



KISUNLA™ (donanemab-azbt) OVERVIEW

A ONCE-MONTHLY AMYLOID-TARGETING THERAPY FOR PATIENTS WITH EARLY SYMPTOMATIC ALZHEIMER'S DISEASE (AD) AND CONFIRMED AMYLOID POSITIVITY¹

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.

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

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



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The purpose of this document is to provide healthcare organizations with an overview of Kisunla that can be distributed to other relevant stakeholders within your system, as appropriate. If you wish to use this document for a live presentation at your health system, please know you can always reach out to a Lilly Account Manager who can further support you or connect you with an Outcomes Liaison.

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For more information on Kisunla, contact your Lilly Account Manager.

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 see additional [Important Safety Information](#) and full [Prescribing Information](#), including [Boxed Warning](#) regarding ARIA, and [Medication Guide](#) for Kisunla.



APPROPRIATE PATIENT POPULATION FOR KISUNLA

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TREATING AD BEGINS WITH UNDERSTANDING THE APPROPRIATE PATIENT POPULATION¹



HAS EARLY SYMPTOMATIC AD¹

Inclusive of MCI or mild dementia (MMSE 20-28)¹



IS AMYLOID POSITIVE¹

Amyloid positivity can be confirmed via a variety of diagnostic tests, such as PET scans, CSF, and blood plasma.² In the Kisunla clinical trial, amyloid positivity was confirmed via amyloid PET scan¹



IS MOTIVATED TO MAINTAIN INDEPENDENCE LONGER

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.

CSF=cerebrospinal fluid; MCI=mild cognitive impairment; MMSE=Mini-Mental State Examination; PET=positron emission tomography.

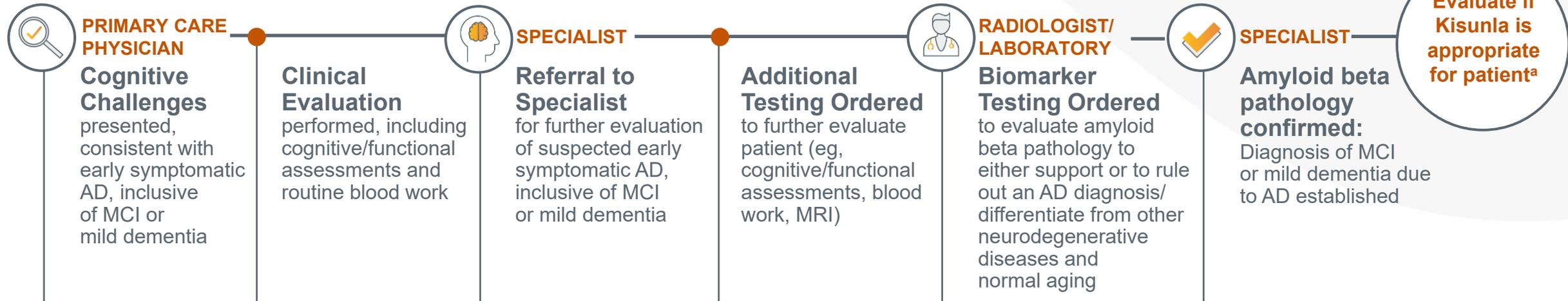
References: 1. Kisunla (donanemab-azbt). Prescribing Information. Lilly USA, LLC. 2. McDade E, Bednar MM, Brashear HR, et al. The pathway to secondary prevention of Alzheimer's disease. *Alzheimers Dement (N Y)*. 2020;6(1):e12069. doi:10.1002/trc2.12069

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





CLINICAL CONSIDERATIONS WITH THE IDENTIFICATION OF AN ELIGIBLE PATIENT FOR KISUNLA¹⁻³



^aA recent brain MRI is required prior to initiating treatment. If a patient experiences symptoms suggestive of ARIA, clinical evaluation should be performed, including MRI testing if indicated.³

Kisunla is for patients with early symptomatic AD with confirmed amyloid positivity who are motivated to maintain independence longer.³

This is a representative patient journey; there are many ways a patient may enter this journey and not all possibilities are presented here.

SELECT IMPORTANT SAFETY INFORMATION

Risk Factors for ARIA and Intracerebral Hemorrhages

- **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.

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

References: 1. Alzheimer’s Association. 2023 Alzheimer’s disease facts and figures. *Alzheimers Dement.* 2023;19(4):1598-1695. 2. Porsteinsson AP, Isaacson RS, Knox S, et al. Diagnosis of early Alzheimer’s disease: clinical practice in 2021. *J Prev Alzheimers Dis.* 2021;8:371-386.

3. Kisunla (donanemab-azbt). Prescribing Information. Lilly USA, LLC.

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FDA-APPROVED ATTs REQUIRE THE CONFIRMATION OF AMYLOID BETA PATHOLOGY TO INITIATE TREATMENT^{1,2}

AS PART OF THE DIAGNOSTIC PROCESS FOR PATIENTS WITH COGNITIVE IMPAIRMENT BEING EVALUATED FOR AD, BIOMARKER TESTING CAN HELP CONFIRM THE PRESENCE OF AMYLOID BETA PATHOLOGY.¹⁻³

CURRENT APPROACHES



AMYLOID PET SCANS

Used to estimate the density of beta-amyloid plaques through PET image interpretation⁴



CSF TESTS

Determine amyloid beta levels measured in cerebrospinal fluid⁴



BLOOD TESTS

Measure the likelihood of presence or absence of amyloid plaques in the brain⁴

CMS covers FDA-approved ATTs under CED for MCI or mild dementia due to AD with confirmed presence of amyloid beta pathology.⁵

SELECT IMPORTANT SAFETY INFORMATION

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

- **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.

ATT=amyloid-targeting therapy; CED=coverage with evidence development; CMS=Centers for Medicare & Medical Services.

References: **1.** Kisunla (donanemab-azbt). Prescribing Information. Lilly USA, LLC. **2.** Leqembi (lecanemab-irmb). Prescribing Information. Eisai R&D Management Co., Ltd. **3.** Porsteinsson AP, Isaacson RS, Knox S, et al. Diagnosis of early Alzheimer's disease: clinical practice in 2021. *J Prev Alzheimers Dis.* 2021;8:371-386. **4.** Iaccarino L, Burnham SC, Dell'Agnello G, et al. Diagnostic biomarkers of amyloid and tau pathology in Alzheimer's disease: an overview of tests for clinical practice in the United States and Europe. *J Prev Alzheimers Dis.* Published online April 6, 2023. doi:10.14283/jpad.2023.43 **5.** CMS.gov. Monoclonal antibodies directed against amyloid for the treatment of Alzheimer's disease (CAG-00460N). Published April 7, 2022. Accessed July 21, 2023. <https://www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=N&ncaid=305>

