COVERAGE AUTHORIZATION REQUEST AND APPEALS GUIDE

Composing a Letter of Medical Necessity

kisunla™ (donanemab-azbt) injection for IV infusion 350 mg/20 mL

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Many health plans require that a Letter of Medical Necessity accompanies a Coverage Authorization Appeals Letter.* The purpose of a Letter of Medical Necessity is to explain the prescribing healthcare provider's (HCP's) rationale and clinical decision-making when choosing a treatment.

This resource, **Composing a Letter of Medical Necessity**, provides information on the process of drafting a Letter of Medical Necessity. Included on the following page is a list of considerations that can be followed when creating a Letter of Medical Necessity. In addition, 2 sample letters are attached to this document and include information that plans often require. Note that some plans have specific Coverage Authorization Forms that must be used to document a Letter of Medical Necessity. Also see **Preparing a Coverage Authorization Appeals Letter** for more information.

Follow the patient's plan requirements when requesting Kisunla; otherwise, treatment may be delayed.

*For Medicare beneficiaries, specific requirements must be met for the HCP to be considered a legal representative of the patient in an appeal. For additional information, please visit https://www.cms.gov/Medicare/CMS-Forms/CMS-Forms/downloads/cms1696.pdf.

INDICATION

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.

SELECT IMPORTANT SAFETY INFORMATION

WARNING: AMYLOID-RELATED IMAGING ABNORMALITIES

Monoclonal antibodies directed against aggregated forms of beta amyloid, including Kisunla, can cause amyloid-related imaging abnormalities (ARIA), characterized as ARIA with edema (ARIA-E) and ARIA with hemosiderin deposition (ARIA-H). ARIA usually occurs early in treatment and is usually asymptomatic, although serious and life-threatening events rarely can occur. Serious intracerebral hemorrhages >1 cm, some of which have been fatal, have been observed in patients treated with this class of medications. Because ARIA-E can cause focal neurologic deficits that can mimic an ischemic stroke, treating clinicians should consider whether such symptoms could be due to ARIA-E before giving thrombolytic therapy in a patient being treated with Kisunla.

ApoE ε4 Homozygotes: Patients who are apolipoprotein E ε4 (ApoE ε4) homozygotes treated with this class of medications, including Kisunla, have a higher incidence of ARIA, including symptomatic, serious, and severe radiographic ARIA, compared to heterozygotes and noncarriers. Testing for ApoE ε4 status should be performed prior to initiation of treatment to inform the risk of developing ARIA. Prior to testing, prescribers should discuss with patients the risk of ARIA across genotypes and the implications of genetic testing results.

Consider the benefit for the treatment of Alzheimer's disease and risk of ARIA when deciding to treat with Kisunla.

Composing a Letter of Medical Necessity

Letter of Medical Necessity Considerations:

1. If required and following patient's consent, include the patient's full name, date of birth, plan identification number, and case identification number if a decision has already been rendered.
2. Add the prescribing HCP's National Provider (NPI) number and specialty.
3. Provide a copy of the patient's records with the following details: patient's history, diagnosis, and condition. Relevant clinical information may include, but is not limited to:
   - Diagnosis of Alzheimer's disease (mild cognitive impairment (MCI) or mild dementia stage of disease), as well as the date of diagnosis.
     - Consider including the patient's ICD-10 diagnosis code(s) as appropriate.
   - Result and Date of Recent Baseline Magnetic Resonance Imaging (MRI) prior to initiating treatment
   - Confirmation of Amyloid Pathology, including type of test, date of test, and test result, for example:
     - Amyloid Positron Emission Tomography (PET) Scan
     - Cerebrospinal Fluid (CSF)
     - Other Amyloid Test
   - Cognitive Assessments with a validated tool (may require more than one), including type of test, date of test, and test result, for example:
     - Clinical Dementia Rating (CDR) Scale
     - Mini-Mental State Exam (MMSE) score
     - Montreal Cognitive Assessment (MoCA)
     - Other Cognitive Test and associated score
   - Functional Assessments with a validated tool (may require more than one), including date of test and test result, for example:
     - The Functional Activities Questionnaire (FAQ) score
     - Other Functional Test and associated score
   - Whether the patient has any history of Amyloid-Related Imaging Abnormalities (ARIA), either ARIA-E or ARIA-H. Please note if there is evidence of ARIA and the date of the MRI, if any.
4. Note the severity of the patient's condition. 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.
   - Please include any co-morbidities, concomitant medications, and all relevant information pertaining to the patient's diagnosis, condition, and symptoms.
5. Document prior treatment, duration of each, and the rationale for discontinuation. It may be beneficial to include Common Procedural Terminology (CPT)-4 and/or J-codes to define prior services/treatments, so that the health plan can conduct research and make a timely determination.
6. Attach clinical documentation which includes clinical rationale per the Kisunla Prescribing Information and/or clinical peer-reviewed literature that supports your recommendation.

