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

AN OVERVIEW OF

TREATING WITH KISUNLA

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.

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

CONSIDERATIONS BEFORE TREATING WITH KISUNLA

Kisunla is indicated for the treatment of Alzheimer's disease (AD) in patients with MCI or mild dementia due to AD with confirmed presence of amyloid beta pathology. After ensuring the criteria below are met, this guide can help your patients get started on Kisunla. First, ensure that they meet the following criteria[1]:

Cognitive evaluation[1]

- Demonstrating **early symptomatic AD**, inclusive of MCI or mild dementia[†]

Amyloid-positivity confirmation[1]

- When sending patient referral paperwork, include all historic amyloid biomaker diagnostic tests[2]

Baseline Brain MRI[1,3]

- Recently obtained **prior to starting treatment** to assess for for pre-existing ARIA (including both FLAIR and T2*GRE)

Testing for ApoE ε4 status[1,3]

- Testing for ApoE ε4 status should be performed prior to initiation of treatment with amyloid-targeting therapies to inform of the risk of developing ARIA
- **Prior to testing**, prescribers should discuss with patients the risk of ARIA across ApoE genotypes and the implications of genetic testing results to patients and their loved ones
- Prescribers should inform patients that if genotype testing is not performed, they can still be treated with Kisunla

[†]The clinical trial included patients with an MMSE score of 20-28[1]

ApoE=apolipoprotein E; ARIA=amyloid-related imaging abnormalities; FLAIR=fluid-attenuated inversion recovery; GRE=gradient-recalled echo imaging; MCI=mild cognitive impairment; MMSE=Mini-Mental State Examination; MRI=magnetic resonance imaging

SELECT IMPORTANT SAFETY INFORMATION

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

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

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STARTING TREATMENT

Infusion

- Provide a complete infusion referral with documentation supporting treatment initiation, including:
  - Medical records confirming cognitive impairment using a validated tool, such as MMSE, MoCA, or other assessment
  - Type of test, results, and date of diagnostic testing confirming Aß pathology
  - A recent brain MRI prior to initiating treatment to monitor for pre-existing ARIA[1]
  - Confirmation of patient enrollment in coverage with evidence development registry, if insured by Medicare
- Kisunla is an IV infusion administered over approximately **30 minutes once every 4 weeks**[1]
- Patients should be observed for a minimum of **30 minutes post-infusion** to monitor for IRRs and hypersensitivity[1]

Monitoring

- After baseline brain MRI, **conduct a brain MRI** before infusions 2, 3, 4, and 7 and if symptoms consistent with ARIA occur[1]

Dosing Considerations

- Consider stopping dosing based on removal of amyloid plaques to minimal levels consistent with a visually negative amyloid PET scan[1]

In a Phase 3 clinical trial, dosing was stopped based on observed effects on amyloid imaging. Amyloid PET values may increase after treatment with Kisunla is stopped. There are no data beyond the 76-week duration of TRAILBLAZER-ALZ 2 to guide whether additional dosing with Kisunla may be needed for longer-term clinical benefit.[1]

In clinical trials, completion of active treatment was based on amyloid PET levels measured at week 24, week 52, and week 76. If amyloid plaque level was <11 Centiloids on a single PET scan or 11 to <25 Centiloids on 2 consecutive PET scans, subjects taking Kisunla were eligible to switch to placebo.[1]

For reference, <24.1 Centiloids on an amyloid PET scan is consistent with a negative visual read.[5]

The safety and efficacy of Kisunla were evaluated in a Phase 3, randomized, double-blind, placebo-controlled study that assessed disease progression in early symptomatic Alzheimer's disease (AD) (including those with MCI or mild dementia) by reducing amyloid plaques. The study was powered to test the results of Kisunla in the low-medium tau population* (N=1182) and allowed enrollment of high tau participants so Kisunla could also be tested in the overall population (the low-medium tau population plus high tau participants) (N=1736). Participants were included in the study if they had confirmed presence of amyloid pathology. 1736 patients were randomized 1:1 to receive 700 mg of Kisunla every 4 weeks for the first 3 infusions, and then 1400 mg every 4 weeks (n=860) or placebo (n=876) for a total of up to 72 weeks. The primary efficacy endpoint was change in the iADRS score from baseline to 76 weeks (impact on cognitive and functional decline). ARIA-monitoring MRI was performed before infusions 1, 2, 3, 4, and 7.[1,4]

