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

INFUSION CHECKLIST

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.

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.

KISUNLA™ INFUSION CHECKLIST

STEP 1: PRE-INFUSION

- ☐ Review the active order form or medical record to confirm the dose and infusion number
- ☐ Ensure required MRI has been completed prior to infusions 1, 2, 3, 4, and 7 and inquire if any ARIA was detected[1]
- ☐ Consult with the prescriber prior to providing the infusion if[1]:
  - Assessment is positive for signs/symptoms of ARIA, such as: headache, confusion, visual changes, dizziness, nausea, gait difficulty, status epilepticus, and seizure
  - MRI has not been completed or shows radiographic evidence of ARIA

STEP 2: COUNSELING

- ☐ Counsel patients through the treatment journey by discussing key steps
- ☐ Answer questions about how Kisunla works and potential side effects, such as ARIA and infusion-related reactions[1]
- ☐ Remind patients that support is available through Lilly Support Services™ for Kisunla at 1-800-LillyRx (1-800-545-5979)

STEP 3: INFUSION[1]

- ☐ Equilibrate vials to room temperature; visually inspect for particulate matter and do not use if it is discolored or foreign particles are seen. Kisunla solution is clear to opalescent, colorless to slightly yellow to slightly brown
- ☐ Calculate volume, withdraw, and dilute using aseptic technique into an infusion bag containing 0.9% sodium chloride injection to final concentration of 4 mg/mL to 10 mg/mL. Discard any unused portion left in the vial
- ☐ Gently invert the Kisunla diluted solution to mix completely. Do not shake
- ☐ Visually inspect the diluted solution prior to administration
- ☐ Administer the entire diluted solution via IV over approximately 30 minutes
- ☐ 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
- ☐ Promptly discontinue the infusion upon the first observation of any signs or symptoms consistent with a hypersensitivity-type reaction
- ☐ If infusion-related reactions occur, 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

STEP 4: POST-INFUSION[1]

- ☐ After the infusion is complete, flush the administration set only with 0.9% sodium chloride to ensure entire dose, including residual volume, is administered
- ☐ Observe the patient post-infusion for a minimum of 30 minutes to evaluate for infusion and hypersensitivity reactions
- ☐ Provide your patients with reminders about adverse event signs and symptoms, when to call their clinicians, upcoming infusion appointments, and imaging steps

ARIA=amyloid-related imaging abnormalities; 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.

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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]

Obtain recent baseline brain MRI prior to initiating treatment. Perform an MRI prior to infusions 2, 3, 4, and 7. If a patient experiences symptoms suggestive of ARIA, clinical evaluation should be performed, including an MRI if indicated. 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.

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

ARIA-E=amyloid-related imaging abnormalities-edema; ARIA-H=amyloid-related imaging abnormalities-hemosiderin deposition; Q4W=every four weeks.

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.

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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. 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.

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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Reference: 1. Kisunla (donanemab-azbt). Prescribing Information. Lilly USA, LLC.

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