Clinical Policy: Donanemab-azbt (Kisunla)

Reference Number: PA.CP.PHAR.594
Effective Date: 11/2024
Last Review Date: 10/2024

Description
Donanemab-azbt (Kisunla™) is a monoclonal antibody targeting amyloid beta.

FDA Approved Indication(s)
Kisunla is indicated for the treatment of Alzheimer's disease (AD). Treatment with Kisunla should be initiated in patients with mild cognitive impairment (MCI) or mild dementia stage of disease, the population in which treatment was initiated in the clinical trials.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness® that Kisunla is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Alzheimer's Disease (must meet all)**:**

1. Diagnosis of MCI due to AD or mild AD dementia (see *Appendix E*);
2. Prescribed by or in consultation with a geriatrician or neurologist;
3. Age ≥ 60 and ≤ 85 years;
4. Documentation of the presence of beta-amyloid plaques as verified by one of the following (a or b):
   a. Positron emission tomography scan;
   b. Cerebrospinal fluid testing;
5. Documentation of one of the following baseline cognitive tests (a or b; *see Appendix D*):
   a. Mini-Mental State Examination (MMSE) score of 20-28;
   b. Montreal Cognitive Assessment (MoCA) score ≥ 16;
6. Documentation of one of the following baseline functional tests and the resulting score (a, b, or c):
   a. Functional Assessment Questionnaire (FAQ) score ≤ 9;
   b. Functional Assessment Staging Test (FAST) score of 3-4;
   c. Clinical Dementia Rating-Sum of Boxes (CDR-SB) of 0.5-9;
7. Documentation of recent (within the last year) brain magnetic resonance imaging (MRI) demonstrating all of the following (a-e):
   a. Absence of amyloid-related imaging abnormalities-edema (ARIA-E);
   b. ≤ 4 cerebral microhemorrhages;
   c. ≤ 1 area of superficial siderosis;
   d. Absence of any macrohemorrhage;
   e. Absence of any severe white matter disease;

8. Member has no history of transient ischemic attacks (TIA), stroke, or seizures within the past 12 months;
9. Member is not currently taking concomitant anticoagulant or antiplatelet therapy;
10. Prescriber attestation that the prescriber has discussed with the member the potentially increased risk of amyloid-related imaging abnormalities (ARIA) in those who are ApoE4 genetic homozygotes;
11. Kisunla is not prescribed concurrently with Leqembi;
12. Dose does not exceed 1,400 mg every 4 weeks.

Approval duration: 3 months (3 doses of infusion only)

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Alzheimer's Disease (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy as evidenced by slowed decline in cognition;
3. Documentation of one of the following baseline cognitive tests (a or b; *see Appendix D*):
   a. MMSE score of 20-28;
   b. MoCA score ≥ 16;
4. Documentation of one of the following baseline functional tests and the resulting score (a, b, or c):
   a. FAQ score ≤ 9;
   b. FAST score of 3-4;
   c. CDR-SB of 0.5-9;
5. Prior to the 4th and 7th infusions, documentation of a recent (within the last month) brain MRI and ARIA symptom status showing all of the following (a, b, c and d):
   a. Absence of any macrohemorrhage (> 1 cm at greatest diameter; symptomatic or not);
   b. Member does not have any symptoms of amyloid-related imaging abnormalities-hemosiderin deposition (ARIA-H) and has ≤ 4 cerebral microhemorrhages;
   c. Member does not have any symptoms of ARIA-E or only has mild symptoms (i.e., discomfort noticed, but no disruption of normal daily activity);
   d. Fluid attenuation inversion recovery (FLAIR) hyperintensity is confined to the sulcus and/or cortex/subcortex white matter, and in any one location is < 5 cm;
6. Member is not currently taking concomitant anticoagulant or antiplatelet therapy;
7. Kisunla is not prescribed concurrently with Leqembi;
8. If request is for a dose increase, new dose does not exceed 1,400 mg every 4 weeks.

Approval duration:

- **Members with < 4 total infusions: up to the 4th total infusion**

- **Members with < 7 total infusions but ≥ 4 total infusions: up to the 7th total infusion**
- **Members with ≥ 7 total infusions: 6 infusions per PA approval**

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AD: Alzheimer's disease
ARIA-E: amyloid-related imaging abnormalities-edema
ARIA-H: amyloid-related imaging abnormalities-hemosiderin deposition
CDR-SB: Clinical Dementia Rating-Sum of Boxes
CMS: Centers for Medicare and Medicaid Services
DLB: dementia with Lewy bodies
FAQ: Functional Assessment Questionnaire
FAST: Functional Assessment Staging Test
FDA: Food and Drug Administration
FLAIR: fluid attenuation inversion recovery
FTD: frontotemporal dementia
IADL: instrumental activity of daily living
MCI: mild cognitive impairment
MMSE: Mini-Mental State Examination
MoCA: Montreal Cognitive Assessment
MRI: magnetic resonance imaging
PPA: primary progressive aphasia
TIA: transient ischemic attack

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): serious hypersensitivity to donanemab-azbt or to any of the excipients of Kisunla
- Boxed warning(s): increased risk of ARIA

Appendix D: Dementia Rating Scales

- MoCA is a highly sensitive tool for early detection of MCI and has been widely adopted in clinical settings. The maximum score is 30 points. The following ranges may be used to grade severity: 18-25 = mild cognitive impairment, 10-17 = moderate cognitive impairment and < 10 = severe cognitive impairment. However, research for these severity

ranges has not been established yet. The average MoCA score for MCI is 22 (range 19-25) and the average MoCA score for Mild AD is 16 (range 11-21).