*There were 2 primary analysis populations based on tau PET imaging with flortaucipir: 1) low-medium tau level population (SUVR of ≥1.10 and ≤1.46), and 2) combined population of low-medium plus high tau (SUVR>1.46).[1]

Aß=amyloid-ß; iADRS=integrated Alzheimer's Disease Rating Scale; IRR=infusion-related reaction; IV=intravenous; MoCA=Montreal Cognitive Assessment; MRI=magnetic resonance imaging; PET=positron emission tomography; SUVR=standardized uptake value ratio; ARIA=amyloid-related imaging abnormalities; MMSE=Mini-Mental State Examination.

SELECT IMPORTANT SAFETY INFORMATION

Risk Factors for ARIA and Intracerebral Hemorrhages (ICH)

- **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.
- In Study 1, 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 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.

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

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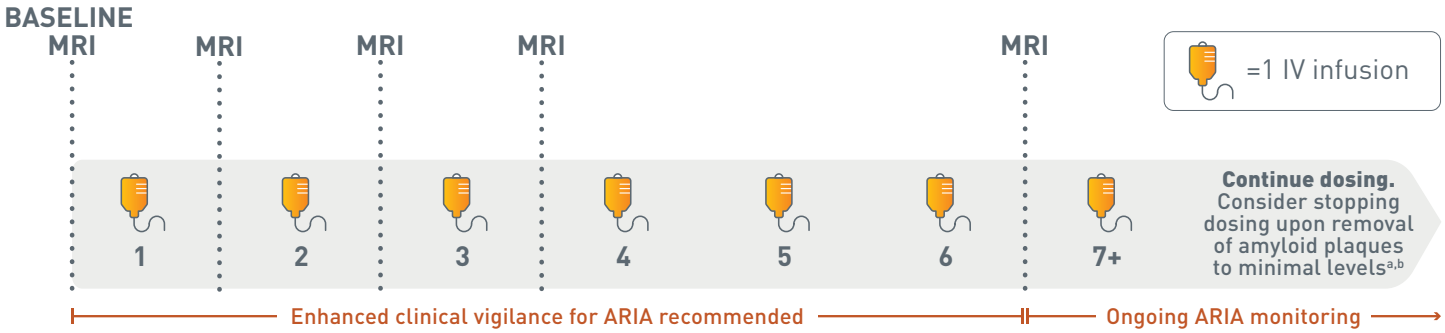
INITIATING AND MONITORING TREATMENT[1]

Infusions should be administered every 4 weeks. If an infusion is missed, resume administration every 4 weeks at the scheduled dose as soon as possible.[1]

If a patient experiences symptoms suggestive of ARIA, clinical evaluation should be performed, including MRI if indicated.[1]



ARIA=amyloid-related imaging abnormalities; IV=intravenous; MRI=magnetic resonance imaging

[a] In clinical trials, completion of active treatment was based on amyloid PET levels measured at week 24, week 52, and week 76. If amyloid plaque level was <11 Centiloids on a single PET scan or 11 to <25 Centiloids on 2 consecutive PET scans, subjects taking Kisunla were eligible to switch to placebo.[1]

[b] For reference, <24.1 Centiloids on an amyloid PET scan is consistent with a negative visual read.[5]

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.[1] See Prescribing Information for additional dosing considerations.

