Mass General Brigham
Health Plan

Alzheimer's Agents
Adlarity (donepezil patch)
Aduhelm (adacanumab-avwa)
Leqembi ((lecanemab-irmb)
Effective 10/02/2023

Plan	☒ MassHealth UPPL ☐Commercial/Exchange	**Program Type**	☒ Prior Authorization ☐ Quantity Limit ☐ Step Therapy
Benefit	☒ Pharmacy Benefit ☒ Medical Benefit		
Specialty Limitations	Aduhelm and Leqembi are designated as a specialty medication and must be filled at a contracted specialty pharmacy when obtained through the pharmacy benefit.		
Contact Information	**Medical and Specialty Medications** All Plans | Phone: 877-519-1908 | Fax: 855-540-3693		
	Non-Specialty Medications All Plans | Phone: 800-711-4555 | Fax: 844-403-1029		
Exceptions	Aduhelm and Leqembi is available on both the medical and pharmacy benefits.		

Overview
Adlarity® (donepezil patch) is indicated for the treatment of mild, moderate, and severe dementia of the Alzheimer's type.

Aduhelm® (aducanumab-avwa) is the first disease modifying therapy approved for the treatment of Alzheimer's disease. Of note, aducanumab received FDA approval based on a surrogate endpoint (reduction in amyloid-β plaques) and has not yet been shown to provide a clinical benefit. Aducanumab is a human immunoglobulin (IgG1) monoclonal antibody directed against aggregated soluble and insoluble forms of amyloid-β, a defining pathophysiological feature of Alzheimer's disease. A second disease modifying therapy, Leqembi (lecanemab-irmb), initially received accelerated approval similar to Aduhelm, but subsequently received a traditional approval after a clinical benefit was established. Of note, while Leqembi appears to be a safer alternative than Aduhelm, there a black box warning for amyloid-related imaging abnormalities (ARIA), particularly those patients who are apolipoprotein E (ApoE) ε4 homozygotes.

Drugs that require PA†
Cholinesterase Inhibitors
Adlarity (donepezil patch)
Disease Modifying Agents
Aduhelm (aducanumab-avwa) Leqembi (lecanemab-irmb)

†Use of donepezil-containing products in members less than 18 years of age is discussed in the MassHealth Pediatric Behavioral Health Medication Initiative guideline

The **Pediatric Behavioral Health Medication Initiative** may apply to MassHealth members <18 years of age due to polypharmacy, age, and/or drug restrictions. As indicated within this guideline, please refer to the **Pediatric Behavioral Health Initiative** guideline to assess appropriateness of therapy.

Coverage Guideline
Authorization may be granted for new members to the plan who are currently receiving treatment with requested medication excluding when the product is obtained as samples or via manufacturer's patient assistance programs, when continuation of therapy criteria is met.
OR
Authorization may be granted for members when all the following criteria are met:

Adlarity (donepezil patch)
ALL of the following:
1. Diagnosis of Alzheimer's disease or dementia
2. Requested quantity is ≤ 4 units/28 days
3. Medical necessity for use instead of donepezil tablets or ODT *(e.g., forgetfulness/compliance as medical necessity for once-weekly patch is acceptable unless there are claims for daily scheduled medications)*

Aduhelm (aducanumab-avwa)
ALL of the following:
1. Diagnosis of mild cognitive impairment (MCI) or mild dementia associated with Alzheimer's Disease
2. Prescriber is a specialist in the treatment of dementia or Alzheimer's disease (e.g., neurologist, geriatric psychiatrist, geriatrician who specializes in treating dementia)
3. Medical records documenting baseline (within the past three months) cognitive function based on **ONE** of the following objective assessments:
    a. Mini Mental State Exam (MMSE) score ≥ 24
    b. Montreal Cognitive Assessment (MoCA) score ≥ 15
    c. Saint Louis University Mental Status Examination (SLUMS) score ≥16.1
4. Medical records documenting confirmed evidence of clinically significant AD neuropathology based on **ONE** of the following:
    a. Cerebral Spinal Fluid (CSF) biomarkers
    b. Amyloid positron emission tomography (PET)
5. Member has had a brain magnetic resonance imaging (MRI) in the previous 12 months
6. Appropriate dose
7. The member and/or authorized representative (e.g., power of attorney, invoked health care proxy) has been informed of the known and potential risks and lack of established clinical benefit associated with Aduhelm treatment
8. Inadequate response, adverse reaction, or contraindication to Leqembi (lecanemab)
9. Member does **NOT** have ANY of the following non-AD neurodegenerative disorders:
    a. Probable dementia with Lewy bodies by consensus criteria
    b. Suspected frontotemporal degeneration
    c. Dementia in down syndrome
10. Member has **NOT** had ANY of the following in the past year:
    a. Stroke or transient ischemic attack
    b. Any unexplained loss of consciousness
11. Member does **NOT** have coagulopathy or requirement for therapeutic anticoagulation and/or dual antiplatelet therapy (only aspirin ≤325 mg/day monotherapy is allowed)
12. Member does **NOT** have ANY of the following neurological or psychiatric conditions:

a. Uncontrolled seizure disorder
b. Uncontrolled mood disorder, anxiety disorder or psychosis