Sample Letter of Medical Necessity

HCPs can follow this format for patients who are **NOT** currently receiving treatment with Kisunla™ (donanemab-azbt).

[Date]
[Prior authorization/appeals department]
[Name of health plan]
[Mailing address]

Re: **[Patient's name]**
[Plan identification number]
[Date of birth]
[Case identification number]

To whom it may concern:

I am writing to provide additional information to support my claim for **[patient's name]**'s treatment of **[mild cognitive impairment (MCI) or mild dementia stage of Alzheimer's disease]** with Kisunla (donanemab-azbt). In brief, treatment with Kisunla **700 mg IV every 4 weeks for 3 infusions, then 1400 mg IV every 4 weeks thereafter** is medically appropriate and necessary for this patient. This letter outlines the patient's medical history and previous treatments to support my recommendation for treatment with Kisunla.

[Patient's history, diagnosis, condition, and symptoms*:
Patient must have a diagnosis for an indication of Kisunla. Kisunla is indicated for the treatment of Alzheimer's disease (AD) in patients with mild cognitive impairment (MCI) or mild dementia stage of disease. Please reference the guidance on page 2 and include any co-morbidities, confirmation of amyloid positivity, concomitant medications, and all relevant information pertaining to the patient's diagnosis, condition, and symptoms.]

Past Treatments†	Start/Stop Dates	Reason(s) for Discontinuation

[Please detail all that apply and add additional lines as needed.]

[Provide clinical rationale for this treatment; this information may be found in the Kisunla Prescribing Information and/or clinical peer-reviewed literature.]

[Insert your recommendation summary here, including your professional opinion of the patient's likely prognosis or disease progression without treatment with Kisunla.]

Please feel free to contact me, **[HCP's name]**, at **[office phone number]** for any additional information you may require. We look forward to receiving your timely response and approval of this claim.

Sincerely,

_____

[Physician's name and signature]
[Physician's medical specialty]
[Physician's NPI #]
[Physician's practice name]
[Phone #]
[Fax #]

_____

[Patient's name and signature]

Encl: Medical records
Clinical trial information

*Include patient's medical records and supporting documentation.
†Identify drug name, strength, dosage form, and therapeutic outcome.

Sample Letter of Medical Necessity

HCPs can follow this format for patients who **HAVE** been treated with Kisunla™ (donanemab-azbt) and may have experienced a treatment interruption.

[Date]
[Prior authorization/appeals department]
[Name of health plan]
[Mailing address]

Re: **[Patient's name]**
[Plan identification number]
[Date of birth]
[Case identification number]

To whom it may concern:

I am writing to provide additional information to support my claim for **[patient's name]'s** treatment of **[mild cognitive impairment (MCI) or mild dementia stage of Alzheimer's disease]** with Kisunla (donanemab-azbt). In brief, treatment with Kisunla **700 mg IV every 4 weeks for 3 infusions, then 1400 mg IV every 4 weeks thereafter** is medically appropriate and necessary for this patient. This letter outlines the patient's medical history and previous treatments to support my recommendation for treatment with Kisunla.

[In this section, describe the severity of the patient's Alzheimer's Disease at the time when the patient was first prescribed Kisunla. In addition, include the results of any safety monitoring MRIs.]