In a Phase 3 clinical trial, dosing was stopped in response to observed effects on amyloid imaging. Amyloid PET values may increase after treatment with Kisunla is stopped. There are no data beyond the 76-week duration of TRAILBLAZER-ALZ 2 to guide whether additional dosing with Kisunla may be needed for longer-term clinical benefit.[1]

For infusions 1 to 3, initiate treatment of Kisunla at 700 mg. At infusion 4, increase to 1400 mg. Infusions should be administered every 4 weeks.[1]

SELECT IMPORTANT SAFETY INFORMATION

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, 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.

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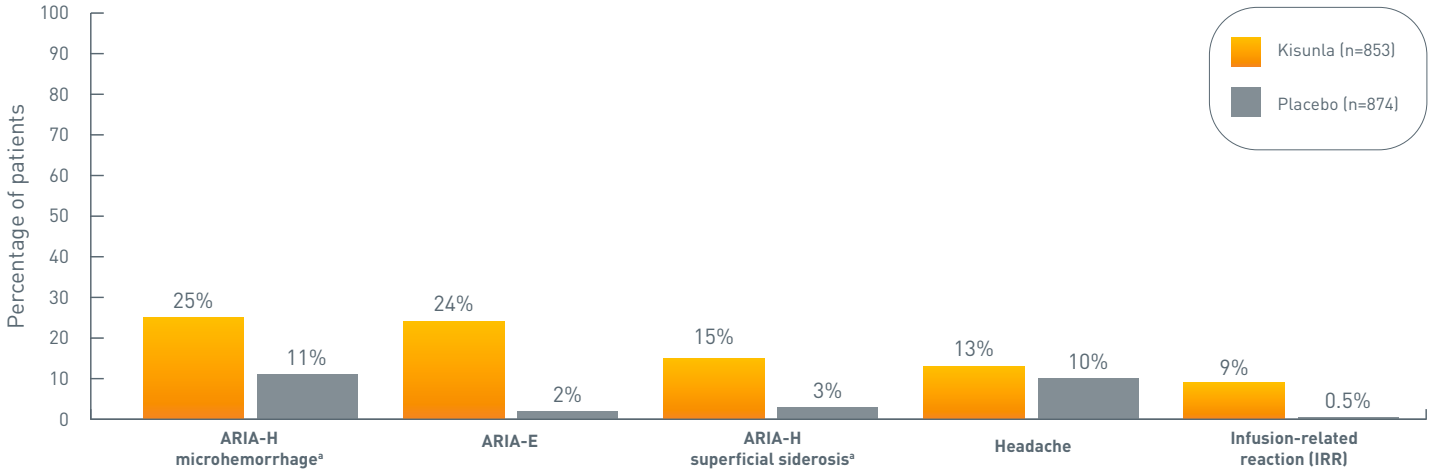
THE SAFETY OF KISUNLA WAS STUDIED IN MORE THAN 1900 PATIENTS IN CLINICAL TRIALS[1*]

- ARIA-E (edema) includes brain edema or sulcal effusions[1]
- ARIA-H (hemosiderin deposition) most commonly includes microhemorrhage and superficial siderosis[1]

Thirteen percent of patients on Kisunla discontinued treatment due to adverse reactions vs 4% on placebo. The most common adverse reaction leading to discontinuation was infusion-related reaction (4% of patients on Kisunla vs 0% on placebo).[1]

Adverse Reactions Reported in ≥5% of Patients Treated With Kisunla and ≥2% Higher Than Placebo in TRAILBLAZER-ALZ 2[1]



[a] As assessed by MRI. A participant could have both microhemorrhage and superficial siderosis.[1]
*1912 patients with Alzheimer's disease (AD) received Kisunla once monthly for ≥6 months.[1]

ARIA=amyloid-related imaging abnormalities; ARIA-E=amyloid-related imaging abnormalities-edema; ARIA-H=amyloid-related imaging abnormalities-hemosiderin deposition

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 can be serious and life-threatening events can occur. Serious intracerebral hemorrhages >1 cm, some fatal, have been observed 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.

