MEDICAL COVERAGE POLICY	
SERVICE: Lecanemab-irmb (Leqembi™)	
Policy Number:	**301**
Effective Date:	**09/01/2023**
Last Review:	**08/24/2023**
Next Review Date:	**08/24/2024**

Important note:
Unless otherwise indicated, this policy will apply to all lines of business.
Even though this policy may indicate that a particular service or supply may be considered medically necessary and thus covered, this conclusion is not based upon the terms of your particular benefit plan. Each benefit plan contains its own specific provisions for coverage and exclusions. Not all benefits that are determined to be medically necessary will be covered benefits under the terms of your benefit plan. You need to consult the Evidence of Coverage (EOC) or Summary Plan Description (SPD) to determine if there are any exclusions or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and your plan of benefits, the provisions of your benefits plan will govern. However, applicable state mandates will take precedence with respect to fully insured plans and self-funded non-ERISA (e.g., government, school boards, church) plans. Unless otherwise specifically excluded, Federal mandates will apply to all plans. With respect to Medicare-linked plan members, this policy will apply unless there are Medicare policies that provide differing coverage rules, in which case Medicare coverage rules supersede guidelines in this policy. Medicare-linked plan policies will only apply to benefits paid for under Medicare rules, and not to any other health benefit plan benefits. CMS's Coverage Issues Manual can be found on the CMS website. Similarly, for Medicaid-linked plans, the Texas Medicaid Provider Procedures Manual (TMPPM) supersedes coverage guidelines in this policy where applicable.

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PRIOR AUTHORIZATION: Required

POLICY:

For Medicare plans, please refer to applicable NCD (National Coverage Determination).

For Medicaid plans, please confirm coverage as outlined in the Texas Medicaid TMPPM.

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:

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

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
        ii. Lumbar puncture: CSF (i.e. Aβ42, Aβ41/ Aβ40 ratio, tau/ Aβ42 ratio) assay with high evidence of concordance with amyloid PET scan to assess the presence of amyloid deposition

    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 ε4 genetic testing to assess risk of amyloid-related imaging abnormalities (ARIA), i.e. brain swelling and bleeds
8. Risks of ARIA discussed with member or caregiver
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 (≤ 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 an < 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)
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.

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

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.
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)
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
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.

OVERVIEW:

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, visuoperceptual 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 (Aβ) accumulation is considered to 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-Aβ 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 Aβ 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 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:

CODES: 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:	
CPT Not Covered:	

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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:	

CMS: NCD 200.3 Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease (AD) – Medicare 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.
Effective date: 04/07/2022. Implementation date 12/12/2022.

POLICY HISTORY:

Status	Date	Action
New	08/24/2023	New policy

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 may modify it at a later date based upon the evolution of the published clinical evidence. Should additional scientific studies become available and 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.

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