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

INFUSION PREPARATION HANDBOOK

FOR ADMINISTRATION OF 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 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 see additional Important Safety Information and full Prescribing Information, including Boxed Warning regarding ARIA, and Medication Guide for Kisunla.

Lilly

IMPORTANT RESOURCES

Training Assistance

Review important training information with the **Kisunla Infusion Training Module**.

Insurance Coverage Information

For more information on insurance coverage and reimbursement requirements, visit **kisunla.lilly.com/support-resources** or scan this QR code.

Kisunla Infusion Center Locator Tool

Access the Kisunla alternate infusion center locator tool using this QR code or by visiting **www.infusionlocator.kisunla.com**

Register your practice as offering Kisunla at **infusionlocator.kisunla.com/admin**

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.

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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TREATMENT READINESS

Prior to each infusion

CHECK

- Review the active infusion order form or medical record to confirm the dose and infusion number
- Confirm that the medical record contains complete and current clinical documentation prior to every treatment (hold the infusion and notify the prescriber if documentation is missing), including:
  - Presence of amyloid beta pathology prior to first infusion[1]
  - Recent baseline MRI prior to infusion 1 and prior to infusions 2, 3, 4, and 7[1]
- Consult with the prescriber prior to providing the infusion if:
  - Assessment is positive for signs/symptoms of ARIA, such as: headache, confusion, visual changes, dizziness, nausea, and gait difficulty. Focal neurologic deficits may also occur[1]
  - MRI has not been completed or shows radiographic evidence of ARIA[1]

INFORM

- Inform patients about the risk of side effects, their signs and symptoms, and when to consult with their prescriber

DISCUSS

- Discuss what to expect from the infusion process and next steps
- Anticipate the possibility of providing support to patients with treatment reminders and/or transportation arrangements
- **Remind your patient that Lilly Support Services™ can provide assistance at 1-800-LillyRx (1-800-545-5979)**

ARIA=amyloid-related imaging abnormalities; MRI=magnetic resonance imaging.

SELECT IMPORTANT SAFETY INFORMATION

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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.

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KISUNLA DOSING AND PREPARATION[1]

1 MONTHLY INFUSION

30-MINUTE DURATION

- The recommended dosage of Kisunla is 700 mg every 4 weeks for 3 infusions, then 1400 mg every 4 weeks
- Kisunla is an IV infusion administered over approximately 30 minutes. Observe the patient for at least 30 minutes after the infusion for infusion-related and hypersensitivity reactions
- If an infusion is missed, resume administration every 4 weeks at the scheduled dose as soon as possible
- Consider stopping dosing based on removal of amyloid plaques to minimal levels consistent with a visually negative amyloid PET scan[1*†‡]

*In the 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]

†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]

Preparation and Reconstitution for Kisunla[1]

IV infusion Q4W	Kisunla dosage administered over ~30 minutes	Kisunla volume	Volume of 0.9% sodium chloride injection diluent	Final volume of diluted solution to be infused[a]
Infusions 1, 2, and 3	700 mg	40 mL	30 to 135 mL	70 to 175 mL
	2 vials of Kisunla needed			
Infusion 4+	1400 mg	80 mL	60 to 270 mL	140 to 350 mL
	4 vials of Kisunla needed			

[a]Final concentration of diluted solution is 4 mg/mL to 10 mg/mL.[1]

ARIA=amyloid-related imaging abnormalities; ARIA-E=amyloid-related imaging abnormalities-edema; ARIA-H=amyloid-related imaging abnormalities-hemosiderin deposition; ATT=amyloid-targeting therapy; IV=intravenous; MRI=magnetic resonance imaging; PET=positron emission tomography; Q4W=every 4 weeks

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.

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STORAGE GUIDE[1]

When your Kisunla shipment arrives, make sure it is cold and there is no damage. Should you have concerns about your shipment, or if it doesn't arrive, please contact your specialty distributor.

