Effective: January 1, 2023

Prior Authorization Required
If REQUIRED, submit supporting clinical documentation pertinent to service request.

<table>
<thead>
<tr>
<th>Applies to:</th>
<th>Yes ☒ No ☐</th>
</tr>
</thead>
<tbody>
<tr>
<td>Commercial Products</td>
<td></td>
</tr>
<tr>
<td>☐ Harvard Pilgrim Health Care Commercial products; Fax 617-673-0988</td>
<td></td>
</tr>
<tr>
<td>☐ Tufts Health Plan Commercial products; Fax 617-673-0988</td>
<td></td>
</tr>
<tr>
<td>CareLinkSM – Refer to CareLink Procedures, Services and Items Requiring Prior Authorization</td>
<td></td>
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<tr>
<td>Public Plans Products</td>
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<tr>
<td>☐ Tufts Health Direct – A Massachusetts Qualified Health Plan (QHP) (a commercial product); Fax 617-673-0988</td>
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<tr>
<td>☐ Tufts Health Together – MassHealth MCO Plan and Accountable Care Partnership Plans; Fax 617-673-0988</td>
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<tr>
<td>☐ Tufts Health RITogether – A Rhode Island Medicaid Plan; Fax 617-673-0988</td>
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<tr>
<td>☒ Tufts Health Unify* – OneCare Plan (a dual-eligible product); Fax 617-673-0956</td>
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<tr>
<td>☒*The MNG applies to Tufts Health Unify members unless a less restrictive LCD or NCD exists.</td>
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<tr>
<td>Senior Products</td>
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<tr>
<td>☒ Harvard Pilgrim Health Care Stride Medicare Advantage; Fax 617-673-0956</td>
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<tr>
<td>☒ Tufts Health Plan Senior Care Options (SCO), (a dual-eligible product); Fax 617-673-0956</td>
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<tr>
<td>☒ Tufts Medicare Preferred HMO, (a Medicare Advantage product); Fax 617-673-0956</td>
<td></td>
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<tr>
<td>☒ Tufts Medicare Preferred PPO, (a Medicare Advantage product); Fax 617-673-0956</td>
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Note: While you may not be the provider responsible for obtaining prior authorization, as a condition of payment you will need to ensure that prior authorization has been obtained.

Overview

Alzheimer’s disease (AD) is a currently irreversible brain disorder that progressively degrades memory, cognitive function, and ability to carry out tasks of daily living. AD is the number one cause of dementia in older Americans, contributing to 60-80% of cases. Over 6 million older Americans are believed to have AD. This prevalence is expected to rise to 14 million by 2060 barring effective interventions (such as lifestyle changes, treatment of risk factors, and possibly combinations of Alzheimer’s drugs). AD is the sixth leading cause of death in the United States but may rank from fifth to as high as third (after heart disease and cancer) as a cause of death for older Americans. Women are more likely to have AD than men, although this is in part because women live longer. (AA 2021, NIA 2021, CDC 2021, Rajan 2021, Brookmeyer 2018, 2019.) Most individuals with AD become symptomatic after age 65. Alzheimer’s can be fatal anywhere between 2 and 20 years of symptom onset, but 8 years on average (in those with onset before age 75 years). However, pathophysiologic changes in the brain (including amyloid-beta [Aβ] plaques and neurofibrillary tangles of tau) may be evident up to decades before symptoms occur. Among 70-year-olds, 61% of those with AD die within a decade (compared to only 30% of those without AD). However, most persons who have evidence of AD pathology but are asymptomatic will not develop AD dementia during their lifetimes. (Ganguli 2005, Brookmeyer 2018, AA 2021, Dilworth 2008, Sperling 2011, CMS 2013, Jack 2010).

Food and Drug Administration (FDA) Approved Indications:

- Aduhelm™ (aducanumab-avwa) is an IgG1 human monoclonal anti-amyloid beta antibody indicated for the treatment of patients with Alzheimer disease (AD) exhibiting mild cognitive impairment or mild dementia. The rationale for the use of Aduhelm™ (Aducanumab-avwa) is based on the hypothesis that the accumulation of amyloid beta is a main driver of AD. The deposition of amyloid beta plaques in the brain occurs before the onset of clinical symptoms and dementia. Aduhelm™ (aducanumab-awwa) has been shown to reduce the accumulation of amyloid beta, thus potentially slowing disease progression.
Nationally Covered Indication(s):
The Centers for Medicare & Medicaid Services (CMS) issued a National Coverage Determination (NCD for monoclonal antibodies directed against amyloid for the treatment of Alzheimer’s disease (AD). The NCD utilizes a Coverage with Evidence Development (CED) to establish a dual coverage pathway for individuals with mild cognitive impairment (MCI) due to AD or mild AD dementia, both with confirmed presence of amyloid beta pathology consistent with AD to be covered according to their FDA approval pathway:

