



MEDICAL COVERAGE POLICY

SERVICE: Lecanemab-irmb (Leqembi™)

Policy Number: 301

Effective Date: 11/01/2024

Last Review: 08/12/2024

Next Review: 08/12/2025

Important note: Unless otherwise indicated, medical policies will apply to all lines of business.

Medical necessity as defined by this policy does not ensure the benefit is covered. This medical policy does not replace existing federal or state rules and regulations for the applicable service or supply. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan documents. See the member plan specific benefit plan document for a complete description of plan benefits, exclusions, limitations, and conditions of coverage. In the event of a discrepancy, the plan document always supersedes the information in this policy.

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PRIOR AUTHORIZATION: **Required**

POLICY: Please review the plan's EOC (Evidence of Coverage) or Summary Plan Description (SPD) for details.

For Medicare plans, please refer to appropriate Medicare [NCD \(National Coverage Determination\) 200.3 Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease \(AD\)](#).

For Medicaid plans, please confirm coverage as outlined in the [Texas Medicaid Provider Procedures Manual | TMHP](#) (TMPPM). Texas Mandate HB154 is applicable for Medicaid plans.

Baylor Scott & White Health Plan (BSWHP) may consider lecanemab (Leqembi™) medically necessary for the treatment of Alzheimer's disease (AD) in adult patients when ALL of the following criteria are met:

For initiation of treatment, documentation from the member's medical records must be submitted showing member meets all criteria:

1. Member has a diagnosis of Alzheimer's disease (AD); **AND**
 2. The medication is prescribed by or in consultation with a neurologist, geriatric psychiatrist, or geriatrician; **AND**
 3. Member age is 50 to 90 years; **AND**
 4. The member must have a documented diagnosis of mild cognitive impairment (MCI) due to AD or mild dementia stage of AD as confirmed by both:
 - a. One or more of the following cognitive tests with scores:
 - i. MMSE (Mini-Mental State Exam) score 21-30
 - ii. CDR-GS (Clinical Dementia Rating-Global Scale) score = 0.5 or 1
 - iii. MoCA (Montreal Cognitive Assessment) score ≥16
- AND**
- b. Amyloid beta (Aβ) deposits consistent with a diagnosis of AD as confirmed by one of the following (must submit a copy of imaging results or diagnostic immunoassay):
 - i. Amyloid PET; **OR**
 - ii. Lumbar puncture: CSF assay with results consistent with diagnosis of Alzheimer's disease. Biomarkers include but are not limited to: A-beta 42 peptide



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(A β 42), phospho-tau (P-tau) and total tau (T-tau) proteins, ATI index (A β 42/ T-tau).

AND

5. Specialist has ruled out other conditions or causative factors that could be viewed as AD (ex. Lewy body dementia, cerebrovascular disease, Parkinson's disease, vitamin B12 deficiency, etc.); **AND**
6. Prior to lecanemab administration, member must be on stable dose if taking the following drugs:
 - a. AD symptomatic treatment (ex. donepezil, rivastigmine, galantamine, memantine) for 12 weeks
 - b. Anticoagulant therapy (ex. enoxaparin, warfarin, Eliquis, Pradaxa, Xarelto), for 4 weeks

AND

7. Apolipoprotein E ϵ 4 genetic testing to assess risk of amyloid-related imaging abnormalities (ARIA), i.e. brain swelling and bleeds; **AND**
8. Risks of ARIA discussed with member or caregiver; **AND**
9. The member does NOT have any of the following:
 - a. Submitted baseline MRI (within 1 year) with any of the following:
 - i. More than four microhemorrhages (\leq 10 mm at greatest diameter)
 - ii. A single microhemorrhage $>$ 10 mm at greatest diameter
 - iii. An area of superficial siderosis
 - iv. Evidence of vasogenic edema
 - v. Evidence of cerebral contusion, encephalomalacia, aneurysms, vascular malformations, or infection lesions
 - vi. Evidence of multiple lacunar infarcts or stroke involving a major vascular territory, severe small vessel, or white matter disease
 - vii. Space occupying lesions
 - viii. Brain tumors (meningiomas or arachnoid cysts $<$ 10 mm at greatest diameter are not exclusionary)
 - b. Any medical or neurological condition (other than AD) that might be a contributing cause of cognitive impairment
 - c. Seizures, stroke, or transient ischemic attack (TIA) in the past 12 months
 - d. History of cerebrovascular abnormalities
 - e. Bleeding disorder not under adequate control (ex. platelet count $<$ 50,000 or INR $>$ 1.5 for patients not on warfarin)

AND

10. Lecanemab will not be used in combination with any other amyloid beta-directed antibodies (ex. aducanumab).

Initial approval of lecanemab will be for 6 months.