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



MECHANISM OF ACTION

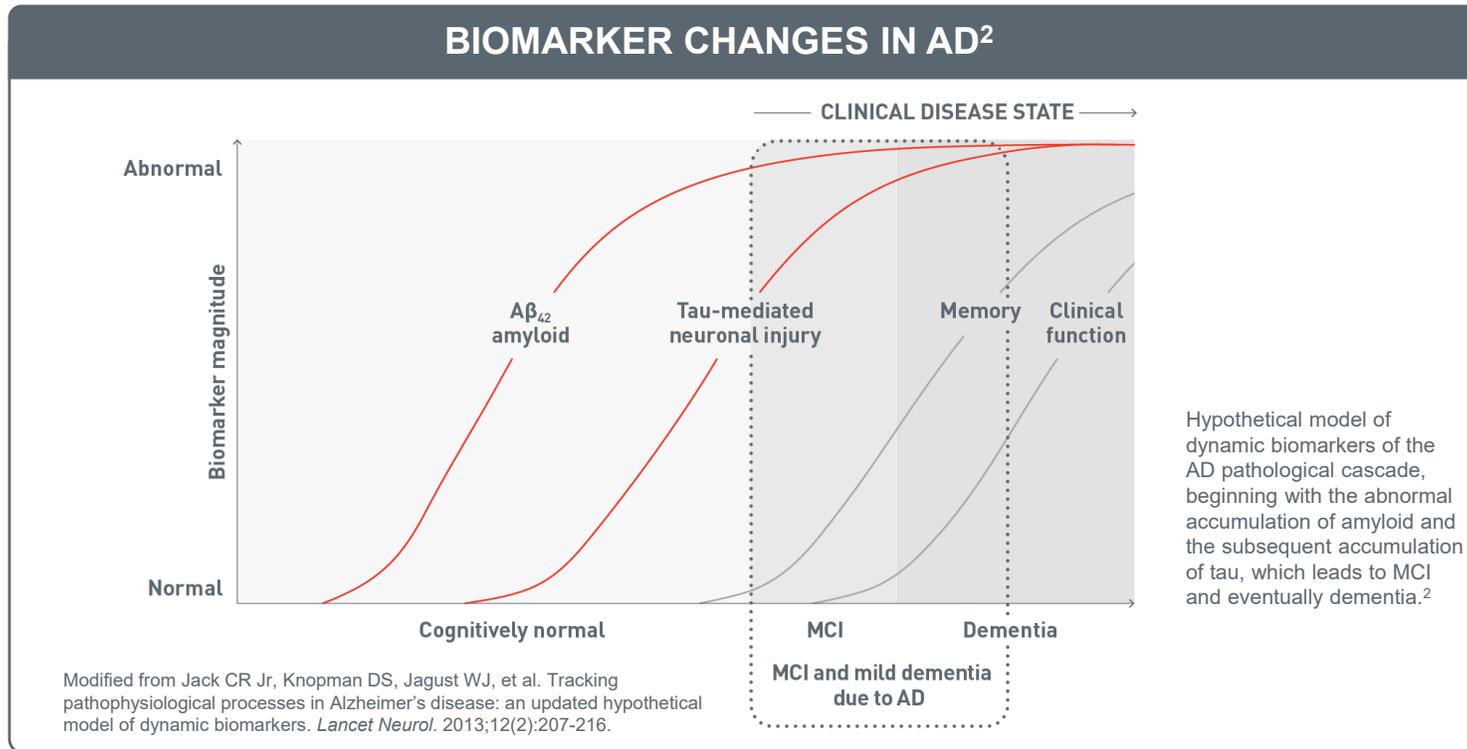
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AMYLOID, A KEY BIOMARKER, REPRESENTS AN OPPORTUNITY TO TREAT EARLY AND SLOW DISEASE PROGRESSION IN AD¹



- Amyloid plaques may begin to accumulate in the brain **approximately 20 years before symptoms present¹**
- Tau, another key biomarker, follows the accumulation of amyloid and is correlated with disease progression and cognitive decline¹
- As part of the diagnostic process, biomarker testing can confirm the presence of key underlying pathology, including amyloid¹
- Acting early could give patients with early symptomatic AD an opportunity to benefit from Disease Modifying Therapies (DMTs)¹

Aβ=amyloid beta.

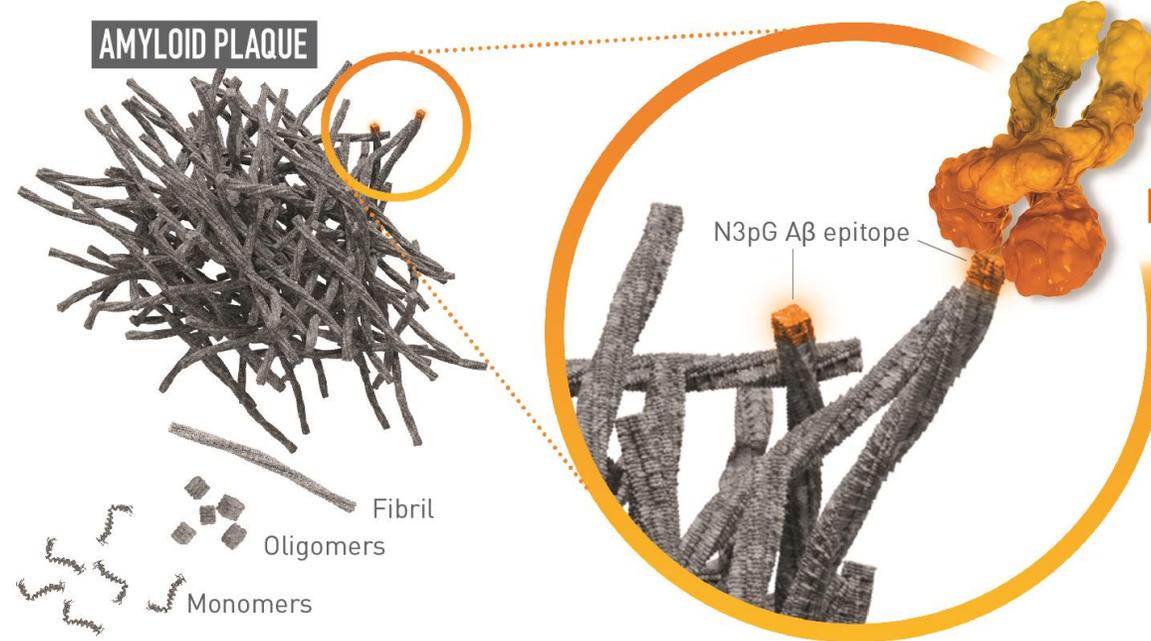
References: 1. Porsteinsson AP, Isaacson RS, Knox S, et al. Diagnosis of early Alzheimer's disease: clinical practice in 2021. *J Prev Alzheimers Dis.* 2021;8:371-386. 2. Jack CR Jr, Knopman DS, Jagust WJ, et al. Tracking pathophysiological processes in Alzheimer's disease: an updated hypothetical model of dynamic biomarkers. *Lancet Neurol.* 2013;12(2):207-216.

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KISUNLA TARGETS FULLY FORMED AMYLOID BETA PLAQUES¹

TARGET OF KISUNLA^{1,2}



Kisunla

TARGETS FULLY FORMED AMYLOID BETA PLAQUES

Kisunla is a humanized IgG1 monoclonal antibody directed against insoluble N-truncated pyroglutamate found in amyloid beta plaques in the brain—a defining feature of Alzheimer’s disease (AD).¹

SELECT IMPORTANT SAFETY INFORMATION

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

- 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.

IgG1=immunoglobulin gamma 1; N3pG=N-terminal, third amino acid, pyroglutamate formation.

References: 1. Kisunla (donanemab-azbt). Prescribing Information. Lilly USA, LLC. 2. Drolle E, Hane F, Lee B, et al. Atomic force microscopy to study molecular mechanisms of amyloid fibril formation and toxicity in Alzheimer’s disease. *Drug Metab Rev.* 2014;46(2):207-223.

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TRIAL DESIGN

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TRAILBLAZER-ALZ 2

A PHASE 3 STUDY THAT ASSESSED DISEASE PROGRESSION IN EARLY SYMPTOMATIC AD BY REDUCING AMYLOID PLAQUES^{1,2}

ASSESSED IN 2 POPULATIONS^{1,2}



The study was powered to test the results of Kisunla in the low-medium tau population.

The study allowed enrollment of participants with high tau levels, so Kisunla could also be tested in the overall population (low-medium tau plus high tau levels).

