Oscar Clinical Guideline: Leqembi (lecanemab-irmb) (PG138 Ver. 3)

Leqembi (lecanemab-irmb)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by the gradual decline of cognitive functions, including memory, thinking, and reasoning abilities. It is the most common cause of dementia in older adults, affecting millions of people worldwide. The disease primarily impacts individuals over 65 years of age, but early-onset Alzheimer's can occur in people as young as 40.

The exact cause of Alzheimer's is not entirely understood, but it is believed to involve a combination of genetic, environmental, and lifestyle factors. At the microscopic level, the disease is associated with the accumulation of amyloid-beta (A**β**) plaques and neurofibrillary tangles in the brain, leading to neuronal dysfunction and cell death.

Currently, there is no cure for Alzheimer's disease. Treatment primarily focuses on managing symptoms and improving the quality of life for patients. The available treatments can be divided into symptomatic treatments, disease-modifying therapies, and non-pharmacological interventions.

- Symptomatic treatments: These medications aim to alleviate cognitive and behavioral symptoms, such as memory loss and confusion. They include cholinesterase inhibitors (e.g., donepezil, rivastigmine, and galantamine) and the NMDA receptor antagonist memantine. These drugs can help manage symptoms, but they do not address the underlying disease progression.
- Disease-modifying therapies: Disease-modifying therapies aim to target the underlying pathophysiology of Alzheimer's disease, with the goal of slowing down or halting its progression. Two notable examples of these therapies include LEQEMBI™ (lecanemab-irmb) and ADUHELM® (aducanumab-avwa).
- Non-pharmacological interventions: A comprehensive approach to Alzheimer's disease treatment should not only focus on pharmacological options, such as symptomatic treatments and disease-modifying therapies, but also consider non-pharmacological interventions and caregiver support to provide the best possible care for patients and their families. Non-pharmacological interventions, including cognitive stimulation, physical activity, and social engagement, play a vital role in managing Alzheimer's disease and improving patients' quality of life. These interventions contribute to preserving cognitive function, postponing symptom progression, and adopting a more comprehensive approach to patient care.

LEQEMBI™ (lecanemab-irmb) is an amyloid beta-directed antibody that specifically targets aggregated forms of Aβ, promoting their clearance from the brain. It is indicated for the treatment of Alzheimer's disease in patients with mild cognitive impairment or mild dementia stage, 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 those studied.

Definitions

"**ADAS-Cog (Alzheimer's Disease Assessment Scale - Cognitive Subscale)**" is a widely used cognitive test specifically designed to evaluate the cognitive function of individuals with Alzheimer's disease. It assesses various cognitive domains, such as memory, language, praxis, and orientation. The ADAS-Cog has multiple versions with different numbers of items; the 14-item version is often used in clinical trials. Higher scores on the ADAS-Cog indicate greater cognitive impairment.

"**ADCOMS (Alzheimer's Disease Composite Score)**" is a composite score that combines selected items from the CDR-SB, MMSE, and ADAS-Cog to create a single measure of cognitive and functional performance in Alzheimer's disease. The ADCOMS has been developed specifically for use in clinical trials to detect treatment effects in the early stages of the disease.

"**Alzheimer's disease (AD)**" is a progressive neurodegenerative disorder characterized by a decline in cognitive functions, such as memory, thinking, and reasoning abilities. It is the most common cause of dementia in older adults.

"**Amyloid-beta (Aβ) plaques**" are abnormal protein deposits that accumulate in the brain and are associated with Alzheimer's disease. They consist of amyloid-beta peptides, which are thought to contribute to neuronal dysfunction and cell death.

"**CDR-SB (Clinical Dementia Rating Scale Sum of Boxes)**" is a widely used tool to assess the severity of dementia, particularly Alzheimer's disease. It measures cognitive and functional performance in six domains: memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care. Each domain is rated on a scale from 0 (no impairment) to 3 (severe impairment), resulting in a sum of boxes score ranging from 0 to 18, with higher scores indicating greater severity of dementia.

"**Cholinesterase inhibitors**" is a class of drugs used to treat Alzheimer's disease by increasing the levels of the neurotransmitter acetylcholine in the brain, which can help improve cognitive function. Examples include donepezil, rivastigmine, and galantamine.

"**Dementia**" is a general term for a decline in mental ability severe enough to interfere with daily life. It is not a specific disease but an overall term that describes a wide range of symptoms associated with a decline in memory or other thinking skills.

"**Disease-modifying therapies**" refer to treatments that aim to target the underlying pathophysiology of a disease, with the goal of slowing down or halting its progression.

"**Experimental or Investigational**" are terms used to describe treatments, procedures, or services that are not considered standard of care or have not been proven to be safe and effective for a specific condition. These treatments are generally not covered by the Plan.

"**MMSE (Mini-Mental State Examination)**" is a brief, 30-point questionnaire that is used to assess cognitive function in older adults. It measures various cognitive domains, including orientation, registration, attention and calculation, recall, and language. The MMSE is scored from 0 to 30, with lower scores indicating more severe cognitive impairment.

"**Neurofibrillary tangles**" are abnormal accumulations of the protein tau inside brain cells that are also associated with Alzheimer's disease. These tangles disrupt the normal functioning of cells and are thought to contribute to cell death.

"**NMDA receptor antagonist**" is a type of drug that blocks the NMDA receptor, a protein involved in the communication between brain cells. Memantine is an NMDA receptor antagonist used to treat Alzheimer's disease.

