Drug Coverage Policy

Effective Date 9/1/2024
Coverage Policy Number.....IP0200
Policy Title.....Aduhelm

Neurology – Aduhelm

- Aduhelm® (aducanumab-avwa intravenous infusion – Biogen)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Cigna Healthcare Coverage Policy

Aduhelm, an amyloid beta-directed antibody, is indicated for the **treatment of Alzheimer's disease**.[1]

This indication is approved under accelerated approval based on reduction in amyloid beta plaques observed in patients treated with Aduhelm.[1] Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trial(s).

Disease Overview
An estimated 6.9 million Americans ≥ 65 years of age are living with Alzheimer's dementia in 2024, with 73% of these people ≥ 75 years of age.[2] The number and proportion of older adults who have mild cognitive impairment due to Alzheimer's disease is difficult to estimate; however, a rough approximation suggests that 5 to 7 million older Americans may have mild cognitive

impairment due to Alzheimer's disease. People with mild cognitive impairment due to Alzheimer's disease have biomarker evidence of brain changes due to the disease in addition to subtle problems with memory and thinking. Biomarker evidence includes abnormal levels of amyloid beta as evidenced on positron emission tomography (PET) scans and in analysis of cerebrospinal fluid, and decreased metabolism of glucose as shown on PET scans. These cognitive problems may be noticeable to the individual family members and friends, but not to others, and they do not interfere with the person's ability to carry out everyday activities. The mild changes in cognitive abilities occur when the brain can no longer compensate for the damage and death of nerve cells due to Alzheimer's disease.

Clinical Efficacy
The current Aduhelm efficacy information is insufficient to determine if the medication demonstrates any clinically meaningful benefits. In the absence of additional clinical trials, there is not enough information to support approval.

Due to the lack of clinical efficacy data and safety concerns, **approval is not recommended** for Aduhelm. The current Aduhelm efficacy information is insufficient to determine if the medication demonstrates any clinically meaningful benefits; whereas, safety concerns have been demonstrated in clinical trials. In the absence of additional clinical trials, there is not enough information to support approval.

Conditions Not Covered

Aducanumab (Aduhelm) is considered to be experimental, investigational, or unproven due to insufficient data establishing safety, efficacy, and improved health outcomes for any condition, including the following:

1. **Alzheimer's Disease.** Due to the lack of clinical efficacy data, approval is not recommended for Aduhelm. The prescribing information for Aduhelm states that it was approved under accelerated approval based on reduction in amyloid beta plaques observed in patients treated with Aduhelm.[1] FDA has required a randomized, controlled trial evaluation post-marketing to establish efficacy of Aduhelm. Results are expected in 2030.

   Two identical, Phase III, double-blind, placebo-controlled, randomized trials of high- and low-dose Aduhelm (ENGAGE and EMERGE) were conducted in patients with Alzheimer's disease (patients with confirmed presence of amyloid pathology and mild cognitive impairment or mild dementia stage of disease).[1,3] Approximately halfway through the two Phase III studies, a planned interim analysis met prespecified futility criteria and the trials were terminated prior to completion. A post-hoc analysis of the trials revealed that EMERGE did reach statistical significance on its primary efficacy endpoint, estimating a high-dose treatment effect corresponding to a 22% relative reduction in the Clinical Dementia Rating–Sum of Boxes (CDR-SB) score compared with placebo (P = 0.01). Efficacy was not demonstrated in the low-dose arm of EMERGE or in either treatment arm of ENGAGE. Of note, the minimum clinically important difference for the primary endpoint of CDR-SB is generally considered to be 1 to 2 on a scale from 0 to 18.[4] The 22% reduction in CDR-SB detected in the high-dose arm in EMERGE reflected an absolute difference of 0.39, which does not qualify as clinically significant.

   Aduhelm can cause amyloid related imaging abnormalities-edema (ARIA-E) and amyloid related imaging abnormalities-hemosiderin deposition (ARIA-H), which includes microhemorrhage and superficial siderosis, which can be observed on magnetic resonance imaging (MRI).[1] A recent (within 1 year) MRI of the brain should be obtained prior to initiating treatment with Aduhelm. The safety of Aduhelm in patients with any pre-treatment localized superficial siderosis, ten or

more brain microhemorrhages, and/or with a brain hemorrhage > 1 cm within one year of treatment initiation has not been established. Enhanced clinical vigilance for asymptomatic amyloid related imaging abnormalities (ARIA) is recommended during the first eight doses of treatment with Aduhelm, particularly during titration, because the majority of ARIA was observed during this time. MRIs of the brain should be obtained prior to the seventh infusion (first dose of 10 mg/kg) and 12th infusion (sixth dose of 10 mg/kg) of Aduhelm to evaluate for the presence of asymptomatic ARIA. If ten or more new incident microhemorrhages or greater than two focal areas of superficial siderosis (radiographic severe ARIA-H) are observed, treatment may be continued with caution only after a clinical evaluation and a follow-up MRI demonstrate radiographic stabilization (i.e., no increase in size or number of ARIA-H).

Coding / Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Experimental/Investigational/Unproven:

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

References

1. Aduhelm® intravenous infusion [prescribing information]. Cambridge, MA: Biogen; August 2023.
2. Alzheimer's Association. Alzheimer's disease facts and figures-2024. Available at: https://www.alz.org/media/Documents/alzheimers-facts-and-figures.pdf. Accessed on June 6, 2024.
3. Budd Haeberlein S, Aisen PS, Barkhof F, et al. Two randomized phase 3 studies of aducanumab in early Alzheimer's Disease. *J Prev Alzheimers Dis*. 2022;2(9):197-210.
4. Alexander GC, Emerson S, Kesselheim AS. Evaluation of aducanumab for Alzheimer Disease scientific evidence and regulatory review involving efficacy, safety, and futility. *JAMA*. 2021;325(17):1717-1718.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	**Conditions Not Covered.** **Updated** from 'Alzheimer's disease, mild cognitive impairment or dementia stage of disease' and 'Alzheimer's disease, moderate or severe cognitive impairment or dementia stage of disease' into single Alzheimer's Disease aggregate. **Updated** title from 'Aducanumab' to 'Neurology – Aduhelm'	9/1/2024

The policy effective date is in force until updated or retired.