Amyloid Beta-Directed Monoclonal Antibodies for Alzheimer's Disease
ADUHELM® (aducanumab-avwa)
LEQEMBI® (lecanemab-irmb)

The purpose of this document is to assist providers enrolled in the Connecticut Medical Assistance Program (CMAP) with the information needed to support a medical necessity determination for treatment with amyloid beta-directed monoclonal antibodies for Alzheimer's Disease (AD). By clarifying the information needed for prior authorization of services, HUSKY Health hopes to facilitate timely review of requests so that individuals obtain the medically necessary care they need as quickly as possible.

ADUHELM is an amyloid beta-directed monoclonal antibody indicated for the treatment of Alzheimer's disease. ADUHELM was FDA approved in June 2021 under accelerated approval based on a reduction in amyloid beta plaques observed in patients treated with ADUHELM. On July 8, 2021, the FDA approved an updated label that states that the treatment should be initiated only in Alzheimer's 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. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trial(s).

LEQEMBI is an amyloid beta-directed monoclonal antibody indicated for the treatment of AD. Treatment with LEQEMBI should be initiated in patients with mild cognitive impairment (MCI) or mild dementia stage of disease, the population in which treatment was initiated in clinical trials. The Food and Drug Administration (FDA) approved LEQEMBI in January 2023 under an accelerated approval based on a reduction in amyloid beta plaques. In July 2023, the FDA granted full approval based on a confirmatory trial. There are no safety or effectiveness data on initiating treatment at earlier or later stages of the disease than were studied.

Both ADUHELM and LEQEMBI can cause amyloid related imaging abnormalities (ARIA), characterized as ARIA with edema (ARIA-E) and ARIA with hemosiderin deposition (ARIA-H). ARIA is usually asymptomatic, although rarely serious and life-threatening events can occur. Serious intracerebral hemorrhage greater than 1 cm have occurred in patients treated with this class of medications. Patients treated with this class of medications, who are ApoE ε4 homozygotes, have a higher incidence of ARIA, including symptomatic and serious ARIA, compared to heterozygotes and noncarriers.

CLINICAL GUIDELINE

Coverage guidelines for amyloid-beta directed monoclonal antibodies for AD are made in accordance with the DSS definition of Medical Necessity. The following criteria are guidelines *only*. Coverage determinations are based on an individual assessment of the member and their unique clinical needs. If the guidelines conflict with the definition of Medical Necessity, the definition of Medical Necessity shall prevail. The guidelines are as follows:

Treatment with LEQEMBI or ADUHELM is considered medically necessary when **ALL** of the following criteria are met:

Initial Authorization

A. The individual has a diagnosis of early Alzheimer's disease (mild cognitive impairment (MCI) due to AD, or mild Alzheimer's dementia); **AND**
B. The individual has confirmed presence of amyloid pathology verified by positron emission tomography (PET) scan or cerebrospinal fluid (CSF) testing; **AND**
C. The individual is 50 years of age or older; **AND**
D. Treatment is prescribed by or in consultation with a neurologist, geriatrician, or geriatric psychiatrist; **AND**
E. The individual must have objective evidence of cognitive impairment at baseline as evidenced by achieving one of the following scores using any of the assessment tools specified below:
    1. Mini-Mental State Exam (MMSE) score of 22-30; **OR**
    2. Clinical Dementia Rating-Global Score (CDR-GS) of 0.5 or 1; **OR**
    3. Montreal Cognitive Assessment (MoCA) score of 17-30; **AND**
F. Testing for ApoE ε4 Homozygote status has been performed prior to initiation of treatment and the implications of genetic test results regarding the risk of developing ARIA has been discussed with the patient and/or caregiver; **AND**
G. The individual has had a recent brain magnetic resonance imaging (MRI) within the last year to assess for pre-existing ARIA or other significant cerebral pathology. The MRI must demonstrate all of the following:
    1. No evidence of other significant pathological findings (e.g., hemorrhages); **AND**
    2. No evidence of other clinically significant lesions that could indicate a dementia diagnosis other than AD; **AND**
H. The individual does not have a history of stroke, transient ischemic attacks (TIA) or seizures documented within the last 12 months; **AND**
I. The individual is not on therapeutic anticoagulation except for aspirin at a prophylactic dose; **AND**
J. The individual does not have a bleeding disorder that is inadequately controlled; **AND**
K. The individual does not have any other neurologic disorders that may be contributing to cognitive impairment above and beyond that which is caused by AD; **AND**
L. The individual does not have any contraindications to amyloid testing (e.g., PET, CSF testing) or to an MRI brain scan (e.g., metallic implants, cardiac pacemaker/defibrillator); **AND**
M. The individual (and/or caregivers) considering LEQEMBI or ADUHELM therapy have been provided with information on the requirements for treatment and expected outcomes, potential side effects, risks (including the risks of ARIA), and burdens related to administration and monitoring; **AND**
N. For LEQEMBI:
    1. LEQEMBI will not be used in combination with any other amyloid beta-directed antibodies (e.g., ADUHELM); **AND**
    2. The treating physician will follow all other FDA requirements related to dosing, administration, and monitoring. This includes the use of MRI to monitor for ARIA prior to the 5th, 7th, and 14th infusions and as needed if the individual experiences symptoms suggestive of ARIA
O. For ADUHELM:
    1. ADUHELM will not be used in combination with any other amyloid beta-directed antibodies (e.g., LEQEMBI); **AND**
    2. The treating physician will follow all other FDA requirements related to dosing, administration, and monitoring for ARIA including the use of MRI prior to the 5th, 7th, 9th, and 12th infusions and as needed if the individual experiences symptoms suggestive of