ELIGIBILITY

- Confirmed presence of amyloid pathology
- MCI or mild dementia

PRIMARY ENDPOINT

- Change in iADRS score from baseline to 76 weeks (impact on cognitive and functional decline)

TREATMENT PERIOD

- 1:1 randomization to Kisunla (n=860) or placebo (n=876) treatment arms at week 0
- Treated until amyloid plaques reached a minimal level^b (assessed with amyloid PET scans at 24, 52, and 76 weeks), discontinuation, or study completion (76 weeks)

DOSING AND ADMINISTRATION

- Administered via once-monthly (Q4W) IV infusion (for up to 72 weeks)
- Kisunla: Q4W 700 mg, increased to 1400 mg at fourth infusion
- Placebo: Q4W
- ARIA-monitoring MRI before infusions 1, 2, 3, 4, and 7

^aThere 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

^bIn the protocol, if the amyloid plaque level was < 11 Centiloids on a single PET scan or 11 to < 25 Centiloids on 2 consecutive PET scans, the patient was eligible to be switched to placebo.² For reference, < 24.1 Centiloids on an amyloid PET scan is consistent with a negative visual read.³

SELECT IMPORTANT SAFETY INFORMATION

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

- **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 $\epsilon 4$ 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.

iADRS=integrated Alzheimer's Disease Rating Scale; IV=intravenous; Q4W=every 4 weeks; SUVR=standardized uptake value ratio.

References: 1. Kisunla (donanemab-azbt). Prescribing Information. Lilly USA, LLC. 2. Sims JR, Zimmer JA, Evans CD, et al; for TRAILBLAZER-ALZ 2 Investigators. Donanemab in early symptomatic Alzheimer disease: the TRAILBLAZER-ALZ 2 randomized clinical trial. *JAMA*. 2023;330(6):512-527. 3. 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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BASELINE DEMOGRAPHICS AND CLINICAL CHARACTERISTICS IN TRAILBLAZER-ALZ 2 IN AN EARLY SYMPTOMATIC AD PATIENT POPULATION¹

BASELINE DEMOGRAPHICS AND CLINICAL CHARACTERISTICS IN THE OVERALL POPULATION^{1,2}

	Kisunla (n=860)	Placebo (n=876)
Female, n (%)	493 (57.3)	503 (57.4)
Mean age, years (SD)	73.0 (6.2)	73.0 (6.2)
Race, n (%) ^a		
White	781 (90.9)	807 (92.1)
American Indian or Alaskan Native	2 (0.2)	0 (0.0)
Asian	57 (6.6)	47 (5.4)
Black or African American	19 (2.2)	21 (2.4)
ApoE ε4 carrier, n (%)	598 (69.8)	621 (71.2)
ApoE ε4 homozygotes, n (%)	143 (16.7)	146 (16.7)
AChEI and/or memantine use, n (%)	521 (60.6)	538 (61.4)
MMSE score, mean (SD) ^b	22.4 (3.8)	22.2 (3.9)
MCI (MMSE ≥27) ^c n (%)	146 (17.0)	137 (15.7)
Mild AD (MMSE 20-26) ^c n (%)	713 (82.9)	738 (84.3)
Moderate AD (MMSE <20) ^c n (%)	1 (0.1)	0
Amyloid PET Centiloids, mean (SD) ^d	103.5 (34.5)	101.6 (34.5)
Flortaucipir SUVR, mean (SD) ^{c,e}	1.34 (0.25)	1.35 (0.26)

^aRace data were self-reported by participants within fixed categories.¹

^bLast nonmissing MMSE score prior to or at the start of study treatment.¹

^cBased on screening data.¹

^dAssessed via amyloid and tau PET.¹

^eAssessed via amyloid and tau PET. Global tau uptake was measured using a composite neocortical SUVR with white matter signal reference.¹

AChEI=acetylcholinesterase inhibitor; ApoE=apolipoprotein E; SD=standard deviation.

References: 1. Sims JR, Zimmer JA, Evans CD, et al; for TRAILBLAZER-ALZ 2 Investigators. Donanemab in early symptomatic Alzheimer disease: the TRAILBLAZER-ALZ 2 randomized clinical trial. *JAMA*. 2023;330(6):512-527. 2. Kisunla (donanemab-azbt). Prescribing Information. Lilly USA, LLC.

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.

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



KISUNLA EFFICACY IN EARLY SYMPTOMATIC AD

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EFFICACY ENDPOINTS IN TRAILBLAZER-ALZ 2: CHANGE FROM BASELINE AT 76 WEEKS^{1,2}

PRIMARY ENDPOINT	KEY SECONDARY ENDPOINTS		OTHER ENDPOINTS
<p>iADRS</p> <p>Validated integrated assessment of cognition and function from the ADAS-Cog₁₃ and ADCS-iADL measuring global disease severity across the AD continuum as a single summary score</p>	<p>CDR-SB^a</p> <p>Continuous measure of dementia severity based on summed clinical ratings of cognition and function</p>	<p>ADAS-Cog₁₃</p> <p>Measures cognition performance</p> <p>ADCS-iADL</p> <p>Measures instrumental activities of daily living</p> <p>PATHOLOGY BIOMARKERS</p> <p>Amyloid plaque deposition and tau deposition</p>	<p>CDR-GS^{a,b}</p> <p>Categorical global staging of dementia severity</p> <p>MMSE</p> <p>Measures cognitive function</p>

^aCDR is a clinician-rated assessment of cognition and function.

^bAdjusted for multiplicity.

SELECT IMPORTANT SAFETY INFORMATION

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

- 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.

ADAS-Cog₁₃=Alzheimer’s Disease Assessment Scale–Cognitive Subscale; ADCS-iADL=Alzheimer’s Disease Cooperative Study–instrumental Activities of Daily Living subscale; CDR=Clinical Dementia Rating; CDR-GS=Clinical Dementia Rating Global Score; CDR-SB=Clinical Dementia Rating scale Sum of Boxes.

References: 1. Kisunla (donanemab-azbt). Prescribing Information. Lilly USA, LLC. 2. Sims JR, Zimmer JA, Evans CD, et al; for TRAILBLAZER-ALZ 2 Investigators. Supplement 1: I5T-MC-AAC1 Clinical Study Protocols. Donanemab in early symptomatic Alzheimer disease: the TRAILBLAZER-ALZ 2 randomized clinical trial. *JAMA*. 2023;330(6):512-527.

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THE POWER OF KISUNLA WAS MEASURED ON A VALIDATED, INTEGRATED SCALE OF COGNITION AND FUNCTION¹

iADRS: AN INTEGRATED ASSESSMENT OF COGNITION AND DAILY FUNCTION^{1*}

iADRS Measures AD Severity and Reflects the Impact of Cognitive Loss on the Ability to Complete Daily Tasks¹⁻³

Cognitive Ability (ADAS-Cog₁₃)



- Memory
- Language
- Orientation
- Attention
- Planning and execution of movements



- Clearing the dishes
- Disposing of garbage
- Making meals
- Obtaining beverages
- Using household appliances

Functional Ability (ADCS-iADL)



- Writing
- Reading
- Keeping appointments
- Shopping
- Getting around
- Finding belongings
- Selecting clothes
- Engaging in hobbies



- Having conversations
- Using the telephone
- Talking about current events
- Watching television
- Being left alone

*The primary efficacy endpoint was change in the iADRS score from baseline to 76 weeks (18 months). The iADRS is a combination of 2 scores: the ADAS-Cog₁₃ and the ADCS-iADL. The total score ranges from 0 to 144, with lower scores reflecting worsening cognitive and functional performance.¹

SELECT IMPORTANT SAFETY INFORMATION

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

- 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.