[Patient's history, diagnosis, condition, and symptoms*:
Patient must have a diagnosis for an indication of Kisunla. Kisunla is indicated for the treatment of Alzheimer's disease (AD) in patients with mild cognitive impairment (MCI) or mild dementia stage of disease. Please reference the guidance on page 2 and include any co-morbidities, confirmation of amyloid positivity, concomitant medications, and all relevant information pertaining to the patient's diagnosis, condition, and symptoms.]

Past Treatments†	Start/Stop Dates	Reason(s) for Discontinuation

[Please detail all that apply and add additional lines as needed.]

[Provide clinical rationale for this treatment; this information may be found in the Kisunla Prescribing Information and/or clinical peer-reviewed literature.]

[Insert your recommendation summary here, including your professional opinion of the patient's likely prognosis or disease progression without treatment with Kisunla.]

Please feel free to contact me, **[HCP's name]**, at **[office phone number]** for any additional information you may require. We look forward to receiving your timely response and approval of this claim.

Sincerely,

[Physician's name and signature]
[Physician's medical specialty]
[Physician's NPI #]
[Physician's practice name]
[Phone #]
[Fax #]

[Patient's name and signature]

Encl: Medical records
Clinical trial information

*Include patient's medical records and supporting documentation.
†Identify drug name, strength, dosage form, and therapeutic outcome.

IMPORTANT SAFETY INFORMATION FOR Kisunla™ (donanemab-azbt)

WARNING: AMYLOID-RELATED IMAGING ABNORMALITIES

Monoclonal antibodies directed against aggregated forms of beta amyloid, including Kisunla, can cause amyloid-related imaging abnormalities (ARIA), characterized as ARIA with edema (ARIA-E) and ARIA with hemosiderin deposition (ARIA-H). ARIA usually occurs early in treatment and is usually asymptomatic, although serious and life-threatening events rarely can occur. Serious intracerebral hemorrhages >1 cm, some of which have been fatal, have been observed in patients treated with this class of medications. Because ARIA-E can cause focal neurologic deficits that can mimic an ischemic stroke, treating clinicians should consider whether such symptoms could be due to ARIA-E before giving thrombolytic therapy in a patient being treated with Kisunla.

ApoE ε4 Homozygotes: Patients who are apolipoprotein E ε4 (ApoE ε4) homozygotes (approximately 15% of Alzheimer's disease patients) treated with this class of medications, including Kisunla, have a higher incidence of ARIA, including symptomatic, serious, and severe radiographic ARIA, compared to heterozygotes and noncarriers. Testing for ApoE ε4 status should be performed prior to initiation of treatment to inform the risk of developing ARIA. Prior to testing, prescribers should discuss with patients the risk of ARIA across genotypes and the implications of genetic testing results. Prescribers should inform patients that if genotype testing is not performed, they can still be treated with Kisunla; however, it cannot be determined if they are ApoE ε4 homozygotes and at higher risk for ARIA.

Consider the benefit of Kisunla for the treatment of Alzheimer's disease and potential risk of serious adverse events associated with ARIA when deciding to initiate treatment with Kisunla.

Kisunla is **contraindicated** in patients with known serious hypersensitivity to donanemab-azbt or to any of the excipients. Reactions have included anaphylaxis.

Amyloid-Related Imaging Abnormalities (ARIA)

Kisunla can cause ARIA-E, which can be observed on magnetic resonance imaging (MRI) as brain edema or sulcal effusions, and ARIA-H, which includes microhemorrhage and superficial siderosis. ARIA can occur spontaneously in patients with Alzheimer's disease (AD), particularly in patients with MRI findings suggestive of cerebral amyloid angiopathy, such as pretreatment microhemorrhage or superficial siderosis. ARIA-H generally occurs with ARIA-E.

ARIA usually occurs early in treatment and is usually asymptomatic, although serious and life-threatening events, including seizure and status epilepticus, rarely can occur. When present, reported symptoms associated with ARIA may include, but are not limited to, headache, confusion, visual changes, dizziness, nausea, and gait difficulty. Focal neurologic deficits may also occur. Symptoms associated with ARIA usually resolve over time. In addition to ARIA, intracerebral hemorrhages (ICH) >1 cm in diameter have occurred in patients treated with Kisunla.

Incidence of ARIA

Symptomatic ARIA occurred in 6% (52/853) of patients treated with Kisunla. Clinical symptoms associated with ARIA resolved in approximately 85% (44/52) of patients.