- Store refrigerated at 2°C to 8°C (36°F to 46°F)
- Keep the vial in the outer carton to protect from light
- Do not freeze or shake
- If refrigeration is not available, may be stored at room temperature (20°C to 25°C [68°F to 77°F]) for up to 3 days

INFUSION PREPARATION

- ☐ Kisunla solution for infusion should be prepared and administered by a qualified healthcare professional using aseptic technique.[1]
- ☐ Gather all other supplies needed, including IV bags, tubing, different-sized bags, saline, and syringes.
- ☐ Allow Kisunla to warm to room temperature before preparation.[1]
- ☐ Inspect the content of the vial for particulate matter and discoloration prior to administration. Kisunla solution is clear to opalescent, colorless to slightly yellow to slightly brown. Discard if discolored, or foreign particles are observed.[1]
- ☐ Calculate the volume of Kisunla required to prepare the infusion solution. Each vial contains a Kisunla concentration of 350 mg/20 mL.[1] Use a new syringe for each vial. More than one vial is needed for a full dose.[1]
  - — 700 mg of Kisunla: 40 mL
  - — 1400 mg of Kisunla: 80 mL
- ☐ Withdraw required volume of Kisunla and further dilute into an infusion bag containing 0.9% sodium chloride injection, to a final concentration of 4 mg/mL to 10 mg/mL. Each vial is for one-time use only. Discard any unused portion left in the vial.[1]
- ☐ Do not shake. Gently invert prepared infusion bag to mix. Visually inspect the Kisunla diluted solution for particles or discoloration prior to administration. Do not use if it is discolored, opaque, or foreign particles are seen. Use prepared dosing solution immediately.[1]
- ☐ Administer the diluted infusion solution via IV infusion over approximately 30 minutes.[1]
  - — If not used immediately or if infusion is interrupted, store the dosing solution under refrigeration for up to 72 hours at 2°C to 8°C (36°F to 46°F) or for up to 12 hours at room temperature (20°C to 25°C [68°F to 77°F]), assuming dilution has taken place using aseptic techniques. Storage times include the duration of infusion
- ☐ If a serious infusion-related reaction or hypersensitivity occurs, stop the infusion immediately and treat per orders/protocol as clinically indicated.[1]
- ☐ Flush the line with 0.9% sodium chloride injection at the end of the infusion.[1]
- ☐ Plan to observe the patient post-infusion for a minimum of 30 minutes to evaluate for any infusion-related or hypersensitivity reactions.[1]

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HOW TO INITIATE AND MONITOR TREATMENT WITH KISUNLA

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]

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]

[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]

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

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ADDITIONAL SAFETY INFORMATION

Amyloid-related imaging abnormalities (ARIA)

ARIA is a potential side effect associated with amyloid-targeting therapies, including Kisunla, and may occur when these therapies reduce amyloid plaques in the brain that have been accumulating for years. ARIA is usually asymptomatic, although serious and life-threatening events, including seizure and status epilepticus, rarely can occur. Fatal events of intracerebral hemorrhages >1cm in patients taking Kisunla have been observed. 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[1,3]

There are 2 types of ARIA detected on an MRI scan in patients with Alzheimer's disease (AD)[1]:

- ARIA-H, for hemosiderin deposition, refers to areas of bleeding in the brain or the lining of the brain
- ARIA-E, for edema, refers to swelling of the brain

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[1]

Patients should have an MRI to monitor for ARIA prior to infusions 1, 2, 3, 4, and 7. If a patient experiences symptoms suggestive of ARIA, clinical evaluation should be performed, including MRI if indicated[1]

Enhanced clinical vigilance for ARIA by the prescriber, infusion center staff, and patient is recommended during the first 24 weeks[1]

If ARIA is observed, the prescriber may change dosing based on clinical symptoms and radiographic severity. See Prescribing Information for additional dosing considerations[1]

ARIA can occur at any time during treatment, and patients can have more than one episode, but the majority of cases occurred early and were asymptomatic[1]

See full Prescribing Information for complete recommendations on ARIA management.