- If approved by the FDA based upon evidence of efficacy from a change in a surrogate endpoint (e.g., amyloid reduction) considered as reasonably likely to predict clinical benefit, the drug may be covered in a randomized controlled trial conducted under an investigational new drug (IND) application.
- If approved by the FDA based upon evidence of efficacy from a direct measure of clinical benefit, the drug may be covered in CMS approved prospective comparative studies.

The Centers for Medicare & Medicaid Services (CMS) proposes to cover FDA approved monoclonal antibodies directed against amyloid for the treatment of Alzheimer’s disease (AD) under Coverage with Evidence Development (CED) in CMS approved randomized controlled trials that satisfy the coverage criteria specified below, and in trials supported by the National Institutes of Health (NIH). All trials must be conducted in a hospital-based outpatient setting.

For any CMS approved trials, or trials supported by the NIH, that include a beta amyloid positron emission tomography (PET) scan as part of the protocol, it has been determined that these trials also meet the CED requirements included in the Beta Amyloid Positron Emission Tomography in Dementia and Neurodegenerative Disease NCD (220.6.20), and one beta amyloid PET scan will be covered per patient, if the patient did not previously receive a beta amyloid PET scan.

Nationally Non-Covered Indication(s):
Monoclonal antibodies directed against amyloid for the treatment of AD provided outside of the CMS approved randomized controlled trials and trials supported by the NIH or a CMS -approved study, as appropriate based on the FDA -approval type, are nationally non-covered.

See NCA - Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer’s Disease (CAG-00460N) - Decision Memo (cms.gov) for additional information.

Clinical Guideline Coverage Criteria
CMS may cover Aduhelm™ (aducanumab-avwa) when all the following clinical criteria is met:

Initial Authorization Criteria:
1. The Member is enrolled in a CMS-approved randomized controlled trial for Aduhelm™ (aducanumab-avwa) or a trial supported by the National Institutes of Health (NIH), and the trial is conducted in a hospital-based outpatient setting.

2. The Member has documented clinical evidence of mild cognitive impairment (MCI) due to AD or mild AD dementia based on the National Institute on Aging and the Alzheimer's Association (NIA-AA) criteria

3. Aduhelm™ (aducanumab-avwa) is prescribed by a Neurologist who specializes in the treatment of Alzheimer’s Disease

4. The Member is between 50 and 85 years of age

5. There is documented evidence of amyloid pathology consistent with AD as evidenced by ONE of the following tests:
   a. An Amyloid Positron Emission Tomography (PET scan); or
   b. 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)

6. The Provider attests that the Member does not have:
   a. Any neurological or other medical condition (other than AD) that may significantly contribute to cognitive decline; or
   b. Expected death from any cause during the duration of the study; or
   c. Any medical condition other than AD likely to increase significant adverse events
Reauthorization Criteria:

CMS may cover Aduhelm™ (aducanumab-avwa) when all the following clinical criteria is met:

1. The Member is enrolled in a CMS-approved randomized controlled trial for Aduhelm™ (aducanumab-avwa) or a trial supported by the National Institutes of Health (NIH), and the trial is conducted in a hospital-based outpatient setting.

2. Member meets all initial criteria when starting Aduhelm™ (aducanumab-avwa) therapy

3. Medical records confirm that the member has received scheduled MRIs (e.g., pre-7th infusion, pre-12th infusion, and every 12 months thereafter) for ARIA monitoring and there is no evidence of severe ARIA-H that would warrant discontinuation of treatment

4. For members who have been receiving the medication for more than 12 months, documentation of change from baseline PET scan or CSF analysis confirming ONE of the following obtained at or around 18 months of treatment:
   a. Amyloid PET scan demonstrating a reduction in amyloid plaques from baseline noted by both of the following:
      i. Composite Standard Uptake Value Ratio (SUVR) reduction of at least 0.2 points; and
      ii. Amyloid PET Centiloid reduction of at least 50%.
   OR
   b. CSF results demonstrating a reduction in tau pathophysiology and neurodegeneration from baseline as noted by both of the following:
      i. P-Tau reduction of at least 20 pg/mL; and
      ii. T-Tau reduction of at least 110 pg/mL