References: 1. 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. 2. Wessels AM, Rentz DM, Case M, et al. Integrated Alzheimer's Disease Rating Scale: clinically meaningful change estimates. *Alzheimers Dement (N Y)*. 2022;8:e12312. doi.org/10.1002/trc2.12312 3. Wessels AM, Dennehy EB, Dowsett SA, et al. Meaningful clinical changes in Alzheimer disease measured with the iADRS and Illustrated using the donanemab TRAILBLAZER-ALZ study findings. *Neurol Clin Pract*. 2023;13(2):e200127. doi:10.1212/CPJ.0000000000200127

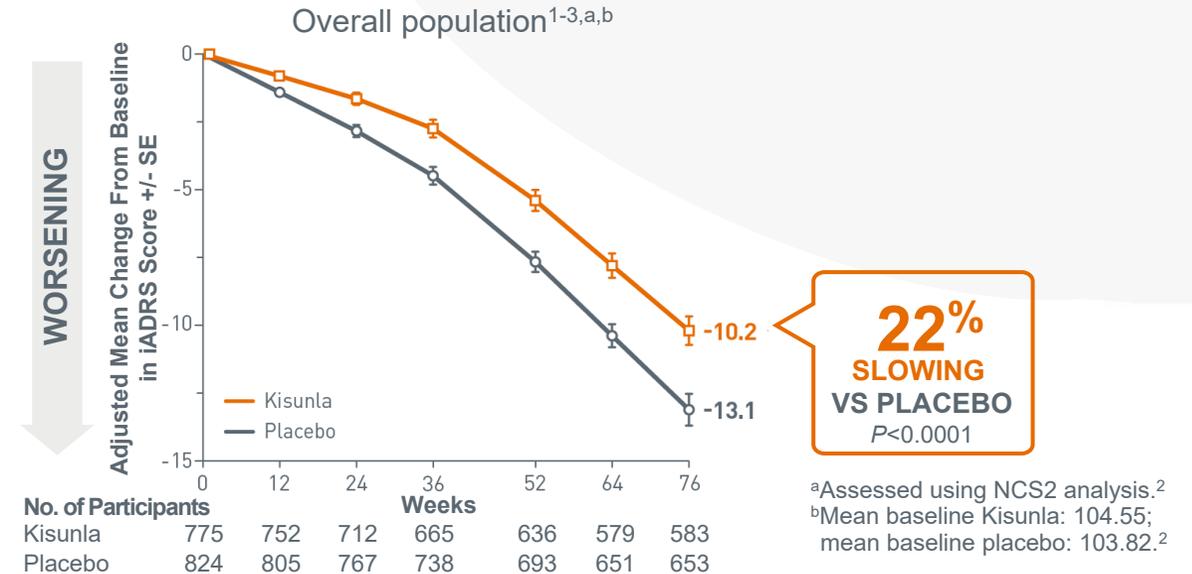
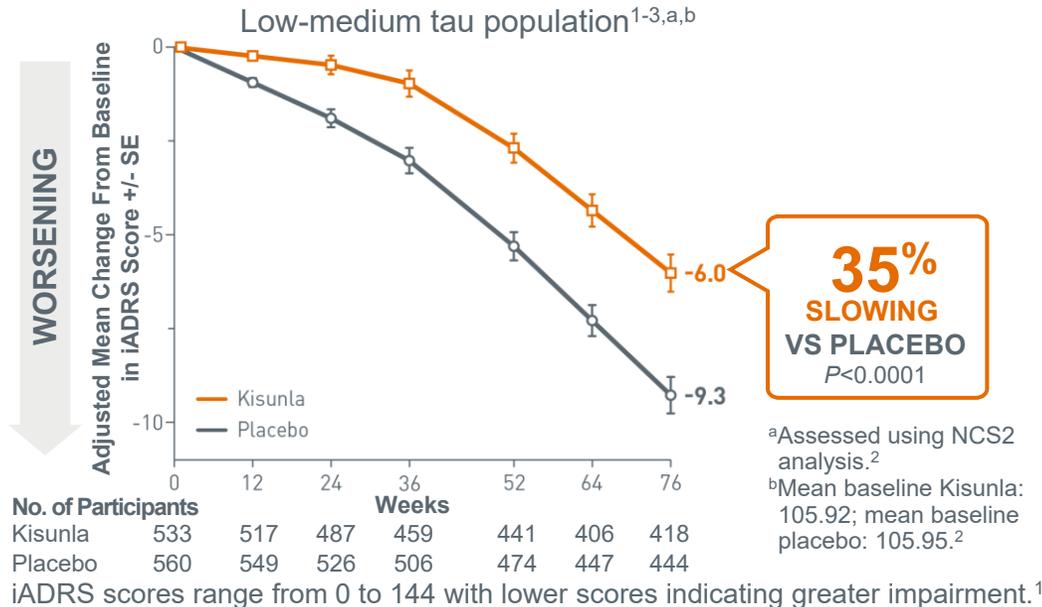
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KISUNLA CAN HELP SLOW COGNITIVE AND FUNCTIONAL DECLINE IN PATIENTS WITH EARLY SYMPTOMATIC AD¹⁻³

iADRS CHANGE FROM BASELINE THROUGH 76 WEEKS¹⁻³



Testing for tau pathology is not required per the Prescribing Information or for CMS reimbursement.¹

SELECT IMPORTANT SAFETY INFORMATION

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

- 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.

NCS2=natural cubic spline with 2 degrees of freedom; SE=standard error.

References: 1. Kisunla (donanemab-azbt). Prescribing Information. Lilly USA, LLC. 2. Sims JR, Zimmer JA, Evans CD, et al; for TRAILBLAZER-ALZ 2 Investigators. Donanemab in early symptomatic Alzheimer disease: the TRAILBLAZER-ALZ 2 randomized clinical trial. JAMA. 2023;330(6):512-527. 3. Data on File. Lilly USA, LLC. DOF-DN-US-0053.

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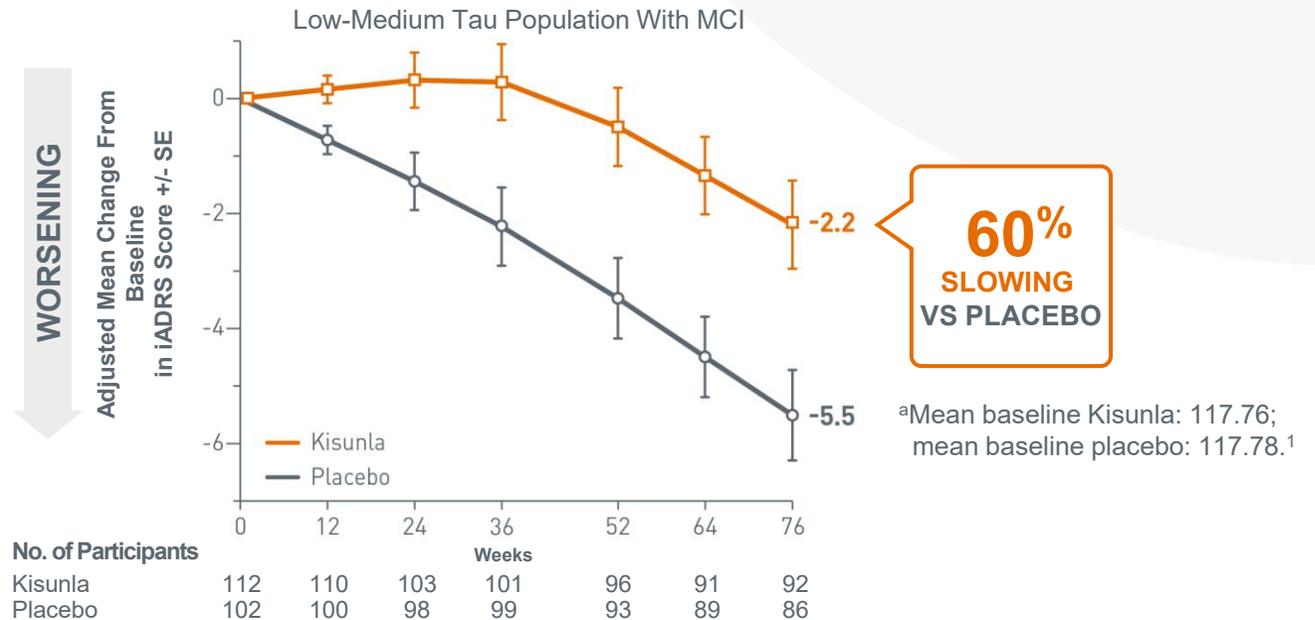


