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 trials.

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. Genetic testing results documenting a mutation in amyloid precursor protein (*APP*), presenilin-1 (*PSEN1*), or presenilin-2 (*PSEN2*), if applicable.
   2. Clinical documentation to support early onset Alzheimer's disease, if applicable.
   3. 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.
      ii. Baseline assessments for any of the following assessment tools:
         a. Clinical Dementia Rating (CDR)-Global Score
         b. Mini-Mental Status Exam (MMSE)
         c. Montreal Cognitive Assessment (MoCA)
   4. Baseline positron emission tomography (PET) scan confirming the presence of amyloid pathology, if applicable.
   5. Lumbar puncture results confirming the presence of elevated phosphorylated tau (P-tau) protein and reduced beta amyloid-42 (AB42) OR low AB42/AB40 ratio, if applicable.
   6. Recent (within one year) brain magnetic resonance imaging (MRI) prior to initiating treatment.

B. Continuation requests (where applicable):
   1. Medical records (e.g., chart notes) of the most recent (less than 1 month prior to continuation request) assessment tool for any of the following:
      i. Clinical Dementia Rating (CDR)-Global Score
      ii. Mini-Mental Status Exam (MMSE)
      iii. Montreal Cognitive Assessment (MoCA)

2. Brain magnetic resonance imaging (MRI) results prior to the 7th dose (first dose of 10 mg/kg) and 12th dose (sixth dose of 10 mg/kg), where applicable.

III. EXCLUSIONS

Coverage will not be provided for members with any of the following conditions:
A. Suspected neurodegenerative etiology of cognitive impairment other than Alzheimer's disease (AD), including but not limited to frontotemporal lobar degeneration (FTLD) or Lewy body disease (i.e., meeting consensus criteria for possible or probable dementia with Lewy bodies).
B. Requirement for therapeutic anticoagulation (e.g., anticoagulants, antiplatelets), except for aspirin at a prophylaxis dose or less (no more than 325mg daily).

IV. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a gerontologist, neurologist, psychiatrist, or neuropsychiatrist.

V. 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 meet one of the following criteria:
   1. Member is 50 years of age or older
   2. 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.
B. Member must have mild cognitive impairment due to AD or mild AD.
C. Member must have objective evidence of cognitive impairment at baseline (Appendix A).
D. Member must have one of the following scores at baseline on any of the following assessment tools:
   1. Clinical Dementia Rating (CDR)-Global Score of 0.5 or 1 (Appendix B).
   2. Mini-Mental Status Exam (MMSE) score of 21 - 30 (Appendix C).
   3. Montreal Cognitive Assessment (MoCA) score of greater than or equal to 12 (Appendix D).
E. Member must meet one of the following criteria:
   1. Have a positron emission tomography (PET) scan confirming the presence of amyloid pathology.
   2. If an amyloid PET scan is unavailable, member must have results from a lumbar puncture confirming the presence of elevated phosphorylated tau (P-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).
F. Member must have a recent brain magnetic resonance imaging (MRI) within one year prior to initiating treatment.

VI. 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 (first reauthorization after initial 6-month approval period) 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 V.
C. The member has been evaluated for evidence of severe amyloid-related imaging abnormalities (ARIA) on MRI prior the 7th dose (first dose of 10 mg/kg) (Appendix E). If 10 or more new incident microhemorrhages or > 2 focal areas of superficial siderosis (radiographic severe ARIA-H) is observed, treatment may be continued with caution only after a clinical evaluation and a follow-up MRI demonstrates radiographic stabilization (i.e., no increase in size or number of ARIA-H).

Authorization of 6 months (second reauthorization) 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 V.
C. The member is receiving benefit from therapy. Benefit is defined as stabilization in score in any of the following measures:
    1. CDR-GS (i.e., score of 0.5 or 1)
    2. MMSE (i.e., score of 21 – 30)
    3. MoCA (i.e., score of greater than or equal to 12)
D. The member has been evaluated for evidence of severe amyloid-related imaging abnormalities (ARIA) on MRI prior to the 12th dose (sixth dose of 10 mg/kg) (Appendix E). If 10 or more new incident microhemorrhages or > 2 focal areas of superficial siderosis (radiographic severe ARIA-H) is observed, treatment may be continued with caution only after a clinical evaluation and a follow-up MRI demonstrates radiographic stabilization (i.e., no increase in size or number of ARIA-H).

Authorization of 12 months (reauthorizations beyond initial 18 months of therapy) 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 V.
C. The member is receiving benefit from therapy. Benefit is defined as stabilization in score in any of the following measures:
    1. CDR-GS (i.e., score of 0.5 or 1)
    2. MMSE (i.e., score of 21 – 30)
    3. MoCA (i.e., score of greater than or equal to 12)

VII. APPENDICES

Appendix A: Summary of clinical and cognitive evaluation for MCI due to AD

- Cognitive concern reflecting a change in cognition reported by patient or information or clinician (i.e. historical or observed evidence of decline over time)
- Objective evidence of impairment in one or more cognitive domains, typically including memory (i.e., formal or bedside testing to establish level of cognitive function in multiple domains)
- Preservation of independence in functional abilities
- Not demented

Appendix B: Clinical Dementia Rating (CDR) Scale

The CDR is obtained through semi-structured interviews of patients and informants with cognitive functioning rated on a 5-point scale in the following domains: memory, orientation, judgement and problem solving, community affairs, home and hobbies, and personal care. The score relates to the member's level of dementia:

- 0 = Normal
- 0.5 = Very Mild Dementia
- 1 = Mild Dementia
- 2 = Moderate Dementia

- 3 = Severe Dementia

Appendix C: Mini-Mental Status Exam (MMSE)
The MMSE is scored on a 30-point scale, with items that assess orientation (temporal and spatial; 10 points), memory (registration and recall; 6 points), attention/concentration (5 points), language (verbal and written, 8 points), and visuospatial function (1 point). The score relates to the member's level of dementia:

- 25 - 30 suggest normal cognition
- 20 – 24 suggests mild dementia
- 13 – 20 suggests moderate dementia
- Less than 12 suggests severe dementia

Appendix D: Montreal Cognitive Assessment (MoCA)
Per MoCA assessment, average scores for the following ranges are:

- Mild Cognitive Impairment: 19 – 25
- Mild Alzheimer's Disease: 11 – 21
- Normal: 26 and above

Appendix E: ARIA MRI Classification Criteria

ARIA Type	Radiographic Severity		
	Mild	Moderate	Severe
ARIA-E	FLAIR hyperintensity confined to sulcus and or cortex/subcortical white matter in one location < 5 cm	FLAIR hyperintensity 5 to 10 cm, or more than 1 site of involvement, each measuring < 10 cm	FLAIR hyperintensity measuring > 10 cm, often with significant subcortical white matter and/or sulcal involvement. One or more separate sites of involvement may be noted.
ARIA-H microhemorrhage	≤ 4 new incident microhemorrhages	5 to 9 new incident microhemorrhages	10 or more new incident microhemorrhages
ARIA-H superficial siderosis	1 focal area of superficial siderosis	2 focal areas of superficial siderosis	> 2 focal areas of superficial siderosis

VIII. REFERENCES

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