Apolipoprotein E ε4 (ApoE ε4) Homozygotes: Patients treated with this class of medications, including Kisunla, who are ApoE ε4 homozygotes have a higher incidence of ARIA, including symptomatic and serious 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.

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

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

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ARIA WITH KISUNLA

ARIA is usually asymptomatic, although rarely serious and life-threatening events can occur.[1]

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.[1]

In TRAILBLAZER-ALZ 2, symptomatic ARIA occurred in 6% (n=52/853) of patients treated with Kisunla. Clinical symptoms associated with ARIA resolved in approximately 85% (n=44/52) of patients.[1]

ARIA-E[1]

ARIA-E (edema) includes brain edema or sulcal effusions

- ARIA-E was observed in 24% (n=201/853) of patients treated with Kisunla compared with 2% (n=17/874) of patients on placebo
- 83% of patients who experienced ARIA-E had complete radiographic resolution when managed according to protocol

ARIA-H[1]

ARIA-H (hemosiderin deposition) most commonly manifests as microhemorrhage and/or superficial siderosis

- ARIA-H was observed in 31% (n=263/853) of patients treated with Kisunla compared with 13% (n=111/874) of patients on placebo[1]
- ARIA-H does not resolve radiographically, but it can stabilize[4]

Intracerebral hemorrhage (>1 cm in diameter)[1]

- Reported in 0.5% (n=4/853) of patients on Kisunla compared to 0.2% (n=2/874) of patients on placebo
- Fatal events of intracerebral hemorrhage in patients taking Kisunla have been observed

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The incidence of ARIA was higher in ApoE ε4 homozygotes (55% on Kisunla vs 22% on placebo) than in heterozygotes (36% on Kisunla vs 13% on placebo) and noncarriers (25% on Kisunla vs 12% on placebo). Among patients treated with Kisunla, symptomatic ARIA-E occurred in 8% of ApoE ε4 homozygotes compared with 7% of heterozygotes and 4% of noncarriers.[1]

The incidence of ARIA-H was 30% (n=106/349) in patients taking Kisunla with a concomitant antithrombotic medication within 30 days compared to 29% (n=148/504) who did not receive an antithrombotic within 30 days of an ARIA-H event. The number of events and limited exposure to non-aspirin antithrombotics limit conclusions about the associated risk of ARIA or intracerebral hemorrhage. Exercise caution when considering administering antithrombotics or thrombolytic agents to patients on 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.[1]

The majority of cases occurred within the first 24 weeks of treatment, but it can occur at any time.[1]

ARIA=amyloid-related imaging abnormalities; ARIA-E=amyloid-related imaging abnormalities-edema; ARIA-H=amyloid-related imaging abnormalities-hemosiderin deposition; MRI=magnetic resonance imaging

SELECT IMPORTANT SAFETY INFORMATION

ARIA Monitoring and Dose Management Guidelines

- Baseline brain MRI and periodic monitoring with MRI are recommended 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.
- 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.

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

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CLASSIFICATION OF THE RADIOGRAPHIC SEVERITY OF ARIA[1]

ARIA MRI CLASSIFICATION CRITERIA[1]

ARIA Type	Radiographic Severity		
	Mild	Moderate	Severe
ARIA-E	FLAIR hyperintensity confined to sulcus and/or cortex/subcortex 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	Less than or equal to 4 new incident microhemorrhages	5 to 9 new incident microhemorrhages	10 or more new incident microhemorrhages
ARIA-H superficial siderosis	1 new[a] focal area of superficial siderosis	2 new focal areas of superficial siderosis	Greater than 2 new focal areas of superficial siderosis

[a]Includes new or worsening superficial siderosis

MAXIMUM ARIA RADIOGRAPHIC SEVERITY OF PATIENTS TREATED WITH KISUNLA[1]

ARIA was classified according to radiographic severity levels in TRAILBLAZER-ALZ 2.[1]

