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** Please note: The Clinical Coverage Guideline (CCG) is intended to supplement certain standard Alignment Health (Alignment) benefit plans and aid in administering benefits. Federal and state law, contract language, etc. take precedence over the CCG (e.g., Centers for Medicare and Medicaid Services [CMS] National Coverage Determinations [NCDs], Local Coverage Determinations [LCDs] or other published documents). The terms of a member's particular Benefit Plan, Evidence of Coverage, Certificate of Coverage, etc., may differ significantly from this Coverage Position. Providers are responsible for the treatment and recommendations provided to the member. The application of the CCG is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations, and any state-specific mandates. Information is current at time of approval by the Quality Improvement Committee (QIC) and are subject to change.*

AHC Aducanumab (Aduhelm)

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MCG Health
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Clinical Indications

- Aduhelm may be covered for the treatment of Alzheimers Disease (AD) if ALL of the following are met:
 - Member is appropriate for treatment, as indicated by ALL of the following:
 - Member is 50 years of age or older: OR
 - If less than 50 years of age, member has a genetic mutation in amyloid precursor protein (APP), presenilin-1 (PSEN1), or presenilin-2 (PSEN2), or other clinical documentation to support early onset AD; AND
 - Member has mild cognitive impairment due to AD or mild AD dementia; AND
 - Member has objective evidence of cognitive impairment at baseline using any of the following assessment tools:
 - Montreal Cognitive Assessment (MoCA) score of greater than or equal to 16; OR
 - Mini-Mental State Examination (MMSE) score of 21-30; OR
 - Clinical Dementia Rating-Global Score (CDR-GS) of 0.5 or 1; AND
 - Confirmed presence of amyloid beta pathology consistent with AD, as indicated by ALL of the following:
 - Member meets one of the following criteria:
 - Have a PET [positron emission tomography] scan confirming the presence of amyloid pathology; OR
 - Have lumbar puncture results confirming the presence of elevated phosphorylated tau (P-tau) protein and/or elevated total tau (T-tau) protein, and reduced beta amyloid-42 (AB42) OR a low AB42/AB40 ratio as determined by the lab assay detected in cerebrospinal fluid (CSF); AND
 - Member has a recent brain MRI [magnetic resonance imaging] within one year prior to initiating treatment to evaluate for pre-existing Amyloid Related Imaging Abnormalities (ARIA)
 - Member must be enrolled in a randomized controlled trial conducted under an investigational new drug (IND) application or National Institutes of Health (NIH)-supported trial.
- Aduhelm is not covered outside of FDA-approved randomized controlled trials, Centers for Medicare and Medicaid Services-approved studies, or National Institutes of Health-supported studies.

Evidence Summary

In June 2021, aducanumab (Aduhelm; Biogen) was approved by the U.S. FDA for treatment of Alzheimer disease. This indication was approved under accelerated approval based on reduction in A- β plaques observed in patients treated with aducanumab. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trial(s).

In July 2021, FDA amended the approved label to emphasize the disease stages studied in the clinical trials. The amended label states, "Treatment with aducanumab 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."

The FDA, under the accelerated approval regulations (21 CFR 601.41), requires that Biogen conduct a randomized, controlled trial to evaluate the efficacy of aducanumab-avwa compared to an appropriate control for the treatment of Alzheimer disease. The trial should be of sufficient duration to observe changes on an acceptable endpoint in the patient population enrolled in the trial. The expected date of trial completion is August 2029 and final report submission to the FDA by February 2030.

For individuals with early Alzheimer disease (mild cognitive impairment [MCI] or mild dementia due to Alzheimer disease) who receive aducanumab, the evidence includes 2 randomized controlled trials (RCTs) and 1 dose-finding and proof of concept phase I trial. Approval by the FDA was based on the reduction in A- β plaques, which was observed in both trials and at all doses. However, there are no satisfactory data clearly establishing that individual changes in amyloid correlate with or predict long term cognitive and functional changes. In the absence of clinical data convincingly demonstrating a clinical effect, it cannot be concluded that the observed reduction in amyloid will translate into a clinical benefit to patients. Cognitive decline in early Alzheimer disease generally occurs over years, and thus the follow-up duration may not be sufficient to conclude whether a drug is effective for this disease or whether the safety profile might change with longer follow-up. Pooled safety data showed that about 35% of patients on aducanumab experienced amyloid-related imaging abnormalities (ARIA) as well an increase in the risk of falling. A confirmatory, prospective and adequately powered trial is necessary to assess the net health benefit of aducanumab in patients with early Alzheimer disease. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome

Committee Approval

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References

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Codes

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