ARIA; **AND**

3. The individual is currently enrolled in a randomized-controlled clinical trial conducted under an investigational new drug (IND) application or National Institutes of Health (NIH)-supported trial.

Reauthorization

Continuation of treatment with LEQEMBI or ADUHELM may be considered medically necessary at six-month intervals if:

A. The individual is continuing to benefit from treatment as evidenced by objective, validated tests used longitudinally for assessment. The expected benefit is slowing of cognitive and functional decline; improvement of current clinical state is not anticipated (a signed letter from the individual's ordering physician is required); **AND**
B. All MRI scans performed per recommended protocol to monitor for ARIA demonstrate that:
    1. The individual shows no evidence of ARIA or if ARIA is present, it is mild, and the individual is asymptomatic; **AND**
    2. The individual does not have unresolved moderate or severe ARIA; **AND**
C. The individual has not manifested severe symptoms (e.g., seizures, stroke-like manifestations) in the presence of ARIA.

NOTE: EPSDT Special Provision

Early and Periodic Screening, Diagnosis, and Treatment (EPSDT) is a federal Medicaid requirement that requires the Connecticut Medical Assistance Program (CMAP) to cover services, products, or procedures for Medicaid enrollees under 21 years of age where the service or good is medically necessary health care to correct or ameliorate a defect, physical or mental illness, or a condition identified through a screening examination. The applicable definition of medical necessity is set forth in Conn. Gen. Stat. Section 17b-259b (2011) [ref. CMAP Provider Bulletin PB 2011-36].

PROCEDURE

Prior authorization is required for LEQEMBI and ADUHELM. Requests for coverage of LEQEMBI and ADUHELM are reviewed in accordance with procedures in place for reviewing requests for physician-administered drugs. Coverage determinations are based upon a review of requested and/or submitted case-specific information.

The following information is needed to review requests:

1. Fully completed Prior Authorization Request Form;
2. Results of PET imaging or CSF testing confirming presence of amyloid pathology;
3. Medical record documentation confirming diagnosis of Alzheimer's disease and absence of any contraindications as outlined in the Clinical Guideline section of this policy;
4. Results from at least one dementia rating scale outlined in the Clinical Guideline section of this policy confirming cognitive impairment at baseline;
5. Results from the most recent brain MRI scan;
6. For ADULHELM requests: evidence of enrollment in a clinical trial;
7. For reauthorization requests: letter from ordering physician documenting the benefits patient is receiving from treatment;
8. Other information as requested by CHNCT.

EFFECTIVE DATE

This Policy is effective for prior authorization requests for amyloid beta-directed monoclonal antibodies

for Alzheimer's Disease for individuals covered under the HUSKY Health Program on or after February 01, 2024.