	ARIA Type		
Radiographic Severity	ARIA-E Percent of all Treated Patients (N=853)	ARIA-H microhemorrhage Percent of all Treated Patients (N=853)	ARIA-H superficial siderosis Percent of all Treated Patients (N=853)
Mild	7.0% (n=59)	17% (n=143)	6% (n=47)
Moderate	15% (n=128)	4% (n=34)	4% (n=32)
Severe	2% (n=14)	5% (n=40)	5% (n=46)

ARIA=amyloid-related imaging abnormalities; ARIA-E=amyloid-related imaging abnormalities-edema; ARIA-H=amyloid-related imaging abnormalities-hemosiderin deposition; FLAIR=fluid-attenuated inversion recovery; MRI=magnetic resonance imaging.

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ARIA MANAGEMENT

DOSING RECOMMENDATIONS FOR PATIENTS WITH ARIA-E[1]

Clinical Symptom Severity[a]	ARIA-E Severity on MRI		
	Mild	Moderate	Severe
Asymptomatic	May continue dosing at current dose and schedule	Suspend dosing[b]	Suspend dosing[b]
Mild	May continue dosing based on clinical judgment	Suspend dosing[b]	
Moderate or Severe	Suspend dosing[b]		

[a] Mild: discomfort noticed, but no disruption of normal daily activity; Moderate: discomfort sufficient to reduce or affect normal daily activity; Severe: incapacitating, with inability to work or to perform normal daily activity.[1]

[b]Suspend until MRI demonstrates radiographic resolution and symptoms, if present, resolve; consider a follow-up MRI to assess for resolution 2 to 4 months after initial identification. Resumption of dosing should be guided by clinical judgment.[1]

DOSING RECOMMENDATIONS FOR PATIENTS WITH ARIA-H[1]

Clinical Symptom Severity	ARIA-H Severity on MRI		
	Mild	Moderate	Severe
Asymptomatic	May continue dosing at current dose and schedule	Suspend dosing[a]	Suspend dosing[b]
Symptomatic	Suspend dosing[a]		

[a]Suspend until MRI demonstrates radiographic stabilization and symptoms, if present, resolve; resumption of dosing should be guided by clinical judgment; consider a follow-up MRI to assess for stabilization 2 to 4 months after initial identification.[1]

[b]Suspend until MRI demonstrates radiographic stabilization and symptoms, if present, resolve. Use clinical judgment when considering whether to continue treatment or permanently discontinue Kisunla.[1]

In patients who develop intracerebral hemorrhage >1 cm in diameter during treatment with Kisunla, suspend dosing until MRI demonstrates radiographic stabilization and symptoms, if present, resolve. Resumption of dosing should be guided by clinical judgment.[1]

ARIA=amyloid-related imaging abnormalities; ARIA-E=amyloid-related imaging abnormalities-edema; ARIA-H=amyloid-related imaging abnormalities-hemosiderin deposition; MRI=magnetic resonance imaging.

SELECT IMPORTANT SAFETY INFORMATION

Risk Factors for ARIA and Intracerebral Hemorrhages (continued)

- **ApoE ε4 Carrier Status:** The risk of ARIA, including symptomatic and serious ARIA, is increased in apolipoprotein E ε4 (ApoE ε4) homozygotes.
- 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.

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

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KISUNLA IS COVERED FOR ELIGIBLE MEDICARE PATIENTS IF THEIR PROVIDER ENROLLS THEM IN A CMS-APPROVED STUDY THAT MEETS THE REQUIREMENTS ESTABLISHED BY CMS

CMS will provide coverage for FDA-approved monoclonal antibodies directed against amyloid for the treatment of Alzheimer's disease under Coverage with Evidence Development (CED) for patients who meet the following criteria:

- Patient must be enrolled in Medicare
- Patient must have a diagnosis of mild cognitive impairment due to AD or mild AD dementia, with documented evidence of beta-amyloid plaque
- Physician must participate in a qualifying registry with an appropriate clinical team and follow-up care

Lilly is committed to supporting patients, providers, and infusion centers in navigating the Medicare reimbursement landscape. To register your patient with CMS, submit here: **https://qualitynet.cms.gov/alzheimers-ced-registry/submission.**

CMS=Centers for Medicare & Medicaid Services.

