Donanemab-azbt (KISUNLA™)

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the medical policy and a health plan or government program (e.g., TennCare), the express terms of the health plan or government program will govern.

POLICY

INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Kisunla is 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.

All other indications are considered experimental/investigational and not medically necessary.

DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
Initial Requests

- Genetic testing results documenting a mutation in amyloid precursor protein (*APP*), presenilin-1 (*PSEN1*), or presenilin-2 (*PSEN2*), if applicable.
- Clinical documentation to support early onset Alzheimer's Disease, if applicable.
- Medical records (e.g., chart notes) documenting the following:
  - Diagnosis of Clinical Stage 3 or 4 Alzheimer's Disease.
  - Baseline (less than 12 months prior to treatment initiation) assessments for any of the following assessment tools:
    - Clinical Dementia Rating-Global Score (CDR-GS)
    - Mini-Mental Status Examination (MMSE)
    - Montreal Cognitive Assessment (MoCA)
- Presence of amyloid pathology documented by either of the following:
  - Baseline positron emission tomography (PET) scan
  - Lumbar puncture results
- Recent (within one year) brain magnetic resonance imaging (MRI) prior to initiating treatment.

Continuation Requests (where applicable)

- Medical records (e.g., chart notes) documenting the most recent (less than 1 month prior to continuation request) assessment tool for any of the following:
  - Clinical Dementia Rating-Global Score (CDR-GS)
  - Mini-Mental Status Exam (MMSE)
  - Montreal Cognitive Assessment (MoCA)

- Brain magnetic resonance imaging (MRI) results prior to the 2nd dose, 3rd dose, 4th dose, and 7th dose.

EXCLUSIONS

- Coverage will not be provided for members with any of the following conditions:
  - Suspected neurodegenerative etiology of cognitive impairment other than Alzheimer's disease (AD), including but not limited to frontotemporal lobar degeneration (FTLD) or Lewy body disease (i.e., meeting consensus criteria for possible or probable dementia with Lewy bodies that lack AD biomarkers of a positive amyloid PET or CSF profile).
  - > 4 cerebral microbleeds, cortical superficial siderosis, or a major vascular contribution to cognitive impairment confirmed via MRI.
  - Cerebral contusion, encephalomalacia, brain aneurysm or other vascular malformation, central nervous system infection, or brain tumor.
  - History of transient ischemic attacks (TIA), stroke, uncontrolled hypertension, or seizures within the past 12 months.
  - Bleeding disorder that is not under adequate control (including a platelet count <50,000 or international normalized ratio [INR] >1.5).
  - Immunologic disorder requiring therapy with immunoglobulins, monoclonal antibodies, immunosuppressants, or plasmapheresis.
- Kisunla will not be used in combination with any other amyloid beta-directed antibodies (e.g., lecanemab).

PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a geriatrician, neurologist, psychiatrist, or neuropsychiatrist.

COVERAGE CRITERIA

Alzheimer's Disease

Authorization of 7 months may be granted for treatment of Alzheimer's Disease (AD) when all of the following criteria are met:

- Member must meet one of the following criteria:
  - Member is 50 years of age or older
  - If less than 50 years of age, member 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.
- Member must have Clinical Stage 3 (cognitive impairment with early functional impact) or Clinical Stage 4 (dementia with mild functional impairment) AD (Appendix A).
- Member must have objective evidence of cognitive impairment at baseline.
- Member must have one of the following scores at baseline (less than 12 months prior to treatment initiation) on any of the following assessment tools:
  - Clinical Dementia Rating-Global Score (CDR-GS) of 0.5 or 1 (Appendix B).
  - Mini-Mental Status Examination (MMSE) score of 21 – 30 (Appendix C).
  - Montreal Cognitive Assessment (MoCA) score of greater than or equal to 16 (Appendix D).
- Member must meet one of the following criteria:
  - Have a positron emission tomography (PET) scan confirming the presence of amyloid pathology.

  - Have results from a lumbar puncture confirming at least one of the following detected in cerebrospinal fluid (CSF) as determined by the lab assay:
    - Low AB42/AB40 ratio
    - Elevated P-Tau/AB42 ratio
    - Elevated T-tau/AB42 ratio
- Member must have a recent brain magnetic resonance imaging (MRI) within one year prior to initiating treatment to evaluate for pre-existing Amyloid Related Imaging Abnormalities (ARIA).
- Member has undergone genotype testing to determine apolipoprotein E ε4 (ApoE ε4) status prior to initiation of the requested medication to inform member of the risk of developing ARIA.
- Member will not use the requested medication in combination with anticoagulants including warfarin, heparin, and direct oral anticoagulants (e.g., dabigatran, rivaroxaban, edoxaban, apiximab, betrixaban).
- If there is concurrent use of antiplatelet agents (e.g., aspirin up to 325 mg/day, clopidogrel, prasugrel, ticagrelor), member will use antiplatelet agent as monotherapy at a standard therapeutic dose (i.e., not using as dual agent anti-platelet therapy).
- Member and/or provider must currently be participating in a provider-enrolled patient registry that collects information on treatments for Alzheimer's disease (e.g., Alzheimer's Network for Treatment and Diagnostics (ALZ-NET)).

