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Medical Drug Clinical Criteria

Subject:	Leqembi (lecanemab)		
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Table of Contents

Overview

This document addresses the use of Leqembi (lecanemab), an amyloid beta-directed antibody indicated for the treatment of Alzheimer's disease.

The manufacturer of Leqembi (lecanemab) submitted the NDA application based on data from a phase 2 and 3 randomized, placebo-controlled study (Clarity AD). Leqembi was FDA approved through an accelerated program, and continued approval is contingent on verification of clinical benefit via a confirmatory trial (not yet completed).

A published Phase 2 study did not meet the primary efficacy endpoint of change from baseline in the Alzheimer's Disease Composite Score (ADCOMS). The key secondary endpoint measuring change on the Clinical Dementia Rating Scale – Sum of Boxes (CDR-SB) was also not met. With regard to the safety results, amyloid-related imaging abnormalities-edema (ARIA-E) incidence was 10% at the highest doses for the overall population and 14.3% for apolipoprotein E4 (ApoE4)-positive subjects (Swanson 2021).

The published phase 3 met its primary endpoint measuring CDR-SB, but clinical significance regarding delay in dementia progression (-0.45 out of 18) was not evident since minimum change of 1 point is considered clinically significant. Safety results showed a 22% total incidence of ARIA with Leqembi compared to 10% in the placebo group. There were no deaths considered related to Leqembi during the double-blind portion of the study. However, two deaths during the open-label phase are considered related to Leqembi by study personnel and being investigated by the manufacturer. Long term efficacy and safety of Leqembi are unknown.

ARIA can be observed on magnetic resonance imaging (MRI) as brain edema or sulcal effusions (ARIA-E) or microhemorrhage and superficial siderosis (ARIA-H).

On April 7, 2022, the Centers for Medicare & Medicaid Services (CMS) released a National Coverage Determination (NCD) for FDA approved monoclonal antibodies (mAb) directed against amyloid beta plaques for the treatment of Alzheimer's disease. CMS concluded that these agents would only be considered under *coverage with evidence development (CED)* when the specified criteria outlined within the NCD are met. Providing further direction, the CMS decision memo asserts that, "*monoclonal antibodies directed against amyloid for the treatment of AD provided outside of a FDA approved randomized controlled trial, CMS approved studies, or studies supported by the NIH, are nationally non-covered*."

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Leqembi (lecanemab)

Requests for Leqembi (lecanemab) for any diagnosis may not be approved.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement

policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J3490	Unclassified drugs (when specified as [Leqembi] (lecanemab))
J3590	Unclassified biologics (when specified as [Leqembi] (lecanemab))

ICD-10 Diagnosis

All diagnoses pend

Document History

New: 01/06/2023
Document History:

- 01/06/2023 – Annual Review: Add new clinical criteria document for Leqembi. Coding Reviewed: Added J3490, J3590. All diagnoses pend.

References

1. Albert MS, DeKosky ST, Dickson D, et.al. The diagnosis of mild cognitive impairment due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimers Dement.* 2011 May; 7(3):270-279. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3312027/. Accessed on November 7, 2022.
2. NCT03887455. A Study to Confirm Safety and Efficacy of Lecanemab in Participants With Early Alzheimer's Disease (Clarity AD). ClinicalTrials.gov. National Institute of Health. U.S. National Library of Medicine. Available at https://clinicaltrials.gov/ct2/show/NCT03887455?term=clarity+ad&draw=2&rank=1. Accessed on November 7, 2022.
3. Swanson CJ, Zhang Y, Dhadda S, et al. A randomized, double-blind, phase 2b proof-of-concept clinical trial in early Alzheimer's disease with lecanemab, an anti-Aβ protofibril antibody. *Alzheimers Res Ther*. 2021 Apr 17;13(1):80. PMID: 33865446; PMCID: PMC8053280. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8053280/ Accessed on November 7, 2022.
4. Van Dyck CH, Swanson CJ, Aisen P, et al. Lecanemab in Early Alzheimer's Disease (Clarity AD). *NEJM*. 2023; 388:9-21. DOI: 10.1056/NEJMoa2212948. Available at https://www.nejm.org/doi/full/10.1056/NEJMoa2212948. Accessed on January 6, 2023.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.