LIMITATIONS
Not Applicable

CODES:

Code	Description
J0172	Injection, aducanumab-avwa, 2 mg
J0174	Injection, lecanemab-irmb, 1mg

DEFINITIONS

1. **HUSKY A**: Connecticut children and their parents or a relative caregiver; and pregnant women may qualify for HUSKY A (also known as Medicaid). Income limits apply.
2. **HUSKY B**: Uninsured children under the age of 19 in higher income households may be eligible for HUSKY B (also known as the Children's Health Insurance Program) depending on their family income level. Family cost-sharing may apply.
3. **HUSKY C**: Connecticut residents who are age 65 or older or residents who are ages 18-64 and who are blind, or have another disability, may qualify for Medicaid coverage under HUSKY C (this includes Medicaid for Employees with Disabilities (MED-Connect), if working). Income and asset limits apply.
4. **HUSKY D**: Connecticut residents who are ages 19-64 without dependent children and who: (1) do not qualify for HUSKY A; (2) do not receive Medicare; and (3) are not pregnant, may qualify for HUSKY D (also known as Medicaid for the Lowest-Income populations).
5. **HUSKY Health Program**: The HUSKY A, HUSKY B, HUSKY C, HUSKY D and HUSKY Limited Benefit programs, collectively.
6. **HUSKY Limited Benefit Program or HUSKY, LBP**: Connecticut's implementation of limited health insurance coverage under Medicaid for individuals with tuberculosis or for family planning purposes and such coverage is substantially less than the full Medicaid coverage.
7. **HUSKY Plus Physical Program (or HUSKY Plus Program):** A supplemental physical health program pursuant to Conn. Gen. Stat. § 17b-294, for medically eligible members of HUSKY B in Income Bands 1 and 2, whose intensive physical health needs cannot be accommodated within the HUSKY Plan, Part B.
8. **Medically Necessary or Medical Necessity**: (as defined in Connecticut General Statutes § 17b-259b) Those health services required to prevent, identify, diagnose, treat, rehabilitate or ameliorate an individual's medical condition, including mental illness, or its effects, in order to attain or maintain the individual's achievable health and independent functioning provided such services are: (1) Consistent with generally-accepted standards of medical practice that are defined as standards that are based on (A) credible scientific evidence published in peer-reviewed medical literature that is generally recognized by the relevant medical community, (B) recommendations of a physician-specialty society, (C) the views of physicians practicing in relevant clinical areas, and (D) any other relevant factors; (2) clinically appropriate in terms of type, frequency, timing, site, extent and duration and considered effective for the individual's illness, injury or disease; (3) not primarily for the convenience of the individual, the individual's health care provider or other health care providers; (4) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the individual's illness, injury or disease; and (5) based

on an assessment of the individual and his or her medical condition.

9. **Prior authorization**: A process for approving covered services prior to the delivery of the service or initiation of the plan of care based on a determination by CHNCT as to whether the requested service is medically necessary.

ADDITIONAL RESOURCES AND REFERENCES:

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3. Centers for Medicare & Medicaid Services. (2022, June 6). Fact sheet - Centers for Medicare & Medicaid Services. www.cms.gov. https://www.cms.gov/files/document/fact-sheet-june-2023.pdf. Accessed on August 3, 2023
4. Centers for Medicare & Medicaid Services Medicare Coverage Database. National Coverage Determination: Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease. April 7, 2022. https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?ncdid=375&ncdver=1. Accessed on August 28, 2023
5. ClinicalTrials.gov. NCT01767311, A Study to Evaluate Safety, Tolerability, and Efficacy of Lecanemab in Subjects With Early Alzheimer's Disease). Available at: https://clinicaltrials.gov/study/NCT01767311. Accessed on July 26, 2023.
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13. Institute for Clinical and Economic Review - Aducanumab for Alzheimer's disease: Final Policy Recommendations. August 5, 2021. Available at: https://icer.org/wp-content/uploads/2020/10/ICER_ALZ_Policy_Recommendations_080521.pdf. Accessed on August 28, 2023.
14. Alzheimer's Association. 2023 Alzheimer's Disease Facts and Figures. Alzheimers Dement. 2023;19(4). DOI 10.1002/alz.13016.
15. Office of the Commissioner. (2023, July 6). FDA converts novel Alzheimer's disease treatment to traditional approval. U.S. Food and Drug Administration. https://www.fda.gov/news-events/press-

announcements/fda-converts-novel-alzheimers-disease-treatment-traditional-approval#:~:text=Action%20Follows%20Confirmatory%20Trial%20to%20Verify%20Clinical%20Benefit&text=Today%2C%20the%20U.S.%20Food%20and,confirmatory%20trial%20verified%20clinical%20benefit. Accessed on August 3, 2023

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PUBLICATION HISTORY

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