For renewal authorization, documentation from the member's medical records must be submitted showing member meets all criteria:



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1. MRI conducted prior to the 5th, 7th, and 14th infusions to monitor for amyloid-related imaging abnormalities (ARIA), i.e. brain swelling and bleeds; **AND**
2. Member must not have any of the following:
 - a. Started new medications that increase risk for ARIA (ex. tPA use since last authorization, antiplatelets, anticoagulants) without documented discussion of ARIA risk and plans for monitoring
 - b. Missed more than two consecutive doses or more than two doses in a 6-month period
 - c. Any medical or neurological condition (other than AD) that might be a contributing cause of cognitive impairment
 - d. Seizures, stroke, or transient ischemic attack (TIA) in the past 12 months
 - e. History of cerebrovascular abnormalities
 - f. Bleeding disorder not under adequate control (ex. platelet count < 50,000 or INR > 1.5 for patients not on warfarin)

AND

3. Clinical documentation must be submitted showing cognition scores have not worsened to moderate or advanced disease as defined by one or more of the following cognitive tests (must submit the same cognition tests used for initial approval):
 - a. MMSE (Mini-Mental State Exam) score 20 or lower
 - b. CDR-GS (Clinical Dementia Rating-Global Scale) score greater than 1
 - c. MoCA (Montreal Cognitive Assessment) score < 16

AND

4. Manageable or no side effects

Renewal approvals will be for 6 months.

Lecanemab-irmb (Leqembi™) for the treatment of all other indications is considered experimental, investigational and/or unproven.

BACKGROUND:

Alzheimer disease (AD) is an irreversible and incurable neurodegenerative disorder that is characterized by progressive memory loss and cognitive decline. AD manifests as impairment in a broad spectrum of cognitive processes, typically presenting with an insidious decline in verbal and nonverbal memory, and gradually progressing to deficits in recognition, language, semantics, attention, executive function, visuospatial and spatial abilities, and sensory and motor skills. Memory loss is a common presenting complaint in individuals with AD. AD is the most common cause of dementia among older adults, affecting more than 5 million Americans.

The pathogenesis of AD is not yet fully understood. Autopsy findings in the brains of patients with AD reveal widespread neuropathological changes including cerebral atrophy, cellular degeneration, reactive gliosis, and neuronal and synaptic losses as well as reductions in esters and enzymes needed for successful neurotransmission. These changes are accompanied by the 2 hallmarks of AD: extracellular plaques consisting of amyloid beta peptide, and intracellular neurofibrillary tangles consisting of abnormally phosphorylated tau protein. Amyloid beta (A β) accumulation is considered to



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be a hallmark of early onset of AD; it is also proposed to be an activator for aggregation of phosphorylated tau. As such, amyloid beta is predicted to be a potentially efficient target for drug/biologic therapy.

Current medications donepezil, rivastigmine, memantine, and galantamine have limitations, as they are not effective in all patients and do not change the course of the disease. Lecanemab was the first anti-A β antibody developed to address disease progression and was granted accelerated approval in June 2021.

Lecanemab (Leqembi™) is the 2nd monoclonal antibody (mAb) for treatment of Alzheimer's Disease (AD) FDA approved under the accelerated approval pathway January 6, 2023 based on a phase 2 study (study 201) which showed reduced accumulation of A β plaque. The FDA granted traditional approval July 6, 2023 based on the results of the confirmatory phase 3 Clarity AD trial.

The lecanemab study 201 core was a double-blind, randomized, placebo-controlled phase 2 study of 856 patients randomized to one of five dose regimens or placebo. The primary endpoint was change from baseline on a weighted composite score consisting of selected items from the CDR-SB, MMSE, and ADAS-Cog 14 at Week 53. Lecanemab had a 64% likelihood of 25% or greater slowing of progression on the primary endpoint relative to placebo at Week 53, which did not meet the prespecified success criterion of 80%. An open label extension of study 201 was initiated to allow patients to receive open-label lecanemab 10mg/kg biweekly for up to 24 months, with an intervening off-treatment period (gap period) ranging from 9 to 59 months (mean 24 months). Lecanemab treatment resulted in significant reduction in amyloid plaques and a slowing of clinical decline. Study 201 is still active but not recruiting with estimated study completion date February 20, 2025.

