Drug Coverage Policy

Effective Date……09/01/2024
Coverage Policy Number……IP0697
Policy Title……Neurology – Kisunla

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- Kisunla™ (donanemab-azbt intravenous infusion - Lilly)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Conditions Not Covered

Donanemab-azbt intravenous infusion (Kisunla) is considered to be experimental, investigational, or unproven due to insufficient data establishing safety, efficacy, and improved health outcomes for any condition.

The current Kisunla efficacy information is insufficient to determine if the medication demonstrates any clinically meaningful benefits. In the absence of additional clinical trials, there is not enough information to support approval.

The efficacy of Kisunla for traditional approval was evaluated in one Phase III randomized, double-blind, placebo-controlled, multicenter, pivotal study (TRAILBLAZER-ALZ2) in patients with mild cognitive impairment due to Alzheimer's disease and mild Alzheimer's disease dementia (n = 1,736).[3] The primary efficacy endpoint was the change from baseline in the integrated Alzheimer's Disease Rating Scale (iADRS) at 76 weeks, an assessment of cognition and daily function with scores ranging from 0 to 144 (lower scores indicate greater impairment). A key secondary endpoint included the change from baseline at 76 weeks in the Clinical Dementia Rating Scale – sum of boxes (CDR-SB), also an assessment of cognition and daily function with scores ranging from 0 to 18 (higher scores indicate greater impairment). For the low/medium tau population, the least-squares mean (LSM) change from baseline at Week 76 in the iADRS score was -6.02 in the Kisunla arm and -9.27 in the placebo arm (treatment difference 3.25; $P < 0.001$). In the combined (low/medium and high tau) population, the LSM change from baseline at Week 76 in the iADRS score was -10.19 in the Kisunla arm and -13.11 in the placebo arm (treatment difference 2.92; $P < 0.001$). In the low/medium tau population, the placebo-adjusted LSM change from baseline at 76 weeks for CDR-SB was -0.67, and in the combined population, the placebo-adjusted LSM change from baseline at 76 weeks for CDR-SB was -0.70. However, this slowing of progression did not achieve clinical significance. The authors of TRAILBLAZER-ALZ2 note that the minimal clinically important difference for the iADRS is a change of 5 points for those with Alzheimer disease with mild cognitive impairment and 9 points for those with Alzheimer disease with mild dementia, and it is 1 to 2 points for the CDR-SB.[3,4]

Additionally, one Phase II, randomized, double-blind, placebo-controlled, multicenter study (TRAILBLAZER-ALZ) was conducted in patients with mild cognitive impairment due to Alzheimer's disease and mild Alzheimer's disease dementia (n = 257).[5] The change from baseline in the iADRS score at 76 weeks was -6.86 in the Kisunla arm and -10.06 in the placebo arm (treatment difference 3.20; $P = 0.04$). The placebo-adjusted change from baseline at 76 weeks for the CDR-SB score was -0.36 and failed to show a significant difference between the two trial groups.

Kisunla can cause amyloid related imaging abnormalities-edema (ARIA-E) and amyloid related imaging abnormalities-hemosiderin deposition (ARIA-H), which includes microhemorrhage and superficial siderosis, which can be observed on magnetic resonance imaging (MRI).[1] A recent (within 1 year) MRI of the brain should be obtained prior to initiating treatment with Kisunla. The safety of Kisunla has not been evaluated in patients with prior cerebral hemorrhage > 1 cm in greatest diameter, more than four microhemorrhages, more than one area of superficial siderosis, severe white matter disease, and vasogenic edema. Enhanced clinical vigilance for asymptomatic amyloid related imaging abnormalities (ARIA) is recommended during the first four doses of treatment with Kisunla, particularly during titration, because the majority of ARIA was observed during this time. MRIs of the brain should be obtained prior to the second, third, fourth, and seventh infusions of Kisunla to evaluate for the presence of asymptomatic ARIA. In addition to ARIA, intracerebral hemorrhages > 1 cm in diameter have occurred in patients treated with Kisunla. Symptomatic ARIA occurred in 6% of patients treated with Kisunla (n = 52/853) in the pivotal trial, and clinical symptoms associated with ARIA resolved in approximately 85% of affected patients (n = 44/52). Including asymptomatic radiographic events, ARIA was observed in 36% of patients treated with Kisunla vs. 14% of patients treated with placebo in the pivotal trial. ARIA-E and ARIA-H were observed in 24% and 31% of patients treated with Kisunla vs. 2% and 13% of patients receiving placebo.

Overview

Kisunla, an amyloid beta-directed antibody, is indicated for the treatment of **Alzheimer's disease**. Per the FDA product information, treatment with Kisunla should be initiated in patients with mild cognitive impairment or mild dementia stage of disease, the population in which treatment was initiated in clinical trials.[1]

Disease Overview
An estimated 6.9 million Americans ≥ 65 years of age are living with Alzheimer's dementia in 2024, with 73% of these people ≥ 75 years of age.[2] The number and proportion of older adults who have mild cognitive impairment due to Alzheimer's disease is difficult to estimate; however, a rough approximation suggests that 5 to 7 million older Americans may have mild cognitive impairment due to Alzheimer's disease. People with mild cognitive impairment due to Alzheimer's disease have biomarker evidence of brain changes due to the disease in addition to subtle problems with memory and thinking. Biomarker evidence includes abnormal levels of amyloid beta as evidenced on positron emission tomography (PET) scans and in analysis of cerebrospinal fluid, and decreased metabolism of glucose as shown on PET scans. These cognitive problems may be noticeable to the individual family members and friends, but not to others, and they do not interfere with the person's ability to carry out everyday activities. The mild changes in cognitive abilities occur when the brain can no longer compensate for the damage and death of nerve cells due to Alzheimer's disease.

Coding Information

Notes:
1. This list of codes may not be all-inclusive since the American Medical Association (AMA) and Centers for Medicare and Medicaid Services (CMS) code updates may occur more frequently than policy updates.
2. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Experimental/Investigational/Unproven:

HCPCS Codes	Description
J0175	Injection, donanemab-azbt, 2 mg

References

1. Kisunla™ intravenous infusion [prescribing information]. Indianapolis, IN: Lilly; July 2024.
2. Alzheimer's Association. Alzheimer's disease facts and figures-2024. Available at: https://www.alz.org/media/Documents/alzheimers-facts-and-figures.pdf. Accessed on July 9, 2024.
3. Sims JR, Zimmer JA, Evans CD, et al, for the TRAILBLAZER-ALZ 2 Investigators. Donanemab in early symptomatic Alzheimer disease: The TRAILBLAZER-ALZ 2 randomized clinical trial. *JAMA*. 2023;330(6):512-527.
4. Andrews JS, Desai U, Kirson NY, et al. Disease severity and minimal clinically important differences in clinical outcome assessments for Alzheimer's disease clinical trials. *Alzheimers Dement*. 2019;5:354-363.
5. Mintun MA, Lo AC, Duggan Evans C, et al. Donanemab in early Alzheimer's disease. *N Engl J Med*. 2021;384(18):1691-1704.

Revision Details

Type of Revision	Summary of Changes	Date
New	New policy	09/01/2024

The policy effective date is in force until updated or retired.