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

Hypersensitivity reactions

Hypersensitivity reactions, including anaphylaxis and angioedema, have occurred in patients who were treated with Kisunla[1]

Promptly discontinue the infusion upon the first observation of any signs or symptoms consistent with a hypersensitivity reaction and initiate appropriate therapy[1]

Kisunla is contraindicated in patients with a history of serious hypersensitivity to donanemab-azbt or to any of the excipients of Kisunla[1]

Infusion-related reactions (IRR)

Signs and symptoms of IRR include chills, erythema, nausea/vomiting, difficulty breathing/dyspnea, sweating, elevated blood pressure, headache, chest pain, and low blood pressure[1]

The majority of IRRs occurred within the first 4 infusions of Kisunla, although they can occur at any time. In clinical trials, infusion reactions occurred during infusion or within 30 minutes post-infusion. Observe the patient post-infusion for a minimum of 30 minutes[1]

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[1]

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LILLY SUPPORT SERVICES FOR KISUNLA

Lilly Support Services™ for Kisunla is a free support program that can partner with your patients to help them stay on track and feel supported

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.

Enroll your patients in Lilly Support Services for Kisunla.

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

*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.

MRI=Magnetic Resonance Imaging; CMS=Centers for Medicare & Medicaid Services

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COMMON QUESTIONS

HOW LONG IS THE INFUSION DURATION? HOW LONG SHOULD THE PATIENT BE MONITORED AFTER INFUSION?

Kisunla is administered via IV infusion over approximately 30 minutes. Patients should be monitored post-infusion for a minimum of 30 minutes to evaluate for infusion reactions and hypersensitivity reactions.[1]

WHAT INFUSION-RELATED REACTIONS (IRR) MAY OCCUR?

Kisunla can cause IRR and hypersensitivity reactions including anaphylaxis and angioedema, some of which may be serious and life threatening. Signs and symptoms of infusion-related reactions include chills, erythema, nausea/vomiting, difficulty breathing/dyspnea, sweating, elevated blood pressure, headache, chest pain, and low blood pressure.[1]

WHAT SHOULD I DO IF A HYPERSENSITIVITY-RELATED REACTION OR AN INFUSION-RELATED REACTION OCCURS?

- Promptly discontinue the infusion upon the first observation of any signs or symptoms consistent with a hypersensitivity reaction, and initiate appropriate therapy based on your center's protocol.[1]
- In the event of an infusion-related reaction, 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.[1]

HOW DO I OBTAIN KISUNLA FOR MY INFUSION SITE?

Kisunla can be shipped from an Authorized Specialty Distributor of Record. Please contact your distributor directly for specific product availability.

WHAT DO I DO IF MY PATIENT MISSES A DOSE?

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

WERE PATIENTS ABLE TO TAKE SYMPTOMATIC ALZHEIMER'S DISEASE (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.[1,2]

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.[1,2]

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.[2]

MUST KISUNLA BE ADMINISTERED VIA AN IV PUMP? IS ADMINISTERING IT TO GRAVITY AN ACCEPTABLE METHOD?

Both methods are acceptable, as long as the infusion is administered over approximately 30 minutes.[1]

IF AN INFUSION IS INTERRUPTED, CAN I RESTART IT? HOW LONG CAN THE IV INFUSION BAG BE USED AFTER PREPARATION, IF ADMINISTRATION IS INTERRUPTED?

After dilution, immediate use is recommended. If the Kisunla diluted solution is not used immediately after preparation, it can be stored under refrigeration for up to 72 hours at 2°C to 8°C (36°F to 46°F) or for up to 12 hours at room temperature: 20°C to 25°C (68°F to 77°F). Do not freeze the Kisunla diluted solution.[1]

WHAT SHOULD I DO IF MY PATIENT EXPERIENCES AN ADVERSE REACTION?