CONTINUATION OF THERAPY

Authorization of 12 months (first reauthorization after the initial 7-month approval period) may be granted for members requesting continuation of therapy when all of the following criteria are met:

- Member has met all initial authorization criteria at the time of initial approval.
- Member has been evaluated for evidence of amyloid-related imaging abnormalities (ARIA) on MRI prior to the 2nd dose, 3rd dose, 4th dose, and 7th dose (Appendix E).
  - For members with radiographic evidence of ARIA-E:
    - Dosing may continue based on clinical judgement, if applicable, for members that meet the following criteria:
      - Member has mild ARIA-E on MRI and is asymptomatic or has mild clinical symptoms
    - Dosing should be suspended until MRI demonstrates radiographic resolution and symptoms resolve for members that meet any of the following criteria:
      - Member has mild ARIA-E on MRI and has moderate or severe clinical symptoms
      - Member has moderate ARIA-E on MRI and is asymptomatic or has mild, moderate, or severe clinical symptoms
      - Member has severe ARIA-E on MRI and is asymptomatic or has mild, moderate, or severe clinical symptoms
  - For members with radiographic evidence of ARIA-H:
    - Dosing may continue for members that meet the following criteria:
      - Member has mild ARIA-H on MRI and is asymptomatic
    - Dosing should be suspended until MRI demonstrates radiographic stabilization and symptoms resolve for members that meet any of the following criteria:
      - Member has mild ARIA-H on MRI and is symptomatic
      - Member has moderate ARIA-H on MRI and is asymptomatic or symptomatic
      - Member has severe ARIA-H on MRI and is asymptomatic or symptomatic
- Member and/or provider continues to participate in a provider-enrolled patient registry that collects information on treatments for Alzheimer's disease (e.g., Alzheimer's Network for Treatment and Diagnostics (ALZ-NET)).

Authorization of 12 months (reauthorizations beyond initial 19 months of therapy) may be granted for members requesting continuation of therapy when all of the following criteria are met:

- Member has met all initial authorization criteria at the time of initial approval.
- Member has a positive clinical response as evidenced by stabilization or slowing of disease progression as documented by any of the following (Note: repeat assessment tool(s) must be the same tool that was submitted upon initial request):
  - CDR-Global Score (i.e., score of 0.5 or 1)
  - MMSE (i.e., decline of 3 points or less per year)
  - MoCA (i.e., score of greater than or equal to 16)

  Note: Continuation requests for members with assessment scores outside of the provided ranges (i.e., mild dementia) or who have progressed greater than the provided rate of decline may be reviewed on a case-by-case basis.
- Member and/or provider continues to participate in a provider-enrolled patient registry that collects information on treatments for Alzheimer's disease (e.g., Alzheimer's Network for Treatment and Diagnostics (ALZ-NET)).

Note: it may be reasonable to consider treatment discontinuation based on a follow-up amyloid PET scan, typically obtained 12 – 18 months after treatment initiation, if the results are read as negative.

APPENDIX

Appendix A: Diagnostic criteria for mild cognitive impairment (MCI) and dementia with mild functional impairment

- Mild cognitive impairment (MCI)/Clinical Stage 3:
  - Cognitive concerns by the patient, knowledgeable informant, or the physician
  - Objective impairment in one or more cognitive domains including memory, executive function, attention, language, or visuospatial skills
  - Generally preserved activities of daily living (ADL)
  - No dementia
- Dementia with mild functional impairment/Clinical Stage 4:
  - Cognitive concerns by the patient, knowledgeable informant, or the physician
  - Performance in the impaired/abnormal range on objective cognitive tests
  - Evidence of decline from baseline, documented by the individual's report or by observer (e.g., study partner) report or by change on longitudinal cognitive testing or neurobehavioral assessments
  - Progressive cognitive and mild functional impairment on instrumental ADL with independence in basic ADL

Appendix B: Clinical Dementia Rating (CDR) Scale

The CDR is obtained through semi-structured interviews of patients and informants with cognitive functioning rated on a 5-point scale in the following domains: memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care. The score relates to the member's level of dementia:

- 0 = Normal
- 0.5 = Very Mild Dementia
- 1 = Mild Dementia
- 2 = Moderate Dementia
- 3 = Severe Dementia

Appendix C: Mini-Mental Status Exam (MMSE)

The MMSE is scored on a 30-point scale, with items that assess orientation (temporal and spatial; 10 points), memory (registration and recall; 6 points), attention/concentration (5 points), language (verbal and written, 8 points), and visuospatial function (1 point). The score relates to the member's level of dementia:

- 25 – 30 suggests normal cognition
- 20 – 24 suggests mild dementia
- 13 – 20 suggests moderate dementia
- Less than 12 suggests severe dementia

Appendix D: Montreal Cognitive Assessment (MoCA)
Per MoCA assessment, average scores for the following ranges are:

- Mild Cognitive Impairment: 19 – 25
- Mild Dementia: 11 – 21
- Normal: 26 and above

Appendix E: ARIA MRI Classification Criteria
Note: For ARIA-H, Radiographic Severity Mild, includes new or worsening superficial siderosis

ARIA Type	Radiographic Severity		
	Mild	**Moderate**	**Severe**
ARIA-E	FLAIR hyperintensity confined to sulcus and or cortex/subcortical white matter in one location < 5 cm	FLAIR hyperintensity 5 to 10 cm in single greatest dimension, or more than 1 site of involvement, each measuring < 10 cm	FLAIR hyperintensity > 10 cm with associated gyral swelling and sulcal effacement. One or more separate/independent sites of involvement may be noted.
ARIA-H microhemorrhage	≤ 4 new incident microhemorrhages	5 to 9 new incident microhemorrhages	10 or more new incident microhemorrhages
ARIA-H superficial siderosis	1 new* focal area of superficial siderosis	2 new focal areas of superficial siderosis	> 2 new areas of superficial siderosis

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

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