- MMSE is a series of questions asked by a health professional designed to test a range of everyday mental skills. The maximum score is 30 points where the following levels of dementia are indicated with a score of:
  - 25 to 30 suggests normal cognition,
  - 21 to 24 suggests mild dementia,
  - 13 to 20 suggests moderate dementia, and
  - less than 12 indicates severe dementia.
  - On average, the MMSE score of a person with Alzheimer's declines about two to four points each year.
- The FAQ measures instrumental activities of daily living (IADLs), such as preparing balanced meals and managing personal finances. Since functional changes are noted earlier in the dementia process with IADLs that require a higher cognitive ability compared to basic activities of daily living, this tool is useful to monitor these functional changes over time. The score range is 0-30. A cut-point of 9 (dependent in 3 or more activities) is recommended to indicate impaired function and possible cognitive impairment.
- FAST is a measure commonly used to assess functional status in patients with dementia. It provides a comprehensive evaluation of functional ability and the potential for a functional decline over time, including physical functional abilities (dressing and grooming), functional language abilities (memory and recognition), and functional activities such as mobility or self-feeding. The FAST score ranges from 1 to 7, categorizing the stages of AD into one of the below:
  - 1: normal aging
  - 2: possible mild cognitive impairment
  - 3: mild cognitive impairment
  - 4: mild dementia
  - 5: moderate dementia
  - 6: moderately severe dementia
  - 7: severe dementia
- CDR-SB assessment is a 5-point scale used to characterize six domains of cognitive and functional performance applicable to Alzheimer’s disease and related dementias: memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care. The information is obtained through an interview of the patient and a reliable informant (e.g., family member). This score is useful for characterizing and tracking a patient's level of impairment/dementia.
  - 0 suggests normal
  - 0.5 to 4 suggests questionable cognitive impairment
  - 0.5 to 2.5 suggests questionable impairment
  - 3.0 to 4.0 suggests very mild dementia
  - 4.5 to 9.0 suggests mild dementia
  - 9.5 to 15.5 suggests moderate dementia
  - 16.0 to 18.0 suggests severe dementia

Appendix E: Diagnosis of Alzheimer’s Disease

- AD
  - Interference with ability to function at work or at usual activities
  - A decline from a previous level of functioning and performing
  - Not explained by delirium or major psychiatric disorder
  - Cognitive impairment established by history-taking from the patient and a knowledgeable informant; and objective bedside mental status examination or neuropsychological testing
  - Cognitive impairment involves a minimum of two of the following domains:
    - Impaired ability to acquire and remember new information
    - Impaired reasoning and handling of complex tasks, poor judgment
    - Impaired visuospatial abilities
    - Impaired language functions (speaking, reading, writing)
    - Changes in personality, behavior, or comportment
  - Insidious onset (gradual onset over months to years, not over hours to days)
  - Clear-cut history of worsening
  - Initial and most prominent cognitive deficits are one of the following:
    - Amnestic presentation (impairment in learning and recall of recently learned information)
    - Nonamnestic presentation in either a language presentation (prominently word-finding deficits), a visuospatial presentation with visual deficits, or executive dysfunction (prominently impaired reasoning, judgment and/or problem solving)
  - No evidence of substantial concomitant cerebrovascular disease, core features of dementia with Lewy bodies (DLB), prominent features of behavioral variant frontotemporal dementia (FTD) or prominent features of semantic or nonfluent/agrammatic variants of primary progressive aphasia (PPA), or evidence of another concurrent, active neurologic or non-neurologic disease or use of medication that could have a substantial effect on cognition
- Mild cognitive impairment due to AD – core clinical criteria
  - Concern regarding change in cognition obtained from the patient, from an informant who knows the patient well, or from a skilled clinician observing the patient
  - Objective evidence of impairment in one or more cognitive domains that is not explained by age or education
  - Preservation of independence in functional abilities
  - Not demented

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
AD	700 mg IV every 4 weeks x 3 doses, then 1,400 mg IV every 4 weeks	1,400 mg every 4 weeks

VI. Product Availability

Single-dose vial for injection: 350 mg/20 mL

VII. References

1. Kisunla Prescribing Information. Indianapolis, IN: Eli Lilly and Co.; July 2024. Available at: https://pi.lilly.com/us/kisunla-uspi.pdf?s=pi. Accessed August 7, 2024.

2. Mintun MA, Lo AC, Duggan Evans C, et al. Donanemab in early Alzheimer's disease. N Engl J Med 2021;384:1691-1704. doi: 10.1056/NEJMoa2100708.
3. Sims JR, Zimmer JA, Evans CD, et al. Donanemab in early symptomatic Alzheimer disease – the TRAILBLAZER-ALZ 2 randomized clinical trial. JAMA 2023; published online: July 17, 2023. doi:10.1001/jama.2023.13239.
4. Centers for Medicare & Medicaid Services. Monoclonal antibodies directed against amyloid for the treatment of Alzheimer's disease. Medicare National Coverage Determination. 200.3; 2022. Available at: https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?ncdid=375&ncdver=1. Accessed July 11, 2024.
5. 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. Alzheimer's & Dementia 2019 Aug;5:354-63.
6. Trzepacz PT, Hochstetler H, Wang S, et al. Relationship between the Montreal Cognitive Assessment and Mini-Mental State Examination for assessment of mild cognitive impairment in older adults. BMC Geriatrics 2015;15:107. https://doi.org/10.1186/s12877-015-0103-3.
7. O'Bryant SE, Waring SC, Cullum CM, et al. Staging dementia using Clinical Dementia Rating Scale Sum of Boxes Scores: a Texas Alzheimer's Research Consortium study. Arch Neurol 2008 August;65(8):1091–1095. doi:10.1001/archneur.65.8.1091.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

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

Reviews, Revisions, and Approvals	Date
Policy created	10/2024