Clarity AD is an 18-month, multicenter, double-blind, phase 3 trial involving persons 50 to 90 years of age with early Alzheimer's disease (mild cognitive impairment or mild dementia due to Alzheimer's disease) with evidence of amyloid on positron-emission tomography (PET) or by cerebrospinal fluid testing. Participants were randomly assigned in a 1:1 ratio to receive intravenous lecanemab or placebo. The primary end point was the change from baseline at 18 months in the score on the Clinical Dementia Rating-Sum of Boxes (CDR-SB; range, 0 to 18, with higher scores indicating greater impairment). The CDR-SB captures function and cognition and is composed of 6 domains: memory, judgment and problem solving, orientation, home and hobbies, community affairs, and personal care. Higher CDR-SB scores are indicative of greater impairment. A total of 1795 participants were enrolled, with 898 assigned to receive lecanemab and 897 to receive placebo. The adjusted least-squares mean change from baseline at 18 months was 1.21 with lecanemab and 1.66 with placebo (difference, -0.45 [-27%]; 95% confidence interval [CI], -0.67 to -0.23; P<0.001). Lecanemab appeared to slow disease progression by about one-quarter, and caused the brain edema (ARIA-E) in one of eight participants. The slower decline translates to a five- to six-month delay in disease progression. Open label studies will answer if clinical benefit persists.

Amyloid related imaging abnormalities (ARIA) have been observed with monoclonal antibodies directed against beta amyloid. ARIA with edema (ARIA-E) can be observed on MRI as brain edema or sulcal effusions, and ARIA with hemosiderin deposition (ARIA-H) includes microhemorrhage and superficial siderosis. ARIA can occur spontaneously in patients with AD, often early in treatment and usually



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asymptomatic, but can lead to serious and life-threatening events including seizure and status epilepticus. Risk of ARIA is increased in apolipoprotein E ε4 (ApoE ε4) homozygotes.

The Centers for Medicare & Medicaid Services (CMS) covers Food and Drug Administration (FDA) approved monoclonal antibodies directed against amyloid for the treatment of AD when furnished in accordance with Section B under coverage with evidence development (CED) for patients who have a clinical diagnosis of mild cognitive impairment (MCI) due to AD or mild AD dementia, both with confirmed presence of amyloid beta pathology consistent with AD. The CED is a paradigm whereby Medicare covers items and services on the condition that they are furnished in the context of approved clinical studies or with the collection of additional clinical data. CMS's decision to use CED is because no trial involving any intervention, alone or combined, has yet demonstrated a meaningful improvement in health outcomes for patients treated with anti-amyloid monoclonal antibodies for the treatment of AD.

CODES:

Important note: Due to the wide range of applicable diagnosis codes and potential changes to codes, an inclusive list may not be presented, but the following codes may apply. Inclusion of a code in this section does not guarantee that it will be reimbursed, and patient must meet the criteria set forth in the policy language.

CPT Codes:	
HCPCS Codes:	J0174 Injection, lecanemab-irmb, 1 mg
ICD10 codes:	Z00.6 Encounter for examination for normal comparison and control in clinical research program G30.0 Alzheimer's disease w/early onset G30.1 Alzheimer's disease w/late onset G30.8 Other Alzheimer's disease G30.9 Alzheimer's disease, unspecified G31.84 mild cognitive impairment, so stated
ICD10 Not covered:	

POLICY HISTORY:

Status	Date	Action
New	08/24/2023	New policy
Updated	08/12/2024	Applied new format and layout. Add CMS NCD hyperlink. Reworded lumbar puncture criteria for clarity.

REFERENCES:

The following scientific references were utilized in the formulation of this medical policy. BSWHP will continue to review clinical evidence related to this policy and make modifications based upon the evolution of the published clinical evidence. Should additional scientific studies become available, and



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they are not included in the list, please forward the reference(s) to BSWHP so the information can be reviewed by the Medical Coverage Policy Committee (MCPC) and the Quality Improvement Committee (QIC) to determine if a modification of the policy is in order.

