Oscar Clinical Guideline: Kisunla (donanemab-azbt) (PG238, Ver. 1)

Kisunla (donanemab-azbt)

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

Kisunla (donanemab-azbt) is a monoclonal antibody that targets amyloid beta plaques in the brain and is approved by the FDA for treatment of early Alzheimer's disease (AD). While clinical trials have shown some potential benefits in slowing cognitive decline, the evidence is limited and the clinical meaningfulness of the observed effects remains uncertain. Additionally, Kisunla (donanemab-azbt) is associated with risks of amyloid-related imaging abnormalities (ARIA) that can be serious. Given the limited evidence of clinically meaningful benefit and potential risks, Kisunla (donanemab-azbt) is considered not medically necessary for the treatment of Alzheimer's disease at this time.

Definitions

"Alzheimer's disease (AD)" is a progressive neurodegenerative disorder characterized by cognitive decline, memory loss, and functional impairment.

"Mild cognitive impairment (MCI)" refers to an early stage of cognitive decline that may progress to dementia.

"Amyloid beta (Aβ)" are protein fragments that accumulate to form plaques in the brains of Alzheimer's patients.

"Amyloid-related imaging abnormalities (ARIA)" refers to brain swelling or bleeding that can occur with anti-amyloid therapies.

Policy Statement on Kisunla (donanemab-azbt) for Alzheimer's Disease Efficacy Information

The use of Kisunla (donanemab-azbt) is considered not medically necessary for the treatment of Alzheimer's disease or any other indication, as the available evidence is insufficient to demonstrate clinically meaningful benefit that outweighs potential risks.

- The phase III TRAILBLAZER-ALZ 2 trial showed Kisunla (donanemab-azbt) slowed cognitive decline by 35.1% in patients with low/medium tau and by 22.3% in the overall population over 76 weeks, as measured by the integrated Alzheimer's Disease Rating Scale (iADRS).
- Secondary outcomes showed modest benefits on measures like the Clinical Dementia Rating Scale-Sum of Boxes (CDR-SB) and activities of daily living.
- Kisunla (donanemab-azbt) substantially reduced amyloid plaque levels but did not significantly affect tau protein levels.
- The earlier phase II TRAILBLAZER-ALZ trial showed a modest 3.2 point difference on the iADRS but failed to meet secondary clinical endpoints.

The use of Kisunla (donanemab-azbt) is associated with significant safety concerns that must be carefully weighed against its modest efficacy. Key risks include:

- Amyloid-Related Imaging Abnormalities (ARIA):
    - ARIA occurred in 36% of patients treated with donanemab compared to 14% on placebo.
    - ARIA-E (edema) occurred in 24% of donanemab patients vs 2% on placebo.
    - ARIA-H (microhemorrhage) occurred in 25% vs 13% on placebo.
    - Symptomatic ARIA occurred in 6% of donanemab patients.
    - Severe ARIA-E occurred in 2%, severe ARIA-H microhemorrhage in 5%, and severe ARIA-H superficial siderosis in 5% of patients.
- Intracerebral Hemorrhage:

    - Intracerebral hemorrhage >1 cm occurred in 0.5% (4/853) of donanemab patients vs 0.2% (2/874) on placebo.
    - Three patients died after developing serious ARIA.
- Increased Risk in ApoE **ε**4 Homozygotes:
    - ARIA incidence was higher in ApoE **ε**4 homozygotes (55%) compared to heterozygotes (36%) and noncarriers (25%).
    - Severe ARIA rates were also higher in homozygotes.
- Other Adverse Effects:
    - Infusion-related reactions occurred in 9% of donanemab patients vs 0.5% on placebo.
    - Hypersensitivity reactions occurred in 3% of donanemab patients vs 0.7% on placebo.
- Testing for ApoE **ε**4 status is recommended before initiating treatment.
- The prescribing information contains a boxed warning about the risk of ARIA.
    - Baseline brain MRI and periodic MRIs are required to monitor for ARIA.
    - Enhanced clinical vigilance for ARIA is recommended during the first 24 weeks of treatment.

Medical Necessity Criteria for Kisunla (donanemab-azbt) for Alzheimer's Disease

Kisunla (donanemab-azbt) is considered not medically necessary for any indication, including for the treatment of Alzheimer's disease.

Experimental or Investigational / Not Medically Necessary

Kisunla (donanemab-azbt) is considered experimental, investigational, and not medically necessary for the treatment of Alzheimer's disease or any other indication for the following reasons:

1. While clinical trials have shown some potential for slowing cognitive decline, the magnitude of benefit is modest and of uncertain clinical significance.
2. Kisunla (donanemab-azbt) is associated with risks of ARIA, which can be serious and potentially life-threatening in some cases.
3. There is insufficient evidence that the potential benefits of Kisunla (donanemab-azbt) outweigh its risks in real-world clinical practice outside of clinical trials.
4. Professional guidelines have not yet recommended routine use of Kisunla (donanemab-azbt) for Alzheimer's disease management.

Given these limitations in the current evidence, Kisunla (donanemab-azbt) is considered not medically necessary for the treatment of Alzheimer's disease or any other indication at this time. The Plan will continue to review emerging evidence on Kisunla (donanemab-azbt) and may reevaluate this policy as new data become available.

Applicable Billing Codes (HCPCS/CPT Codes)

Service(s) name	
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
J0175	Injection, donanemab-azbt, 2 mg
ICD-10 Codes considered experimental or investigational or not considered medically necessary:	
Code	*Description*
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
Z00.6	Encounter For Examination For Normal Comparison And Control In Clinical Research Program

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Clinical Guideline Revision / History Information

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