To learn more about registry requirements and billing and coding for Kisunla, please review the Billing and Coding Guide

SELECT IMPORTANT SAFETY INFORMATION

Risk Factors for ARIA and Intracerebral Hemorrhages (ICH) (continued)

- **Concomitant Antithrombotic or Thrombolytic Medication:** In Study 1, 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.
- 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. 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.
- Consider whether ischemic stroke symptoms could be due to ARIA-E before giving thrombolytic therapy in a patient being treated with Kisunla, because ARIA-E can cause focal neurologic deficits that can mimic an ischemic stroke.
- 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.

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LILLY SUPPORT SERVICES™ FOR KISUNLA GETS YOUR PATIENTS STARTED AND HELPS KEEP THEM ON TRACK WITH KISUNLA

CUSTOMIZED SUPPORT AND RESOURCES FOR YOUR PATIENTS

CARE COORDINATION

This service on behalf of patients helps facilitate confirmation of requirements across their Kisunla treatment team, such as MRIs or other medical documentation to manage Kisunla treatment. Reminders will be provided to HCPs when additional documentation or tests are needed for patients on Kisunla. Lilly Support Services for Kisunla helps patients navigate the logistics associated with treatment to support a smoother experience while on Kisunla.

LILLY-CONDUCTED BENEFITS INVESTIGATION

Lilly Support Services for Kisunla provides assistance to research patient's insurance coverage to help identify the lowest out-of-pocket cost associated with the treatment of Kisunla. A copy of Summary of Benefits will be sent to the HCP's office, infusion center, and patient. Resources for Coverage Authorization and Appeals are also available. CMS registry enrollment information may be shared with the infusion center upon referral.

INFUSION CENTER LOCATOR

Assistance is available to locate an infusion center that is preferable for patients to receive their Kisunla infusion. Register your site on the Kisunla locator tool at infusionlocator.kisunla.com/admin. Lilly Support Services for Kisunla can triage appropriate patient documentation to the chosen infusion center to ensure patients can get started on treatment as soon as possible.*

NURSE NAVIGATOR

Customized support by a registered nurse will be available for patients throughout their treatment journey based on patients' needs. Nurse support helps patients understand what to expect with an infusion, answer questions about treatment and when to contact their HCP if needed, discuss next steps, and offer additional support as needed.

FIELD REIMBURSEMENT MANAGER (FRM) SUPPORT

FRMs are experienced access professionals committed to helping navigate the complex access and reimbursement environment to help patients get access to Kisunla. FRMs are integrated with Support Programs, understand Support Program resources, access challenges, affordability options, and the infusion center network.

*The list of infusion centers provided in the locator is not comprehensive, and other infusion centers may be available to you and your patients. These lists are maintained by a third party, and inclusion in the locator is not an endorsement of any of the centers.

To start your patient, complete the Lilly Support Services for Kisunla Enrollment Form or call 1-800-LillyRx (1-800-545-5979) if you have questions.

Completing the Enrollment Form allows you to enroll the patient in Lilly Support Services for Kisunla, share registry information with your patient's treatment team to support Medicare coverage, send the prescription, and submit the infusion order set.

MRI=magnetic resonance imaging; CMS=Centers for Medicare & Medicaid Services

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

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COMMON QUESTIONS

Were patients able to take symptomatic AD medications in the clinical trial?

Approved standard-of-care symptomatic treatments for AD, such as donepezil and memantine, were permitted in the trial, provided that dosage of such medications was stable within 2 months of starting treatment with Kisunla. No dose modifications of these medications were required.[1,4]

Were anticoagulants allowed in the placebo-controlled studies?

