV. Product Availability

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

V. References

1. Aduhelm Prescribing Information. Cambridge, MA: Biogen, Inc.; August 2023. Available at: https://www.biogencdn.com/us/aduhelm-pi.pdf. Accessed January 09, 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 for Commercial line of business (adopted from CP.PHAR.468); revised to state Aduhelm is not medically necessary based on current available evidence.	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 D; updated Appendix C with boxed warning; references reviewed and updated.	01.09.23	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.

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