"**PET SUVR (Positron Emission Tomography Standardized Uptake Value Ratio)**" is a quantitative measure used in amyloid PET imaging to assess the levels of amyloid-beta plaques in the brain. In the context of Alzheimer's disease, PET SUVR is used to determine the extent of amyloid-beta plaque accumulation in specific brain regions. Higher SUVR values indicate higher levels of amyloid-beta plaques, which are associated with Alzheimer's disease.

"**Symptomatic treatments**" refers to medications that aim to alleviate the cognitive and behavioral symptoms of a disease, such as memory loss and confusion, without addressing the underlying disease progression.

Policy Statement on LEQEMBI™ (lecanemab-irmb) Efficacy Information

Based on the current available efficacy information for LEQEMBI™ (lecanemab-irmb), it is insufficient to determine if the medication demonstrates any clinically meaningful benefits. The primary endpoint in Study 201 (also referred to as Study 1, NCT01767311), which assessed the change from baseline on a weighted composite score consisting of selected items from the CDR-SB, MMSE, and ADAS-Cog 14 at Week 53, did not meet the prespecified success criterion of 80%. The Bayesian analysis indicated that the 10 mg/kg biweekly dose of lecanemab had a 64% probability of bettering placebo by at least 25% less decline on ADCOMS, which was below the required threshold.

While some key secondary efficacy endpoints, such as the change from baseline in amyloid PET SUVR composite at Week 79 and change from baseline in the CDR-SB and ADAS-Cog14 at Week 79, showed less change from baseline in CDR-SB and ADAS-Cog 14 scores at Week 79 in the LEQEMBI group than in patients on placebo, these results were considered "nominal" due to the primary endpoint not being met.

Furthermore, the phase III Clarity AD trial (NCT03887455) and the phase II proof-of-concept trial (Study 201, NCT01767311) provided mixed results. Although the Clarity AD trial showed significant

improvements in the primary efficacy endpoint and key secondary endpoints, the primary efficacy endpoint was not met in Study 201.

Considering the inconclusive findings and the absence of additional clinical trials, there is not enough information to support approval for LEQEMBI™ (lecanemab-irmb) at this time. Further research, including well-designed, large-scale clinical trials, is needed to confirm the clinical benefits and safety of this medication in the treatment of Alzheimer's disease.

Medical Necessity Criteria for LEQEMBI™ (lecanemab-irmb)

Based on the current available efficacy information for LEQEMBI™ (lecanemab-irmb) and the inconclusive findings from the clinical trials, the Plan does not have established Medical Necessity Criteria for authorization of this drug. As the evidence is insufficient to determine any clinically meaningful benefits of LEQEMBI™, the Plan cannot support its approval or usage for the treatment of Alzheimer's disease at this time.

The Plan will continue to monitor the ongoing research and clinical trials related to LEQEMBI™ and will revise our Medical Necessity Criteria accordingly should new, compelling evidence emerge that supports its efficacy and safety in the treatment of Alzheimer's disease. Until then, we encourage healthcare providers and members to explore alternative treatment options with proven efficacy and established medical necessity criteria.

Experimental or Investigational / Not Medically Necessary

LEQEMBI™ (lecanemab-irmb) for any indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven. This determination is based on the lack of sufficient clinical evidence demonstrating the efficacy and safety of LEQEMBI™. Non-covered indications include, but are not limited to, the following:

- the treatment of Alzheimer's disease, including:
    - mild cognitive impairment or mild dementia stage of the disease.
    - moderate to severe Alzheimer's disease or other stages of dementia.
- Treatment of other neurodegenerative disorders or cognitive impairments unrelated to Alzheimer's disease.
- Prophylactic or preventive treatment in individuals without Alzheimer's disease or at risk for developing Alzheimer's disease.

- Use in combination with other experimental or investigational therapies for Alzheimer's disease or other cognitive disorders.

The Plan will continue to monitor the evidence and update the coverage policy as new information becomes available. In the meantime, we encourage healthcare providers and members to consider alternative treatment options with proven efficacy and established medical necessity criteria for the management of Alzheimer's disease and other cognitive disorders.

Applicable Billing Codes (HCPCS/CPT Codes)

CPT/HCPCS Codes considered experimental or investigational or not considered medically necessary:	
Code	*Description*
96365	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour
96366	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hour (List separately in addition to code for primary procedure)
J0174	Injection, lecanemab-irmb, 1mg
ICD-10 Codes considered experimental or investigational or not considered medically necessary:	
Code	*Description*
G30	Alzheimer's disease
G30.0	Alzheimer's disease with early onset
G30.1	Alzheimer's disease with late onset
G30.8	Other Alzheimer's disease
G30.9	Alzheimer's disease, unspecified
G31.84	mild cognitive impairment
F00	Dementia in Alzheimer's disease
F00.0	Dementia in Alzheimer's disease with early onset
F00.1	Dementia in Alzheimer's disease with late onset
F00.2	Dementia in Alzheimer's disease, atypical or mixed type

F00.9	Dementia in Alzheimer's disease, unspecified
F01	Vascular dementia
F01.50	Vascular dementia without behavioral disturbance
F01.51	Vascular dementia with behavioral disturbance
F02	Dementia in other diseases classified elsewhere
F02.80	Dementia in other diseases classified elsewhere without behavioral disturbance
F02.81	Dementia in other diseases classified elsewhere with behavioral disturbance
F03	Unspecified dementia
F03.90	Unspecified dementia without behavioral disturbance
F03.91	Unspecified dementia with behavioral disturbance
F05	Delirium due to known physiological condition

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Clinical Guideline Revision / History Information

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