VENTURA COUNTY
HEALTH CARE PLAN

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Neurology – Aduhelm Utilization Management Medical Policy
- Aduhelm® (aducanumab-avwa intravenous infusion – Biogen/Eisai)

REVIEW DATE: 06/12/2024

OVERVIEW

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.

POLICY STATEMENT

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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

None.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Aduhelm is not recommended in the following situations:

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).

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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.

HISTORY

Type of Revision	Summary of Changes	Review Date

Annual Revision	No criteria changes.	06/07/2023
Annual Revision	No criteria changes.	06/12/2024