Including asymptomatic radiographic events, ARIA was observed with Kisunla: 36% (307/853); placebo: 14% (122/874). ARIA-E was observed with Kisunla: 24% (201/853); placebo: 2% (17/874). ARIA-H was observed with Kisunla: 31% (263/853); placebo: 13% (111/874). There was no increase in isolated ARIA-H for Kisunla vs placebo.

Incidence of ICH

ICH >1 cm in diameter was reported in 0.5% (4/853) of patients after treatment with Kisunla vs 0.2% (2/874) on placebo. Fatal events of ICH have been observed.

Please see Important Safety Information, including Boxed Warning regarding ARIA, on pages 5-7, and click for full Prescribing Information and Medication Guide for Kisunla.

kisunla™ (donanemab-azbt) injection for IV infusion 350 mg/20 mL

IMPORTANT SAFETY INFORMATION FOR Kisunla™ (donanemab-azbt) (continued)

Risk Factors for ARIA and ICH

ApoE ε4 Carrier Status

The risk of ARIA, including symptomatic and serious ARIA, is increased in apolipoprotein E ε4 (ApoE ε4) homozygotes. 17% (143/850) of patients in the Kisunla arm were ApoE ε4 homozygotes, 53% (452/850) were heterozygotes, and 30% (255/850) were noncarriers. The incidence of ARIA was higher in ApoE ε4 homozygotes (Kisunla: 55%; placebo: 22%) than in heterozygotes (Kisunla: 36%; placebo: 13%) and noncarriers (Kisunla: 25%; placebo: 12%). Among patients treated with Kisunla, symptomatic ARIA-E occurred in 8% of ApoE ε4 homozygotes compared with 7% of heterozygotes and 4% of noncarriers. Serious events of ARIA occurred in 3% of ApoE ε4 homozygotes, 2% of heterozygotes, and 1% of noncarriers.

The recommendations for management of ARIA do not differ between ApoE ε4 carriers and noncarriers. Testing for ApoE ε4 status should be performed prior to initiation of treatment to inform the risk of developing ARIA. An FDA-authorized test for detection of ApoE ε4 alleles is not currently available. Currently available tests may vary in accuracy and design.

Radiographic Findings of Cerebral Amyloid Angiopathy (CAA)

Neuroimaging findings that may indicate CAA include evidence of prior ICH, cerebral microhemorrhage, and cortical superficial siderosis. CAA has an increased risk for ICH. The presence of an ApoE ε4 allele is also associated with CAA.

The baseline presence of at least 2 microhemorrhages or the presence of at least 1 area of superficial siderosis on MRI, which may be suggestive of CAA, were identified as risk factors for ARIA. Patients were excluded from enrollment in Study 1 for findings on neuroimaging of prior ICH >1 cm in diameter, >4 microhemorrhages, >1 area of superficial siderosis, severe white matter disease, and vasogenic edema.

Concomitant Antithrombotic or Thrombolytic Medication

In Study 1, baseline use of antithrombotic medication (aspirin, other antiplatelets, or anticoagulants) was allowed. The majority of exposures to antithrombotic medications were to aspirin. The incidence of ARIA-H was 30% (106/349) in patients taking Kisunla with a concomitant antithrombotic medication within 30 days vs 29% (148/504) in patients who did not receive an antithrombotic within 30 days of an ARIA-H event. The incidence of ICH >1 cm in diameter was 0.6% (2/349) in patients taking Kisunla with a concomitant antithrombotic medication vs 0.4% (2/504) in those who did not receive an antithrombotic. The number of events and the limited exposure to non-aspirin antithrombotic medications limit definitive conclusions about the risk of ARIA or ICH in patients taking antithrombotic medications.

One fatal ICH occurred in a patient taking Kisunla in the setting of focal neurologic symptoms of ARIA and the use of a thrombolytic agent. Additional caution should be exercised when considering the administration of antithrombotics or a thrombolytic agent (eg, tissue plasminogen activator) to a patient already being treated with Kisunla.