PATIENTS WITH MCI DUE TO AD AND LOW-MEDIUM TAU HAD A 60% SLOWING OF COGNITIVE AND FUNCTIONAL DECLINE AT 76 WEEKS^{1,2}

- In a prespecified subgroup analysis of low-medium tau participants (n=178) with MCI, treatment with Kisunla slowed decline by 60% on iADRS compared with placebo¹
- This is an exploratory subgroup analysis of patients with MCI stage of AD. No statistical testing was performed; therefore, results should be interpreted with caution

MMSE of 27 and above at baseline.¹

iADRS CHANGE FROM BASELINE THROUGH 76 WEEKS^{1,a}



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.

References: 1. Data on File. Lilly USA, LLC. DOF-DN-US-0041. 2. Sims JR, Zimmer JA, Evans CD, et al; for TRAILBLAZER-ALZ 2 Investigators. Donanemab in early symptomatic Alzheimer disease: the TRAILBLAZER-ALZ 2 randomized clinical trial. *JAMA*. 2023;330(6):512-527.

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





HELP KEEP YOUR PATIENTS IN THE EARLIER STAGES OF DISEASE LONGER¹

37% REDUCED RISK

OF PROGRESSING^a TO THE NEXT STAGE OF DISEASE



CDR-GS: Time to worsening of disease | Overall population

- HR: Overall population=0.63*; 95% CI: 0.51, 0.77; low-medium tau=0.61*; 95% CI: 0.47, 0.80¹
- In the low-medium tau population, a 39% reduced risk vs placebo was observed through 76 weeks (N=1182) P<0.001¹

^aProgression to next clinical stage was defined as any increase in CDR-GS at 2 consecutive visits from baseline. 0=normal, 0.5=very mild dementia; 1=mild dementia; 2=moderate dementia; 3=severe dementia.¹

*The HR is the relative risk reduction for substantial decline achieved by Kisunla vs placebo.¹

SELECT IMPORTANT SAFETY INFORMATION

ARIA Monitoring and Dose Management Guidelines (continued)

- 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.

CI=confidence interval; HR=hazard ratio.

Reference: 1. Sims JR, Zimmer JA, Evans CD, et al; for TRAILBLAZER-ALZ 2 Investigators. Donanemab in early symptomatic Alzheimer disease: the TRAILBLAZER-ALZ 2 randomized clinical trial. *JAMA*. 2023;330(6):512-527.

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





SLOWING OF COGNITIVE AND FUNCTIONAL DECLINE WAS DEMONSTRATED ACROSS ALL SECONDARY CLINICAL ENDPOINTS¹

RESULTS FOR KEY SECONDARY ENDPOINTS AT 76 WEEKS¹⁻⁴

Statistical Significance Achieved	Scale and Impact Measured	Low-Medium Tau Population Kisunla: n=588; Placebo: n=594	Overall Population Kisunla: n=860; Placebo: n=876
		Kisunla vs Placebo Mean Baseline: Kisunla (Placebo); Adjusted Mean Change From Baseline: Kisunla (Placebo)	
✓	CDR-SB^a Cognition and function	36% Baseline: 3.72 (3.64) (-0.67) ^b Change: 1.20 (1.88)	29% Baseline: 3.92 (3.89) (-0.70) ^c Change: 1.72 (2.42)
✓	ADCS-iADL^d Complex function	40% Baseline: 48.20 (48.56) (1.83) ^b Change: -2.76 (-4.59)	28% Baseline: 47.96 (47.98) (1.70) ^e Change: -4.42 (-6.13)
✓	ADAS-Cog₁₃^d Cognition	32% Baseline: 27.41 (27.60) (-1.52) ^b Change: 3.17 (4.69)	20% Baseline: 28.53 (29.16) (-1.33) ^f Change: 5.46 (6.79)

^aAssessed using MMRM analysis.¹ ^bP<0.001 vs placebo.² ^cP<0.0001 vs placebo.¹ ^dAssessed using NCS2 analysis.¹ ^eP=0.0001 vs placebo.¹ ^fP=0.0006 vs placebo.¹

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.

MMRM=mixed model for repeated measures.

References: **1.** Kisunla (donanemab-azbt). Prescribing Information. Lilly USA, LLC. **2.** Sims JR, Zimmer JA, Evans CD, et al; for TRAILBLAZER-ALZ 2 Investigators. Donanemab in early symptomatic Alzheimer disease: the TRAILBLAZER-ALZ 2 randomized clinical trial. *JAMA*. 2023;330(6):512-527. **3.** Wessels AM, Dennehy EB, Dowsett SA, et al. Meaningful clinical changes in Alzheimer disease measured with the iADRS and illustrated using the donanemab TRAILBLAZER-ALZ study findings. *Neurol Clin Pract*. 2023;13(2):e200127. doi:10.1212/CPJ.0000000000200127 **4.** Data on File. Lilly USA, LLC. DOF-DN-US-0054.

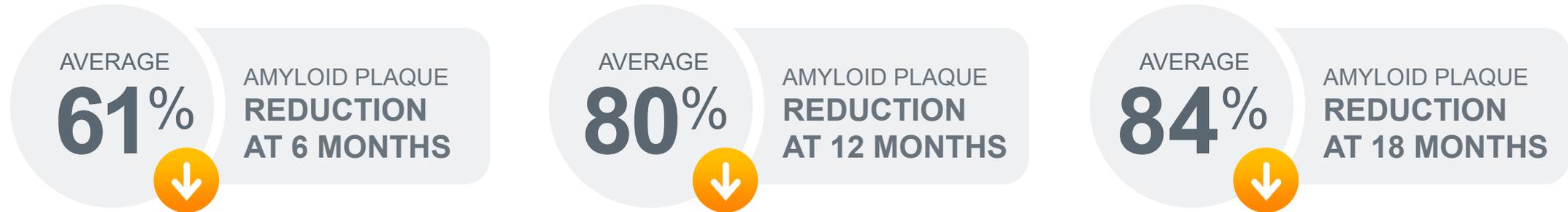
Please see additional [Important Safety Information](#) and full [Prescribing Information](#), including [Boxed Warning](#) regarding ARIA, and [Medication Guide](#) for Kisunla.





KISUNLA DEMONSTRATED REDUCTION IN AMYLOID PLAQUES AS EARLY AS 6 MONTHS^{1,2}

AMYLOID PLAQUE REDUCTION FROM BASELINE IN THE OVERALL POPULATION IN TRAILBLAZER-ALZ^{21,2}



Patients treated with placebo had an average of <1% amyloid plaque reduction from baseline to 18 months.^{1,2}

Mean baseline (n=712) amyloid plaque level for patients treated with Kisunla was 103.7 Centiloids (placebo was 101.4 Centiloids). The mean change from baseline was -62.8 Centiloids at 6 months (n=702), -82.8 Centiloids at 12 months (n=627), and -86.9 Centiloids at 18 months (n=571).^{1,2}

SELECT IMPORTANT SAFETY INFORMATION

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.

