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Section:	Prescription Drugs	**Effective Date:**	January 1, 2025
Subsection:	Central Nervous System Drugs	**Original Policy Date:**	July 26, 2024
Subject:	Kisunla	**Page:**	1 of 5

Last Review Date: December 13, 2024

Kisunla

Description

Kisunla (donanemab-azbt)

Background
Kisunla (donanemab-azbt) is a humanized immunoglobulin gamma 1 (IgG1) monoclonal antibody directed against insoluble N-truncated pyroglutamate amyloid beta. The accumulation of amyloid beta plaques in the brain is a defining pathophysiological feature of Alzheimer's disease (AD). Kisunla reduces amyloid beta plaques (1).

Regulatory Status
FDA-approved indication: Kisunla is an amyloid beta-directed antibody indicated for the treatment of Alzheimer's disease. 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 the clinical trials (1).

Kisunla has a boxed warning regarding amyloid related imaging abnormalities (ARIA). Monoclonal antibodies directed against aggregated forms of beta amyloid, including Kisunla, can cause ARIA, characterized as ARIA with edema and ARIA with hemosiderin deposition. A baseline brain magnetic resonance imaging (MRI) should be obtained prior to initiating treatment. An MRI should also be obtained prior to the 2nd, 3rd, 4th, and 7th infusions (1).

Kisunla carries a warning regarding infusion-related reactions. Consider pre-medication at subsequent dosing with antihistamines, acetaminophen, or corticosteroids (1).

In Study 1 (NCT 04437511), the age of patients ranged from 59 to 86 years, with a median age of 73 years (1). Clinically, AD can be categorized into two phenotypes based on the ages of onset: early-onset AD (EOAD; <65 years) and late-onset AD (LOAD; >65 years), of which LOAD is the more common form worldwide. The proportion of EOAD in all AD cases is between 5% and 10%. Presenilin 1 (*PSEN1*), presenilin 2 (*PSEN2*), and amyloid precursor protein (*APP*) are mostly associated with autosomal dominant forms of EOAD. Apart from genetic factors, mutations are environmentally related. Genetic–environmental interactions may be caused by variation in the age of onset, neuropathological patterns, and disease duration. To date, more than 200 mutations have been described in *PSEN1* throughout the world, but mutations in *PSEN2* are extremely rare (2).

Do not initiate other anti-amyloid agents or central nervous system agents (e.g., cholinesterase inhibitors or memantine) at the same time as Kisunla. Patients should be on a stable dose for 3 months prior to initiating new therapy (3).

The safety and effectiveness of Kisunla in pediatric patients have not been established (1).

Related policies
Leqembi

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Kisunla may be considered **medically necessary** if the conditions indicated below are met.

Kisunla may be considered **investigational** for all other indications.

Prior-Approval Requirements

Diagnosis

Patient must have the following:

Alzheimer’s disease (mild cognitive impairment or mild dementia stage of disease)

AND ALL of the following:

1. 50 years of age or older **OR** if less than 50 years of age, patient has a genetic mutation in amyloid precursor protein (APP), presenilin-1 (PSEN1), or presenilin-2 (PSEN2), or other clinical documentation to support early onset AD
2. Confirmed presence of amyloid pathology by **ONE** of the following:
    a. Amyloid Positron Emission Tomography (PET) scan
    b. Cerebrospinal fluid
    c. Blood/plasma
3. Other causes of dementia (e.g., Lewy body dementia) have been ruled out
4. Patient has mild cognitive impairment as confirmed by **ONE** of the following:
    a. Clinical Dementia Rating (CDR®)-Global score of 0.5 or 1.0 (e.g., *https://knightadrc.wustl.edu/professionals-clinicians/cdr-dementia-staging-instrument/*)
    b. Mini-Mental State Examination (MMSE) score of 20 to 30 (e.g., *https://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/cogimp-smmse.pdf*)
5. A recent (within one year) brain MRI has been obtained or will be obtained prior to initiating treatment with Kisunla
6. Prescriber agrees to monitor for signs and symptoms of amyloid related imaging abnormalities (ARIA) using MRI as clinically appropriate
7. **NO** neurological or other medical condition, other than AD, that may significantly contribute to cognitive decline
8. **NO** medical conditions, other than AD, likely to increase significant adverse events

Prior – Approval *Renewal* Requirements

Diagnosis

Patient must have the following:

Alzheimer's disease (mild cognitive impairment or mild dementia stage of disease)

AND ALL of the following:

1. 50 years of age or older **OR** if less than 50 years of age, patient has a genetic mutation in amyloid precursor protein (APP), presenilin-1 (PSEN1), or presenilin-2 (PSEN2), or other clinical documentation to support early onset AD
2. Reduction in brain amyloid beta plaque as confirmed by PET scan

3. Patient continues to have mild cognitive impairment as confirmed by stabilization in score in **ONE** of the following:
    a. Clinical Dementia Rating (CDR®)-Global score of 0.5 or 1.0 (e.g., *https://knightadrc.wustl.edu/professionals-clinicians/cdr-dementia-staging-instrument/*)
    b. Mini-Mental State Examination (MMSE) score of 20 to 30 (e.g., *https://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/cogimp-smmse.pdf*)
4. Prescriber agrees to continue monitoring for signs and symptoms of ARIA using MRI as clinically appropriate
5. **NO** neurological or other medical condition, other than AD, that may significantly contribute to cognitive decline
6. **NO** medical conditions, other than AD, likely to increase significant adverse events

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Kisunla (donanemab-azbt) is a humanized immunoglobulin gamma 1 (IgG1) monoclonal antibody that reduces amyloid beta plaques in Alzheimer's disease. Patients should have a baseline MRI done prior to initiating therapy with Kisunla and prior to the 2nd, 3rd, 4th, and 7th infusions. The safety and effectiveness of Kisunla in pediatric patients have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Kisunla while maintaining optimal therapeutic outcomes.

References

1. Kisunla [package Insert]. Indianapolis, IN: Eli Lilly and Company; July 2024.
2. Cai, Y., An, S. S., & Kim, S. (2015). Mutations in presenilin 2 and its implications in Alzheimer's disease and other dementia-associated disorders. *Clinical interventions in aging*, *10*, 1163–1172. https://doi.org/10.2147/CIA.S85808.
3. Mintun, M.A., Lo A.C., Duggan Evans C, et al. (2021) Donanemab in early Alzheimer's disease. *N. Engl. J. Med.*, 384,1691-704. DOI: 10.1056/NEJMoa2100708.

Policy History

Date	Action
July 2024	Addition to PA
September 2024	Annual review
December 2024	Annual review. Per SME, updated requirement for amyloid confirmation by PET scan, cerebrospinal fluid, or blood/plasma; updated CDR link; and changed MMSE score to 20 to 30. Also added statement to regulatory section regarding use with other anti-amyloid agents

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 13, 2024 and is effective on January 1, 2025.