13. Member does **NOT** have significant cerebrovascular disease as established by brain MRI showing ANY of the following:
    a. Acute or sub-acute hemorrhage
    b. Prior macro-hemorrhage or prior subarachnoid hemorrhage (unless finding is not due to an underlying structural or vascular hemorrhage)
    c. ≥4 microhemorrhages
    d. Cortical infarct
    e. >1 lacunar infarct
    f. Superficial siderosis
    g. History of diffuse white matter disease
14. Member does **NOT** have ANY of the following cardiovascular conditions:
    a. Uncontrolled hypertension
    b. Coronary artery disease (including unstable angina and myocardial infarction)
    c. Heart failure
    d. Arrhythmia
    e. Clinically significant carotid atherosclerosis and/or peripheral arterial disease
15. Member does **NOT** have ANY uncontrolled clinically significant chronic medical condition (e.g., liver disease, kidney disease, pulmonary disease, autoimmune disease requiring chronic immunosuppression, malignant neoplasm, active chronic infection [HIV, HCV], poorly controlled diabetes mellitus)

Leqembi (lecanemab-irmb)
ALL of the following:

1. Diagnosis of ONE of the following:
    a. Mild cognitive impairment (MCI)
    b. Mild dementia associated with Alzheimer's Disease (AD)
2. Prescriber is a specialist in the treatment of dementia or Alzheimer's disease (e.g., neurologist, geriatric psychiatrist, geriatrician who specializes in treating dementia)
3. Medical records documenting confirmed evidence of clinically significant AD neuropathology based on ONE of the following:
    a. Amyloid PET
    b. Cerebral Spinal Fluid (CSF) biomarkers
4. Member has had a brain magnetic resonance imaging (MRI) within the last 12 months
5. Appropriate dosing
6. Medical records documenting baseline (within the last three months) cognitive function based on ONE of the following objective assessments:
    a. Mini Mental State Exam (MMSE) score ≥ 22
    b. Montreal Cognitive Assessment (MoCA) score ≥ 15
    c. Saint Louis University Mental Status Examination (SLUMS) score ≥ 16.1

<u>Continuation of Therapy</u>
For **Adlarity**, reauthorization by prescriber will infer a positive response to therapy.

For **Aduhelm**, prescriber provides documentation of **ALL** of the following:

1. Appropriate dose
2. Attestation that all MRI monitoring has been completed in accordance with the FDA-approved label

3. Medical records documenting current (within the past 3 months) cognitive function based on ONE of the following objective assessments:
    1. Mini Mental State Exam (MMSE)
    2. Montreal Cognitive Assessment (MoCA)
    3. Saint Louis University Mental Status Examination (SLUMS)
4. **ONE** of the following (Amyloid-related imaging abnormalities-hemosiderin [ARIA-H], microhemorrhages):[*] [‡]
    1. Member has had no new incident microhemorrhage
    2. Member has had 1 to 4 new incident microhemorrhage(s) **AND** microhemorrhages are asymptomatic (no clinical symptoms)
    3. Member has had 5 to 9 new incident microhemorrhages **AND** microhemorrhages are asymptomatic (no clinical symptoms) **AND** the microhemorrhages have been stabilized
    4. Member has had 1 to 9 new incident microhemorrhages **AND** microhemorrhages resulted in mild, moderate or severe clinical symptoms **AND** the microhemorrhages have been stabilized
5. **ONE** of the following (ARIA-H, superficial siderosis): [†] [‡]
    1. Member has had no new incident areas of superficial siderosis
    2. Member has had 1 new incident area of superficial siderosis **AND** superficial siderosis is asymptomatic (no clinical symptoms)
    3. Member has had 2 new incident areas of superficial siderosis **AND** superficial siderosis is asymptomatic (no clinical symptoms) **AND** the superficial siderosis has been stabilized
    4. Member has had 1 to 2 new incident areas of superficial siderosis **AND** superficial siderosis resulted in mild, moderate or severe clinical symptoms **AND** the superficial siderosis has been stabilized
6. **ONE** of the following (Amyloid-related imaging abnormalities-edema [ARIA-E]):
    1. Member has had no new ARIA-E
    2. Member has mild ARIA-E on MRI AND ARIA-E is asymptomatic (no clinical symptoms)
    3. Member has had moderate or severe ARIA-E on MRI AND ARIA-E is asymptomatic (no clinical symptoms) AND the ARIA-E is stable
    4. Member has had mild, moderate or severe ARIA-E on MRI AND ARIA-E resulted in mild, moderate or severe clinical symptoms AND the ARIA-E is stable
7. **ONE** of the following:
    1. Member does **NOT** have ANY of the following:
        i. Initiation of anticoagulation
        ii. Development of active immune-mediated/autoimmune conditions (e.g., Crohn's disease, systemic lupus erythematosus, aplastic anemia, myasthenia gravis, meningitis/encephalitis)
        iii. Initiation of immunomodulatory medications (e.g., cancer immunotherapies, rituximab, azathioprine)
        iv. Development of other neurologic conditions (e.g., intracerebral bleeds, traumatic brain injury, stroke)
    2. Clinical rationale for continued use of Aduhelm[§] in a member with at least one of the above noted conditions