References: 1. Kisunla (donanemab-azbt). Prescribing Information. Lilly USA, LLC. 2. Data on File. Lilly USA, LLC. DOF-DN-US-0029.

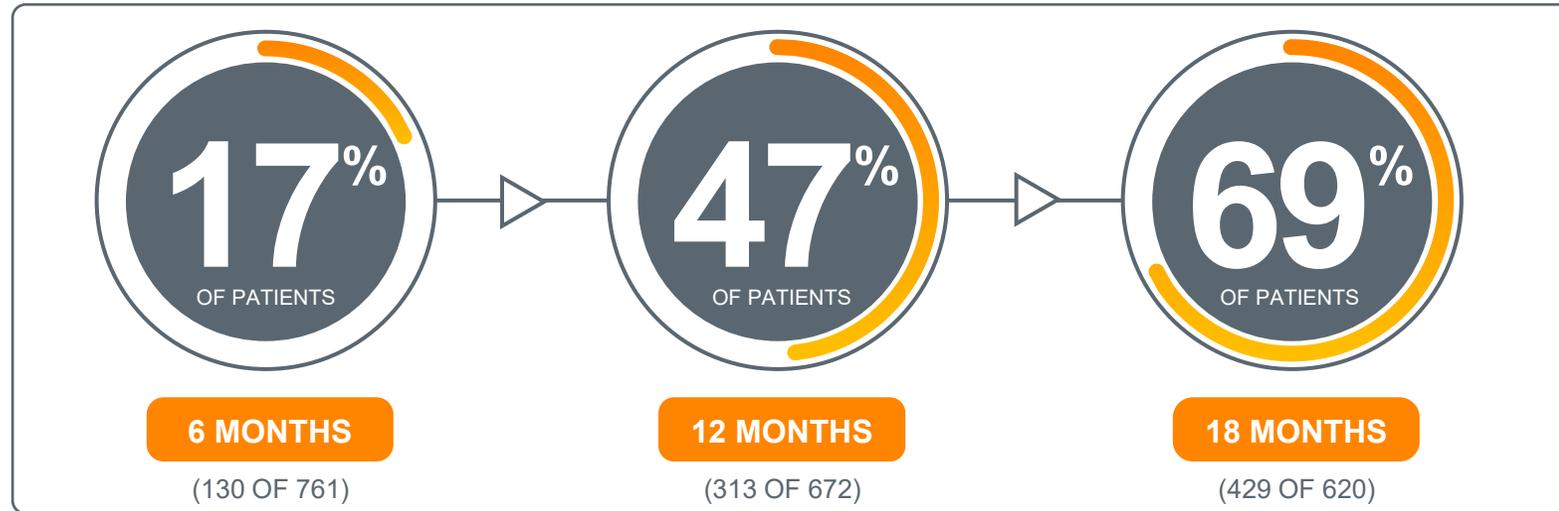
Please see additional [Important Safety Information](#) and full [Prescribing Information](#), including [Boxed Warning](#) regarding ARIA, and [Medication Guide](#) for Kisunla.





NEARLY HALF OF PATIENTS SUCCESSFULLY COMPLETED TREATMENT* BY 1 YEAR¹

PERCENTAGE OF PATIENTS IN THE OVERALL POPULATION ACHIEVING STOPPING CRITERIA* AT KEY TIME POINTS^{1,2†}



Kisunla was stopped based on removal of amyloid plaques to minimal levels on amyloid PET imaging in TRAILBLAZER-ALZ 2.¹

*In the protocol, if the amyloid plaque level was <11 Centiloids on a single PET scan or 11 to <25 Centiloids on 2 consecutive PET scans, the patient was eligible to be switched to placebo. Amyloid PET values may increase after treatment with Kisunla is stopped. There are no data beyond the 76-week duration of the clinical trial to guide whether additional dosing with Kisunla may be needed for longer-term clinical benefit.¹

For reference, <24.1 Centiloids on an amyloid PET scan is consistent with a negative visual read.³

†The mean baseline amyloid levels for patients treated with Kisunla were 103.5 Centiloids for the overall population, and 102.4 Centiloids for the low-medium tau population.⁴

SELECT IMPORTANT SAFETY INFORMATION

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%), and IRRs (9% vs 0.5%).

References: 1. Kisunla (donanemab-azbt). Prescribing Information. Lilly USA, LLC. 2. Data on File. Lilly USA, LLC. DOF-DN-US-0049.

3. 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. 4. Sims JR, Zimmer JA, Evans CD, et al; for TRAILBLAZER-ALZ 2 Investigators. Donanemab in early symptomatic Alzheimer disease: the TRAILBLAZER-ALZ 2 randomized clinical trial. *JAMA.* 2023;330(6):512-527.

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





LOW AMYLOID REACCUMULATION WAS OBSERVED AFTER 1 YEAR FOLLOWING COMPLETION OF TREATMENT¹

PATIENTS IN THIS ANALYSIS MET DOSE-STOPPING CRITERIA AT MONTH 6¹

Mean baseline amyloid level	80.8 Centiloids ^a	Threshold for switching to placebo at 6 months	<11.0 Centiloids	Median amyloid reaccumulation rate from 6 months to 18 months	1.0 Centiloid ^b
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From TRAILBLAZER-ALZ 2, a prespecified analysis of amyloid reaccumulation in patients treated with Kisunla who met dose-stopping criteria at 6 months based on amyloid PET imaging. The median change estimates at 18 months were compared with estimates at 6 months to evaluate the amyloid reaccumulation rates throughout the study.¹ No statistical testing was performed; therefore, results are considered descriptive only. Analyses of post randomization events have a risk for bias; therefore, results should be interpreted with caution.

In a separate modeling analysis of 4 studies (AACD, TB-ALZ, TB-EXT, and TB-ALZ 2) during an off-treatment period, amyloid PET values began to increase with a median rate of 2.80 Centiloids/year.²

^aPatients treated with Kisunla who met dose-stopping criteria at week 24 (amyloid plaque level <11 Centiloids at week 24) and completed the amyloid PET scan at week 76 (n=111; SD: 25.6).¹

^bThe median change in amyloid plaque level was 1.0 Centiloid (Q1: -4.5; Q3: 4.6).¹ On the Centiloid scale, 100 was intended to represent the amount of global amyloid deposition found in a typical mild-moderate AD subject. Since these numbers are mean values, some amyloid-negative scans may show slightly negative values.³

Q1=25th percentile; Q3=75th percentile.

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.

References: 1. Data on File. Lilly USA, LLC. DOF-DN-US-0048. 2. Kisunla (donanemab-azbt). Prescribing Information. Lilly USA, LLC. 3. Klunk WE, Koeppe RA, Price JC, et al. The Centiloid Project: standardizing quantitative amyloid plaque estimation by PET. *Alzheimers Dement.* 2015;11(1):1-15.e1-4. doi:10.1016/j.jalz.2014.07.003

