Reference number(s)
4777-A

STANDARD MEDICARE PART B MANAGEMENT

ADUHELM (aducanumab-avwa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Aduhelm is an amyloid beta-directed antibody 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 disease, the population in which treatment was initiated in clinical trials. There are no safety or effectiveness data on initiating treatment at earlier or later stages of the disease than were studied. 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).

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

II. DOCUMENTATION

The following documentation must be available, upon request, for all submissions:
A. Initial requests:
   1. Medical records (e.g., chart notes) documenting the following:
      i. Diagnosis of mild cognitive impairment due to Alzheimer's disease or mild Alzheimer's disease.
   2. Presence of amyloid pathology documented by either of the following:
      i. Baseline positron emission tomography (PET) scan
      ii. Lumbar puncture results
   3. Current enrollment in a randomized controlled trial conducted under an investigational new drug (IND) application or National Institutes of Health (NIH)-supported trial.
B. Continuation requests:
   1. Continued enrollment in a randomized controlled trial conducted under an investigational new drug (IND) application or National Institutes of Health (NIH)-supported trial.

III. CRITERIA FOR INITIAL APPROVAL

Alzheimer's Disease

Authorization of 6 months may be granted for treatment of Alzheimer's disease (AD) when all of the following criteria are met:

A. Member must have mild cognitive impairment due to AD or mild AD dementia.
B. Member must meet one of the following criteria:
    1. Have a positron emission tomography (PET) scan confirming the presence of amyloid pathology.
    2. Have results from a lumbar puncture confirming at least one of the following detected in cerebrospinal fluid (CSF) as determined by the lab assay:
        i. Presence of elevated phosphorylated tau (P-tau) protein and/or total tau (T-tau) protein, and reduced beta amyloid-42 (AB42)
        ii. Low AB42/AB40 ratio
        iii. Elevated P-Tau/AB42 ratio
        iv. Elevated T-Tau/AB42 ratio
C. Member must currently be enrolled in a randomized controlled trial conducted under an investigational new drug (IND) application or National Institutes of Health (NIH)-supported trial.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

Authorization of 6 months may be granted when all of the following criteria are met:

A. The member is currently receiving therapy with Aduhelm.
B. Aduhelm is being used to treat an indication enumerated in Section III.
C. The member continues to be enrolled in a randomized controlled trial conducted under an investigational new drug (IND) application or National Institutes of Health (NIH)-supported trial.

V. SUMMARY OF EVIDENCE

The contents of this policy were created after examining the following resources:

1. The prescribing information for Aduhelm.
2. The available compendium
    a. Micromedex DrugDex
    b. American Hospital Formulary Service- Drug Information (AHFS-DI)
    c. Lexi-Drugs
    d. Clinical Pharmacology
3. National Coverage Determination (NCD) for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Aduhelm are covered.

VI. EXPLANATION OF RATIONALE

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Using Aduhelm to treat mild cognitive impairment due to Alzheimer's disease or mild Alzheimer's disease (AD) dementia is covered according to the conditions outlined in National Coverage Determination Manual section 200.3- Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease. Monoclonal

antibodies directed against amyloid that are approved by the FDA for the treatment of AD based upon evidence of efficacy from a direct measure of clinical benefit may be covered in CMS-approved prospective comparative studies. Study data for CMS-approved prospective comparative studies may be collected in a registry.

VII. REFERENCES

1. Aduhelm [package insert]. Cambridge, MA: Biogen; February 2023.
2. National Coverage Determination (NCD) for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease (AD) (200.3 – Version 1). https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?ncdid=375&ncdver=1 Accessed May 4, 2023.
3. Fagan AM, Mintun MA, Mach RH, et al. Inverse relation between in vivo amyloid imaging load and cerebrospinal fluid Abeta42 in humans. Ann Neurol. 2006;59(3):512-519.
4. Schindler SE, Gray JD, Gordon BA, et al. Cerebrospinal fluid biomarkers measured by Elecsys assays compared to amyloid imaging. *Alzheimers Dement*. 2018;14(11):1460-1469.
5. Elecsys Phospho-Tau (181P) CSF 2022-12.