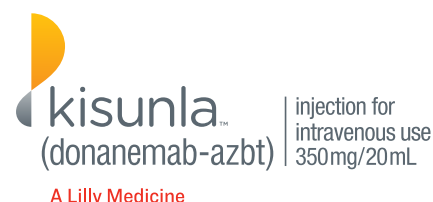


Composing a Letter of Medical Necessity



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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 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 can occur. ARIA can be fatal. 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, the risk of ARIA across genotypes and implications of genetic testing results should be discussed with patients.

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.

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.

Sample Letter of Medical Necessity

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

[Date] Re: [Patient's name]
 [Prior authorization/appeals department] [Plan identification number]
 [Name of health plan] [Date of birth]
 [Mailing address] [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 **350 mg IV for the first infusion, 700 mg IV for the second infusion, 1050 mg IV for the third infusion, then 1400 mg IV every four 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.

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.

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] Re: [Patient's name]
 [Prior authorization/appeals department] [Plan identification number]
 [Name of health plan] [Date of birth]
 [Mailing address] [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 **350 mg IV for the first infusion, 700 mg IV for the second infusion, 1050 mg IV for the third infusion, then 1400 mg IV every four 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.

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.

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 can occur. ARIA can be fatal. 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 treated with this class of medications, including Kisunla, who are apolipoprotein E ε4 (ApoE ε4) homozygotes (approximately 15% of Alzheimer's disease patients) 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, the risk of ARIA across genotypes and the implications of genetic testing results should be discussed with patients.

Consider the benefit for treating Alzheimer's disease and risk of ARIA when deciding to treat 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)

ARIA usually occurs early in treatment and is usually asymptomatic, although serious and life-threatening events, including seizure and status epilepticus, can occur. ARIA can be fatal. 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 Study 1, safety was assessed in patients who received Kisunla Dosing Regimen 1 (n=853) compared to those who received placebo (n=874). In Study 2, the effect of different dosing regimens of Kisunla on ARIA was assessed, including in patients who received Kisunla Dosing Regimen 2 (n=212).

Incidence of ARIA

A lower incidence of ARIA was observed with Dosing Regimen 2 as compared to Dosing Regimen 1. Therefore, Dosing Regimen 2 is the recommended dosage for Kisunla.

In Study 1, symptomatic ARIA-E occurred in 6% of patients through 18 months of treatment with Kisunla.

Clinical symptoms associated with ARIA resolved in approximately 85% of those patients.

Including asymptomatic radiographic events, ARIA, ARIA-E, and ARIA-H were observed with Kisunla: 36%, 24%, and 31% of patients treated with Kisunla, respectively compared to 14%, 2%, and 13% of patients on placebo. There was no increase in isolated ARIA-H for Kisunla vs placebo.

In Study 2, symptomatic ARIA-E occurred in 3% of patients and symptomatic ARIA-H occurred in less than 1% of patients through 12 months of treatment with Kisunla. Clinical symptoms associated with ARIA-E resolved in approximately 67% of patients at 12 months. Including asymptomatic radiographic events, ARIA, ARIA-E, and ARIA-H were observed in 29%, 16%, and 25% of patients treated with Kisunla.

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.



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

Amyloid-Related Imaging Abnormalities (ARIA) (Cont'd)

Incidence of Intracerebral Hemorrhage (ICH)

ICH >1 cm in diameter was reported in 0.5% of patients treated with Kisunla vs 0.2% on placebo in Study 1 and in 1% of patients treated with Kisunla in Study 2. Fatal events of ICH have been observed in patients taking Kisunla.

Risk Factors for ARIA and ICH

ApoE ε4 Carrier Status

The risk of ARIA, including symptomatic and serious ARIA, is increased in ApoE ε4 homozygotes.

Recommendations for management of ARIA do not differ based on ApoE ε4 carrier status. 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 magnetic resonance imaging (MRI), which may be suggestive of CAA, were identified as risk factors for ARIA. Patients were excluded from enrollment in Study 1 and Study 2 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 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 in Study 1, and one fatal intracerebral hemorrhage occurred in the setting of ARIA and the use of a thrombolytic agent in Study 2. 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, and additional caution should be exercised when considering the administration of antithrombotics or a thrombolytic agent (eg, tissue plasminogen activator) to 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.

Monitoring and Dose Management Guidelines

Obtain a recent baseline brain MRI prior to initiating treatment and prior to the 2nd, 3rd, 4th, and 7th infusions. 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.

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.



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

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 with the majority occurring within the first 4 infusions. Most IRRs occurred during the infusion or within 30 minutes after completion of the infusion, however some have occurred hours after an infusion. Signs and symptoms of IRRs include chills, erythema, nausea/vomiting, flushing, 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. Consider pre-treatment with antihistamines, acetaminophen, or corticosteroids prior to subsequent dosing.

Adverse Reactions: The most common adverse reactions reported in $\geq 5\%$ of patients treated with Kisunla and $\geq 2\%$ higher than placebo were ARIA-H microhemorrhage, ARIA-E, ARIA-H superficial siderosis, headache, and IRRs.

Kisunla (donanemab-azbt) injection for intravenous use is available as a 350 mg/20 mL single-dose vial.

Please see full [Prescribing Information](#) for Kisunla, Including Boxed Warning regarding ARIA, and [Medication Guide](#).

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