Yes, these medications were not excluded. However, given that ARIA-H and intracerebral hemorrhages >1 cm in diameter have been observed in patients taking Kisunla, additional caution should be exercised when considering administration of antithrombotic or thrombolytic agents to a patient already being treated with Kisunla. 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 intracerebral hemorrhage in patients taking antithrombotic 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.[1,4]

What should I do if my patients experience ARIA?

- ARIA-E: Patients with mild MRI severity and with lack of symptoms of ARIA-E may continue dosing at current dose and schedule; if mild symptoms are present, patients may continue dosing based on clinical judgment. Patients with moderate or severe findings on MRI or moderate or severe symptoms of ARIA-E should suspend dosing until MRI shows radiographic resolution and symptoms resolve. Resuming dosing should be based on clinical judgement.[1]
- ARIA-H: Patients with mild MRI severity and with lack of symptoms of ARIA-H may continue dosing at current dose and schedule. Patients with moderate or severe findings on MRI or symptoms of ARIA-H should suspend dosing. Suspend until MRI demonstrates radiographic stabilization and symptoms, if present, resolve. For any severe ARIA-H, use clinical judgment when considering whether to continue treatment or permanently discontinue.[1]

Can patients with implants/pacemakers be treated with Kisunla?

The ability to undergo an MRI is a requirement for treatment with Kisunla. In our trials, patients were excluded if they had any contraindications for MRI, including claustrophobia or the presence of contraindicated metal (ferromagnetic) implants/cardiac pacemakers.[4]

What should I discuss with my patient before initiating treatment?

- Discuss what your patient can expect from the infusion process, monitoring requirements, and next steps
- Advise patients to carry information that they are being treated with Kisunla
- Provide additional support as needed with appointment reminders or transportation arrangements
- Remind your patient that Lilly Support Services for Kisunla can provide assistance at **1-800-LillyRx (1-800-545-5979)**

SELECT IMPORTANT SAFETY INFORMATION

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. 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.

ARIA=amyloid-related imaging abnormalities; ARIA-H=amyloid-related imaging abnormalities-hemosiderin deposition; IV=intravenous; MRI=magnetic resonance imaging.

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

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

GET STARTED WITH KISUNLA

- ☐ Enroll your patient in Lilly Support Services for Kisunla by downloading the Enrollment Form at **kisunla.lilly.com/assets/pdf/kisunlaenrollmentform.pdf** or complete digital enrollment via the Digital Enrollment Portal at **enroll.LillySupportServices.Lilly.com**. You and your patient will need to complete and sign the Enrollment Form. Fax completed Enrollment Forms to **1-844-731-2697.** For questions, call **1-800-LillyRx (1-800-545-5979)**
- ☐ Find an infusion center preferable to your patient with our locator tool at **www.infusionlocator.kisunla.com**, or let Lilly Support Services for Kisunla help by requesting infusion center locator support on the Enrollment Form
- ☐ Plan for and promptly schedule monitoring MRIs in advance
- ☐ To find an imaging center, contact your Lilly Alzheimer's Disease Consultant or call **1-800-LillyRx (1-800-545-5979)**
- ☐ Provide your patient with the Getting Started resource

MRI=magnetic resonance imaging

ADDITIONAL SUPPORT FROM YOUR LILLY TEAM

For product-related, infusion, or reimbursement questions, reach out to your Lilly Alzheimer's Disease Consultant or to Lilly Support Services for Kisunla at **1-800-LillyRx (1-800-545-5979)**.

For medical-related questions about Kisunla use or clinical data, speak with a trained medical professional: **1-800-LillyRx (1-800-545-5979)**.

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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.

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.

Important safety information continued on next page.

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IMPORTANT SAFETY INFORMATION FOR KISUNLA™ (DONANEMAB-AZBT) (cont'd)

Radiographic Findings of Cerebral Amyloid Angiopathy (CAA) (con'td)

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.

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.

Important safety information continued on next page.

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IMPORTANT SAFETY INFORMATION FOR KISUNLA™ (DONANEMAB-AZBT) (cont'd)

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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%).

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