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

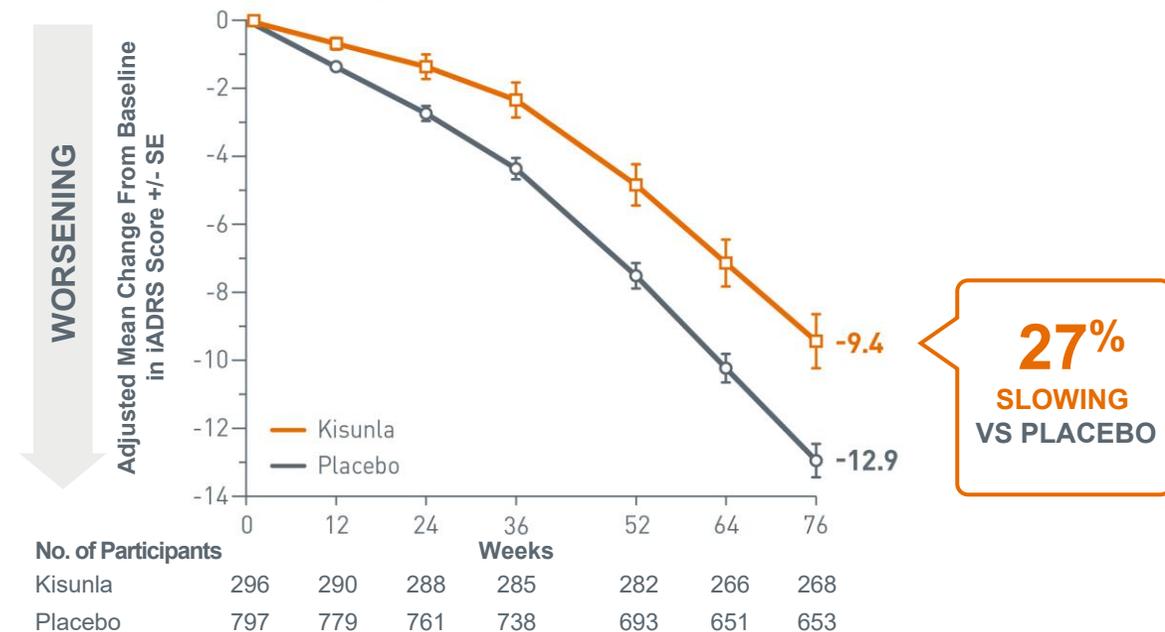




TREATMENT EFFECT IN PATIENTS WHO SWITCHED* TO PLACEBO[†]

OVERALL POPULATION: PATIENTS TAKING KISUNLA WHO SWITCHED TO PLACEBO AT EITHER 24 OR 52 WEEKS¹

iADRS Change From Baseline Through 76 Weeks^{1,a,b}



Mean treatment duration was 47 weeks.¹
No statistical testing was performed, therefore results should be interpreted with caution.¹

*If the amyloid plaque level was <11 Centiloids on a single PET scan or 11 to <25 Centiloids on 2 consecutive PET scans, the patient was eligible to be switched to placebo.²

[†]Based on a post hoc analysis of patients who switched to placebo after a 6- or 12-month PET scan.¹

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.³

^aAssessed using NCS2 analysis.¹

^bMean baseline Kisunla: 105.17; mean baseline placebo: 104.04.¹

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.

References: 1. Data on File. Lilly USA, LLC. DOF-DN-US-0032. 2. Sims JR, Zimmer JA, Evans CD, et al; for TRAILBLAZER-ALZ 2 Investigators. Donanemab in early symptomatic Alzheimer's disease: the TRAILBLAZER-ALZ 2 randomized clinical trial. *JAMA*. 2023;330(6):512-527. 3. Kisunla (donanemab-azbt). Prescribing Information. Lilly USA, LLC.

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



THE SAFETY PROFILE OF KISUNLA

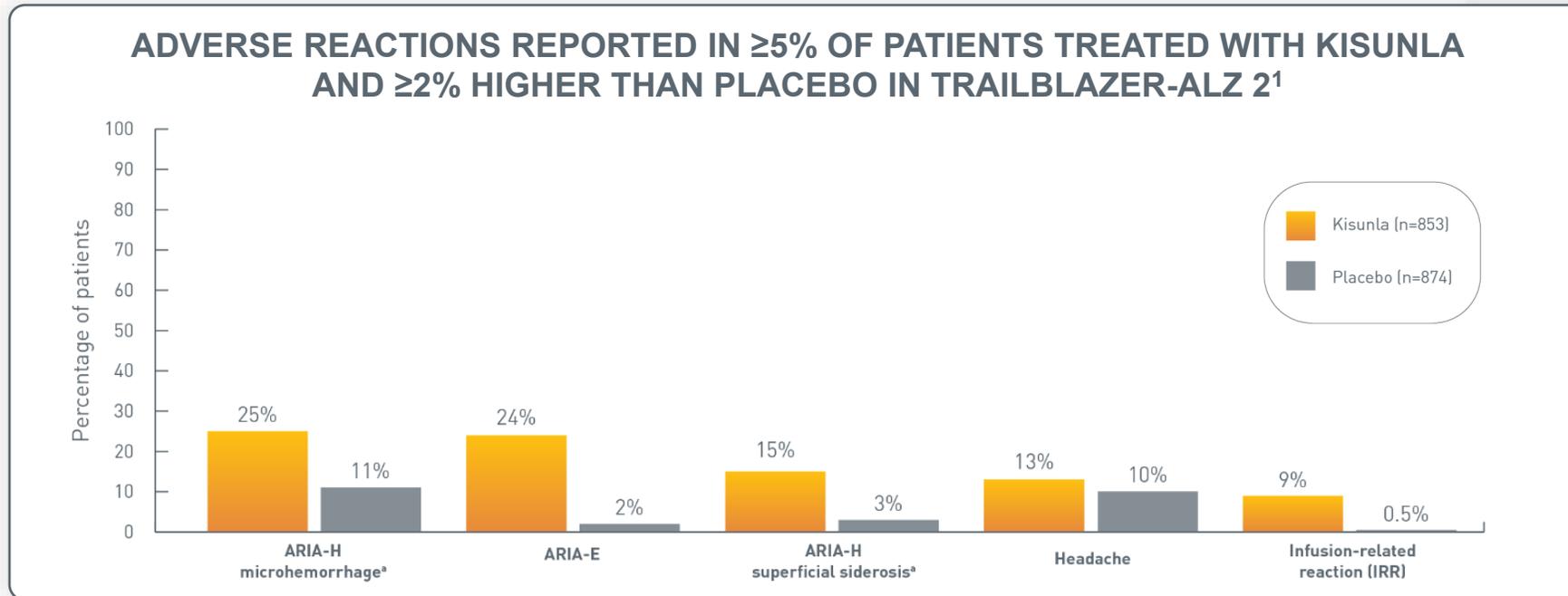
If you have questions about the safety of Kisunla after reviewing this section, your Lilly Account Manager can help you find the right person to answer them. You can also call The Lilly Answers Center at **1-800-LillyRx**.

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





THE SAFETY OF KISUNLA WAS STUDIED IN MORE THAN 1900 PATIENTS IN CLINICAL TRIALS^{1*}



^aAs assessed by MRI. A participant could have both microhemorrhage and superficial siderosis.¹

- ARIA-E (edema) includes brain edema or sulcal effusions¹
- ARIA-H (hemosiderin deposition) most commonly includes microhemorrhage and superficial siderosis¹

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

*1912 patients with AD received Kisunla once monthly for ≥6 months.¹

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

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

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





ARIA WITH AMYLOID-TARGETING THERAPIES

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). Incidence and timing of ARIA vary among treatments. ARIA is usually asymptomatic, although rarely serious and life-threatening events can occur. Serious intracerebral hemorrhage >1 cm, some of which has been fatal, has occurred 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.¹

- 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. Prior to testing, prescribers should discuss with patients the risk of ARIA across genotypes and the implications of genetic testing results¹

Consider the benefit of Kisunla for the treatment of AD and potential risk of serious adverse events associated with ARIA when deciding to initiate treatment with Kisunla.¹

Obtain recent brain MRI prior to initiating treatment with Kisunla. Obtain an MRI prior to infusions 2, 3, 4, and 7, and if symptoms consistent with ARIA occur. Use caution if ARIA is observed on MRI in the presence of clinical symptoms. See Important Safety Information and Prescribing information for dosing considerations if ARIA is observed.^{1,2}

References: 1. Kisunla (donanemab-azbt). Prescribing Information. Lilly USA, LLC. 2. Sims JR, Zimmer JA, Evans CD, et al; for TRAILBLAZER-ALZ 2 Investigators. Donanemab early symptomatic Alzheimer disease: the TRAILBLAZER-ALZ 2 randomized clinical trial. *JAMA*. 2023;330(6):512-527.