5. The Provider attests that the Member does not have any of the following:
   a. Any neurological or other medical condition (other than AD) that may significantly contribute to cognitive decline,
   or
   b. Expected death from any cause during the duration of the study, or
   c. Any medical condition other than AD likely to increase significant adverse events

Limitations

- Initial authorization of Aduhelm is limited to a total of 6 monthly dose if initial authorization criteria are met.
- Reauthorization for Aduhelm may be granted for a period of up to 6 monthly doses (per renewal) when reauthorization criteria are met.
- The plan will not cover:
  - Members who are not enrolled in a CMS-approved randomized controlled trial for Aduhelm™ (aducanumab-avwa) or a trial supported by the National Institutes of Health (NIH), and the trial is conducted in a hospital-based outpatient setting.
  - Members at increased risk for intracranial hemorrhage based on any of the following:
    o History of brain hemorrhage, bleeding disorders, cerebrovascular abnormalities, stroke or Transient Ischemic Attack (TIA)
    o Anticoagulant (e.g., apixaban, dabigatran, enoxaparin, heparin, rivaroxaban, warfarin) or antiplatelet (e.g., aspirin dosed > 325 mg/day, cilostazol, clopidogrel, diprydamole, prasugrel, ticagrelor) medication use
  - Members with a brain MRI that shows evidence of acute or sub-acute hemorrhage or prior subarachnoid hemorrhage
  - Members with a brain MRI that shows evidence of severe ARIA-H
  - Members who are not maintained on a dose of 10 mg/kg
  - Members with a diagnosis of cerebral amyloid angiopathy

Appendix

Dosing Schedule

<table>
<thead>
<tr>
<th>IV Infusion (every 4 weeks)</th>
<th>ADUHELM Dosage (administered over approximately one hour)</th>
</tr>
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<tbody>
<tr>
<td>Infusion 1 and 2</td>
<td>1 mg/kg</td>
</tr>
<tr>
<td>Infusion 3 and 4</td>
<td>3 mg/kg</td>
</tr>
<tr>
<td>Infusion 5 and 6</td>
<td>6 mg/kg</td>
</tr>
<tr>
<td>Infusion 7 and beyond</td>
<td>10 mg/kg</td>
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### ARIA MRI Classification Criteria

<table>
<thead>
<tr>
<th>ARIA Type</th>
<th>Radiographic Severity</th>
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<tbody>
<tr>
<td></td>
<td>Mild</td>
</tr>
<tr>
<td>ARIA-E</td>
<td>FLAIR hyperintensity confined to sulcus and or cortex/subcortical white matter in one location &lt; 5 cm</td>
</tr>
<tr>
<td>ARIA-H microhemorrhage</td>
<td>≤ 4 new incidents microhemorrhages</td>
</tr>
<tr>
<td>ARIA-H superficial siderosis</td>
<td>1 focal area of superficial siderosis</td>
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### Codes

The following code(s) require prior authorization:

#### Table 1: HCPCS Codes

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>J0172</td>
<td>Injection, aducanumab-avwa, 2mg</td>
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</tbody>
</table>

### References:

Background, Product and Disclaimer Information

Medical Necessity Guidelines are developed to determine coverage for benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. We make coverage decisions using these guidelines, along with the Member’s benefit document, and in coordination with the Member’s physician(s) on a case-by-case basis considering the individual Member’s health care needs.

Medical Necessity Guidelines are developed for selected therapeutic or diagnostic services found to be safe and proven effective in a limited, defined population of patients or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in our service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. We revise and update Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

For self-insured plans, coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a Medical Necessity Guideline and a self-insured Member’s benefit document, the provisions of the benefit document will govern. For Tufts Health Together (Medicaid), coverage may be available beyond these guidelines for pediatric members under age 21 under the Early and Periodic Screening, Diagnostic and Treatment (EPSDT) benefits of the plan in accordance with 130 CMR 450.140 and 130 CMR 447.000, and with prior authorization.

Treating providers are solely responsible for the medical advice and treatment of Members. The use of this guideline is not a guarantee of payment or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to eligibility and benefits on the date of service, coordination of benefits, referral/authorization, utilization management guidelines when applicable, and adherence to plan policies, plan procedures, and claims editing logic.