Clinical Policy: Donanemab-azbt (Kisunla)

Reference Number: CP.PHAR.594
Effective Date: 07.02.24
Last Review Date: 11.24
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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 health plans affiliated with Centene Corporation® 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 (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*;
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, and c):
   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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 2 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 –

CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

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	P&T Approval Date
Policy created pre-emptively	10.10.22	11.22
4Q 2023 annual review: updated PEPP criteria to mirror the design of the recently published TRAILBLAZER-ALZ 2 trial as well as functional and cognitive testing requirements from the CMS patient registry; for Initial Approval Criteria: removed the requirement for enrollment in an NIH-sponsored trial since that does not apply to drugs in this class that have obtained full FDA approval (donanemab is applying for full approval instead of accelerated approval); added specialist prescriber requirement; added an exclusion against concomitant use with other anti-amyloid monoclonal antibodies; for consistency with the Leqembi policy, added an exclusion against concomitant use with anticoagulants/antiplatelet therapies, an attestation requirement re: discussing ApoE4 status with the member, and an exclusion if pre-existing stroke, TIA, or seizures; for Continued Therapy: removed the requirement for enrollment in an NIH-sponsored trial; added a requirement for follow-up MRI results to identify new-onset ARIA; added requirement for cognitive and functional testing results to confirm that the member has not progressed beyond the mild stage of AD; added an exclusion for use with concomitant anticoagulant or antiplatelet therapy; added an exclusion against concomitant use with other anti-amyloid monoclonal antibodies; added max dosing limits and Approval Durations; references reviewed and updated.	07.05.23	11.23
RT4: drug is now FDA-approved – criteria updated per FDA labeling: clarified that the initial 3 month auth duration covers the first 3 monthly infusions instead of the first 4 monthly infusions; for Continued Therapy updated the required follow-up MRI	07.11.24	08.24

Reviews, Revisions, and Approvals	Date	P&T Approval Date
schedule, treatment discontinuation thresholds, and MRI-contingent reauth durations to reflect the Kisunla PI; updated the HCPCS code to J0175; references reviewed and updated.		
4Q 2024 annual review: for members with ≥ 7 total infusions – shortened the perpetual reauth duration from 12 infusions per PA approval to 6 infusions per PA approval to align with the approach for Leqembi which is to provide 6 months of perpetual reauthorization at a time; removed the exclusion against concomitant use with Aduhelm since Aduhelm will be completely removed from the market by the time of the posting of these revised criteria; references reviewed and updated.	08.07.24	11.24

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise

professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.