Notes:

- **If the member has had ≥10 new incident microhemorrhages, regardless of clinical severity (including asymptomatic) therapy should be discontinued permanently and the request should be denied.*
- *†If the member has had ≥3 new incident areas of superficial siderosis, regardless of clinical severity (including asymptomatic) therapy should be discontinued permanently and the request should be denied.*

- *‡If the member had a serious event, therapy should be discontinued. Serious events include concern for immediate risk of death (a life-threatening event); inpatient hospitalization or prolongation of existing hospitalization due to symptoms; new persistent or significant disability/incapacity.*

For **Leqembi**, prescriber provides documentation of **ALL** of the following:

1. Appropriate dosing
2. Attestation that all MRI monitoring has been completed in accordance with the FDA approved label
3. Medical records documenting current (within the past three months) cognitive function based on ONE of the following objective assessments:
    a. Mini Mental State Exam (MMSE)
    b. Montreal Cognitive Assessment (MoCA)
    c. Saint Louis University Mental Status Examination (SLUMS)

Limitations

1. Initial approvals will be granted for:
    a. Aduhelm, Leqembi: 6 months
    b. All other agents: 12 months
2. Reauthorizations will be granted for 12 months
3. The following quantity limits apply:

Adlarity	4 units per 28 days

Appendix A - Anticoagulant and Antiplatelet Agents

Members who are utilizing anticoagulant or dual antiplatelet therapy are excluded from utilizing Aduhelm®. Only use of aspirin (≤325 mg/day is allowed). Members utilizing any of the following medications should be denied.

Class	Agents
Direct Thrombin Inhibitors	Dabigatran etexilate mesylate (Pradaxa®)
Factor Xa Inhibitors	Apixaban (Eliquis®) Edoxaban (Savaysa®) Fondaparinux (Arixtra®) Rivaroxaban (Xarelto®)
Low Molecular Weight Heparins	Dalteparin (Fragmin®) Enoxaparin (Lovenox®)
Vitamin K Antagonists	Warfarin
Antiplatelet Agents	Anagrelide (Agrylin®) Cilostazol Clopidogrel (Plavix®) Dipyridamole (±aspirin) Prasugrel (Effient®) Ticagrelor (Brilinta®) Vorapaxar (Zontivity®)

Appendix B - Side-Effect Protocol

ARIA - H (Microhemorrhages)

		New Incident Microhemorrhages		
		Radiographic Severity		
		Mild (1 to 4)	Moderate (5 to 9)	Severe (≥10)
Clinical Symptom Severity	Asymptomatic	Continue treatment; MRI q4w until stable	Suspend treatment; MRI q4w until stable; Restart once stable	Stop Permanently
	Mild	Suspend treatment; MRI q4w until stable Restart once stable and clinical symptoms resolved		Stop Permanently
	Moderate			
	Severe			
	Serious*	Stop Permanently		

ARIA - H (Superficial Siderosis)

		New Incident Areas of Superficial Siderosis (Central Read)		
		Radiographic Severity		
		Mild (1)	Moderate (2)	Severe (≥3)
Clinical Symptom Severity	Asymptomatic	Continue treatment; MRI q4w until stable	Suspend treatment; MRI q4w until stable; Restart once stable	Stop Permanently
	Mild	Suspend treatment; MRI q4w until stable Restart once stable and clinical symptoms resolved		Stop Permanently
	Moderate			
	Severe			
	Serious*	Stop Permanently		

ARIA - E

		ARIA-E Severity on MRI (Central Read)		
		Radiographic Severity		
		Mild	Moderate	Severe
Clinical Symptom Severity	Asymptomatic	Continue treatment; MRI q4w until stable	Suspend treatment; MRI q4w until stable; Restart once stable	
	Mild	Suspend treatment; MRI q4w until stable Restart once stable and clinical symptoms resolved		
	Moderate			
	Severe			
	Serious*	Stop Permanently		

*Serious events include concern for immediate risk of death (a life-threatening event); inpatient hospitalization or prolongation of existing hospitalization due to symptoms; new persistent or significant disability/incapacity.

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Review History

03/16/2022 – Reviewed and Created for March P&T; Match MH criteria Effective 05/01/2022.
01/11/2023 - Reviewed and updated for Jan P&T. Matched MH UPPL criteria. Adlarity was added to pharmacy benefit with PA and QL. Updated approval durations. Effective 3/1/23.
09/13/2023 – Reviewed and updated for P&T. Added Leqembi to criteria. Aduhelm initial criteria: Clarified provider specialty, SLUMS added as another assessment options, changed timeline of MRI scan from 3 to 12 months, and preferred trial of Leqembi. Aduhelm reauth criteria further simplified to require current objective assessments and attestation that all MRI monitoring has been completed. Effective 10/2/23