If your patient experiences an adverse reaction, take appropriate action based on your center's protocol or consult with the patient's prescriber. Adverse reactions should also be reported at **1-800-LillyRx (1-800-545-5979)**.

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 can provide assistance at **1-800-LillyRx (1-800-545-5979)**.

WHAT ASSISTANCE DOES LILLY SUPPORT SERVICES FOR KISUNLA OFFER?

Lilly Support Services for Kisunla can answer questions, provide appointment reminders, complete a benefits investigation, locate infusion centers, provide education on side effects of Kisunla, and support patients and providers in reimbursement processes.

WHAT SHOULD I DO IF I DIDN'T RECEIVE THE INFUSION SHIPMENT I WAS EXPECTING?

Please contact your wholesaler directly.

HOW DO I FIND INFORMATION ABOUT INSURANCE COVERAGE AND REIMBURSEMENT REQUIREMENTS FOR KISUNLA?

The most up-to-date coverage and reimbursement information can be found at **kisunla.lilly.com/hcp/support-resources**.

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

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IMPORTANT SAFETY INFORMATION FOR Kisunla™ (donanemab-azbt)

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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. 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.

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

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

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.

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 for Kisunla.

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References: 1. Kisunla (donanemab-azbt). Prescribing Information. Lilly USA, LLC. **2.** Sims JR, Zimmer JA, Evans CD, et al. Donanemab in early symptomatic Alzheimer disease: the TRAILBLAZER-ALZ 2 randomized clinical trial. *JAMA*. 2023;330(6):512-527. **3.** Barakos J, Purcell D, Suhy J, et al. Detection and management of amyloid-related imaging abnormalities in patients with Alzheimer's disease treated with anti-amyloid beta therapy. *J Prev Alzheimers Dis.* 2022;9(2):211-220. **4.** Tarawneh R, Holtzman DM. The clinical problem of symptomatic Alzheimer disease and mild cognitive impairment. *Cold Spring Harb Perspect Med.* 2012;2(5):a006148. doi:10.1101/cshperspect.a006148. **5.** Navitsky M, Joshi AD, Kennedy I, et al. Standardization of amyloid quantitation with florbetapir standardized uptake value ratios to the Centiloid scale. *Alzheimers Dement.* 2018;14(12):1565-1571.

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SUPPORTING PATIENTS WITH EARLY SYMPTOMATIC AD

BE SUPPORTIVE OF THE PATIENT AND THEIR LOVED ONES

While patients with early symptomatic Alzheimer's disease (AD) may still be independent, many may arrive to appointments with a loved one. Allowing the loved one to remain with the patient could help to relieve some of the anxieties associated with treatment and provide confidence for the patient. Consider the size of your infusion suite to accommodate loved ones and share your facility's policy on guests with patients. At the first appointment, establish a clear care partner who can help make decisions alongside the patient.[4]

APPOINTMENT REMINDERS THROUGH BOTH VERBAL AND WRITTEN COMMUNICATIONS

Patients with early symptomatic AD may have challenges with remembering appointments. Providing multiple appointment reminders through both verbal (ie, phone call) and written (ie, email or text) communications could help with appointment adherence.[4]

OUTLINE THE TREATMENT PROCESS AT EACH APPOINTMENT

Patients with early symptomatic AD may still have many cognitive faculties, but it could still be helpful to outline the treatment process at each appointment and answer questions they may have. These reminders and ongoing support throughout the infusion could go a long way in easing patient anxiety about the process.[4]

Lilly Support Services™ for Kisunla is available to help the patient along the treatment journey. If the patient is not already enrolled in Lilly Support Services for Kisunla, ask them to speak with their HCP about enrollment into the support program or call 1-800-LillyRx (1-800-545-5979) if they have additional questions.

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