Because ARIA-E can cause focal neurologic deficits that can mimic an ischemic stroke, treating clinicians should consider whether such symptoms could be due to ARIA-E before giving thrombolytic therapy in a patient being treated with Kisunla. Advise patients to carry information that they are being treated with Kisunla.

Caution should be exercised when considering the use of Kisunla in patients with factors that indicate an increased risk for ICH and in particular for patients who need to be on anticoagulant therapy or patients with findings on MRI that are suggestive of CAA.

IMPORTANT SAFETY INFORMATION FOR Kisunla™ (donanemab-azbt) (continued)

Radiographic Severity

The majority of ARIA-E radiographic events occurred early in treatment (within the first 24 weeks), although ARIA can occur at any time and patients can have more than one episode. The maximum radiographic severity of ARIA-E in patients treated with Kisunla was mild in 7% (59/853), moderate in 15% (128/853), and severe in 2% (14/853). Resolution on MRI after the first ARIA-E event occurred in 63% of patients treated with Kisunla by 12 weeks, 80% by 20 weeks, and 83% overall after detection. The maximum radiographic severity of ARIA-H microhemorrhage in patients treated with Kisunla was mild in 17% (143/853), moderate in 4% (34/853), and severe in 5% (40/853). The maximum radiographic severity of ARIA-H superficial siderosis in patients treated with Kisunla was mild in 6% (47/853), moderate in 4% (32/853), and severe in 5% (46/853). Among patients treated with Kisunla, the rate of severe radiographic ARIA-E was highest in ApoE ε4 homozygotes 3% (4/143) vs heterozygotes 2% (9/452) or noncarriers 0.4% (1/255). The rate of severe radiographic ARIA-H was highest in ApoE ε4 homozygotes 22% (31/143) vs heterozygotes 8% (38/452) or noncarriers 4% (9/255).

Monitoring and Dose Management Guidelines

Baseline brain MRI and periodic monitoring with MRI are recommended. Enhanced clinical vigilance for ARIA is recommended during the first 24 weeks of treatment with Kisunla. If a patient experiences symptoms suggestive of ARIA, clinical evaluation should be performed, including MRI if indicated. If ARIA is observed on MRI, careful clinical evaluation should be performed prior to continuing treatment.

Recommendations for dosing in patients with ARIA-E and ARIA-H depend on clinical symptoms and radiographic severity. Depending on ARIA severity, use clinical judgment in considering whether to continue dosing, interrupt treatment, or permanently discontinue Kisunla. See Prescribing Information for additional dosing considerations.

There is limited experience in patients who continued dosing through asymptomatic but radiographically mild to moderate ARIA-E. There are limited data for dosing patients who experienced recurrent episodes of ARIA-E.

Hypersensitivity Reactions

Hypersensitivity reactions, including anaphylaxis and angioedema, have occurred in patients who were treated with Kisunla. Promptly discontinue the infusion upon the first observation of any signs or symptoms consistent with a hypersensitivity reaction and initiate appropriate therapy.

Infusion-Related Reactions (IRR)

IRRs were observed with Kisunla: 9% (74/853); placebo: 0.5% (4/874); the majority (70%, 52/74) occurred within the first 4 infusions. IRRs typically occur during infusion or within 30 minutes post-infusion. IRRs were mostly mild (57%) or moderate (39%) in severity. IRRs resulted in discontinuations in 4% (31/853). Signs and symptoms of IRRs include chills, erythema, nausea/vomiting, difficulty breathing/dyspnea, sweating, elevated blood pressure, headache, chest pain, and low blood pressure.

In the event of an IRR, the infusion rate may be reduced, or the infusion may be discontinued, and appropriate therapy initiated as clinically indicated. Pretreatment with antihistamines, acetaminophen, or corticosteroids prior to subsequent dosing may be considered.

Adverse Reactions: The most common adverse reactions reported in ≥5% of patients treated with Kisunla (n=853) and ≥2% higher than placebo (n=874): ARIA-H microhemorrhage (25% vs 11%), ARIA-E (24% vs 2%), ARIA-H superficial siderosis (15% vs 3%), headache (13% vs 10%), IRRs (9% vs 0.5%).

Please click for full Prescribing Information, including Boxed Warning regarding ARIA, and Medication Guide.

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