1. Alonso Vilatela, María Elisa et al. "Genetics of Alzheimer's disease." Archives of medical research vol. 43,8 (2012): 622-31. doi:10.1016/j.arcmed.2012.10.017
2. Alzheimer's Association. "Home." Alzheimer's Disease and Dementia, 2016, www.alz.org/.
3. Bloom, George S. "Amyloid- β and tau: the trigger and bullet in Alzheimer disease pathogenesis." JAMA neurology vol. 71,4 (2014): 505-8. doi:10.1001/jamaneurol.2013.5847
4. Giri, Mohan et al. "Unraveling the genes implicated in Alzheimer's disease." Biomedical reports vol. 7,2 (2017): 105-114. doi:10.3892/br.2017.927
5. Pasanen, Petra et al. "Genetics of dementia in a Finnish cohort." European journal of human genetics : EJHG vol. 26,6 (2018): 827-837. doi:10.1038/s41431-018-0117-3
6. Sun, Xiaojuan et al. " β -Amyloid: the key peptide in the pathogenesis of Alzheimer's disease." Frontiers in pharmacology vol. 6 221. 30 Sep. 2015, doi:10.3389/fphar.2015.00221
7. Tolar, Martin, et al. "Lecanemab, Gantenerumab, BAN2401, and ALZ-801—the First Wave of Amyloid-Targeting Drugs for Alzheimer's Disease with Potential for near Term Approval." Alzheimer's Research & Therapy, vol. 12, no. 1, 2020, doi:10.1186/s13195-020-00663-w.
8. "Dare We Say Consensus Achieved: Lecanemab Slows the Disease | ALZFORUM." Www.alzforum.org, www.alzforum.org/news/conference-coverage/dare-we-say-consensus-achieved-lecanemab-slows-disease. Accessed 21 Feb. 2023.
9. Hayes. Emerging Technology Report Lecanemab (Leqembi) for Alzheimer Disease. Jan 09, 2023.
10. ICER Alzheimer's Disease An assessment of lecanemab Public Meeting March 2023. <https://icer.org/assessment/alzheimers-disease-2022/#overview> Accessed March 21, 2023.
11. IPD Analytics. RxInsights New Drug Review Leqembi (lecanemab-irmb). January 2023.
12. Leqembi (lecanemab-irmb) [prescribing information]. Nutley, NJ: Esai Inc. and Biogen Inc; July 2023.
13. Lin GA, et al. Beta-Amyloid Antibodies for Early Alzheimer's Disease Draft Evidence Report. Institute for Clinical and Economic Review, December 22, 2022. https://icer.org/wp-content/uploads/2021/12/ICER_Alzheimers-Disease_Draft-Report_12222022.pdf
14. McDade, E., Cummings, J.L., Dhadda, S. et al. Lecanemab in patients with early Alzheimer's disease: detailed results on biomarker, cognitive, and clinical effects from the randomized and open-label extension of the phase 2 proof-of-concept study. Alz Res Therapy 14, 191 (2022). <https://doi.org/10.1186/s13195-022-01124-2>
15. Swanson, C.J., 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-A β protofibril antibody. Alz Res Therapy 13, 80 (2021). <https://doi.org/10.1186/s13195-021-00813-8>
16. U.S. Centers for Medicare & Medicaid Services. NCA - Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease (CAG-00460N). www.cms.gov, <https://www.cms.gov/medicare-coverage-database/view/nca.aspx?ncid=305>. Accessed 16 Feb 2023.
17. U.S. Centers for Medicare & Medicaid Services. NCD - Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease (AD) (NCD 200.3). www.cms.gov, <https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?ncid=375&ncdver=1>. Accessed 16 Feb 2023.
18. U.S. Food & Drug Administration. FDA Converts Novel Alzheimer's Disease Treatment to Traditional Approval. FDA News release, <https://www.fda.gov/news-events/press-announcements/fda-converts-novel-alzheimers-disease-treatment-traditional-approval>. July 06, 2023.
19. VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives. Lecanemab-irmb (LEQEMBI) Criteria for Use. February 2023.
20. van Dyck CH, Swanson CJ, Aisen P, et al. Lecanemab in Early Alzheimer's Disease. N Engl J Med. 2023;388(1):9-21. doi:10.1056/NEJMoa2212948



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Note:

Health Maintenance Organization (HMO) products are offered through Scott and White Health Plan dba Baylor Scott & White Health Plan, and Scott & White Care Plans dba Baylor Scott & White Care Plan. Insured PPO and EPO products are offered through Baylor Scott & White Insurance Company. Scott and White Health Plan dba Baylor Scott & White Health Plan serves as a third-party administrator for self-funded employer-sponsored plans. Baylor Scott & White Care Plan and Baylor Scott & White Insurance Company are wholly owned subsidiaries of Scott and White Health Plan. These companies are referred to collectively in this document as Baylor Scott & White Health Plan.

RightCare STAR Medicaid plans are offered through Scott and White Health Plan in the Central Managed Care Service Area (MRSA) and STAR and CHIP plans are offered through SHA LLC dba FirstCare Health Plans (FirstCare) in the Lubbock and West MRSAs.