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





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-E¹

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-H¹

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 placebo¹
- ARIA-H does not resolve radiographically, but it can stabilize²

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.

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

References: 1. Kisunla (donanemab-azbt). Prescribing Information. Lilly USA, LLC. 2. Sims JR, Zimmer JA, Evans CD, et al; for TRAILBLAZER-ALZ 2 Investigators. Donanemab early symptomatic Alzheimer disease: the TRAILBLAZER-ALZ 2 randomized clinical trial. *JAMA*. 2023;330(6):512-527.

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





CLASSIFICATION OF THE RADIOGRAPHIC SEVERITY OF ARIA¹

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

^aIncludes new or worsening superficial siderosis.¹

FLAIR=fluid-attenuated inversion recovery.

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

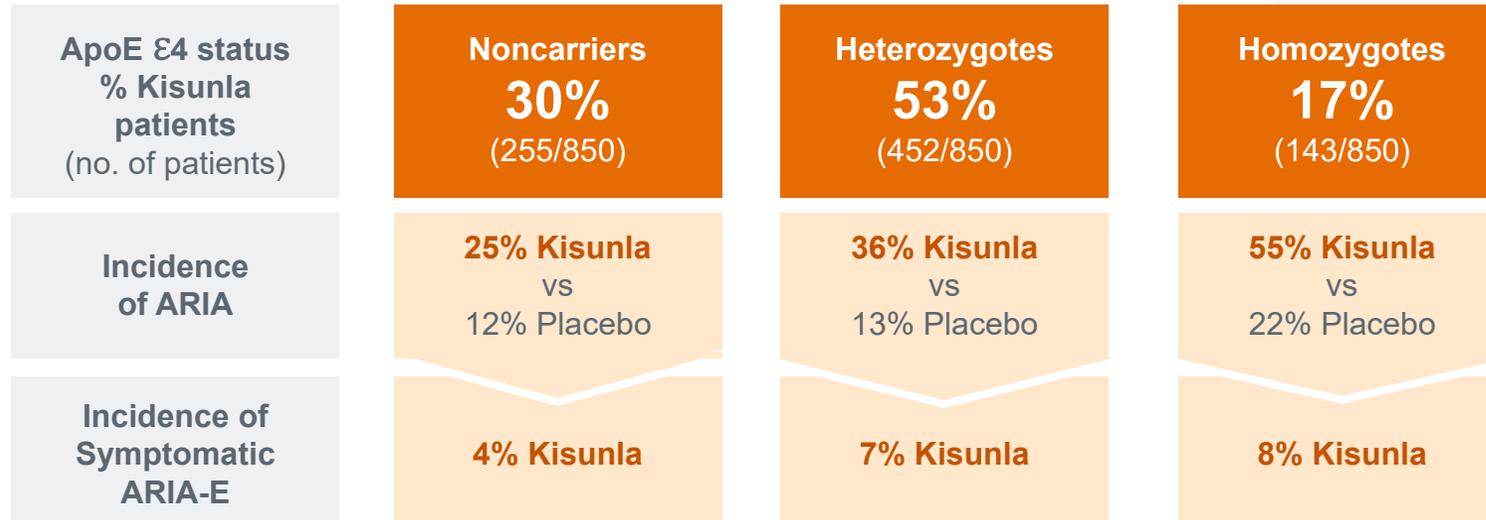
Please see additional Important Safety Information and full Prescribing Information, including Boxed Warning regarding ARIA, and Medication Guide for Kisunla.





UNDERSTANDING ARIA INCIDENCES AND ApoE ε4 CARRIER STATUS

ARIA INCIDENCES AND ApoE ε4 CARRIER STATUS¹



- In patients treated with Kisunla, the risk of ARIA, including symptomatic ARIA, was increased in ApoE ε4 homozygotes compared with heterozygotes and noncarriers as well as in heterozygotes compared with noncarriers. A higher frequency of ARIA-E and ARIA-H was observed for patients with pretreatment microhemorrhage and/or superficial siderosis¹
- For patients treated with Kisunla (n=850), 17% (n=143) were ApoE ε4 homozygotes, 53% (n=452) were heterozygotes, and 30% (n=255) were noncarriers¹
- 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 noncarriers¹

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

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





ARIA MANAGEMENT

DOSING RECOMMENDATIONS FOR PATIENTS WITH ARIA-E¹

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		

^aMild: 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

^bSuspend 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

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

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

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

DOSING RECOMMENDATIONS FOR PATIENTS WITH ARIA-H¹

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		

^aSuspend 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

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



KEY DOSING AND ADMINISTRATION INFORMATION

If you have questions regarding the dosing and administration of Kisunla after reviewing this section, please review additional information found on [kisunla.lilly.com](https://www.kisunla.lilly.com). Your Lilly Account Manager is also always available to help you with additional requests.

Please see 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



ONCE-MONTHLY KISUNLA IS THE FIRST AND ONLY FDA-APPROVED ATT WITH DOSING INSTRUCTIONS THAT ALLOW FOR LIMITED-DURATION TREATMENT^{1†}

1 MONTHLY INFUSION



- 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[‡]

*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

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.

[†]In clinical trials, completion of active treatment was guided by amyloid PET levels measured at week 24, week 52, and week 76. If amyloid plaque level was <11 Centiloids on any 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.²

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.

References: 1. Kisunla (donanemab-azbt). Prescribing Information. Lilly USA, LLC. 2. 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.

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





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

^aIn 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

^bFor reference, <24.1 Centiloids on an amyloid PET scan is consistent with a negative visual read.²

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.

References: 1. Kisunla (donanemab-azbt). Prescribing Information. Lilly USA, LLC. 2. 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.

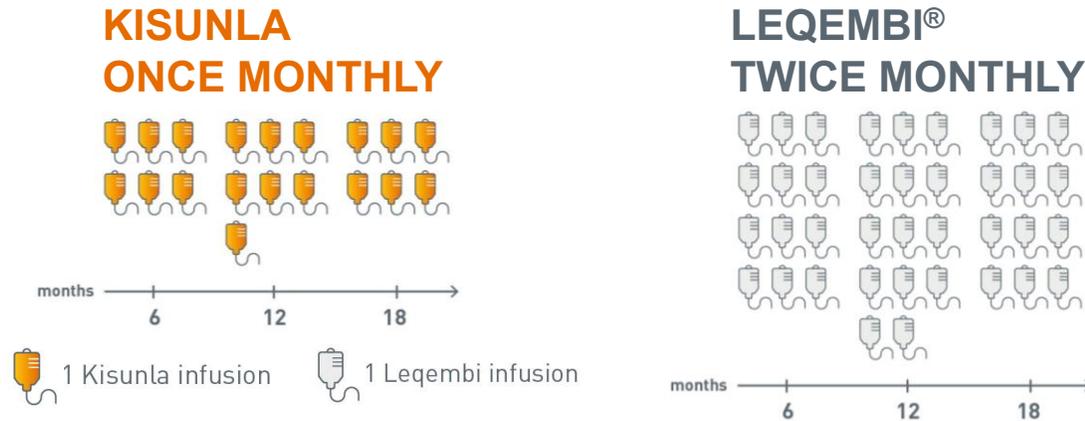
Please see additional [Important Safety Information](#) and full [Prescribing Information](#), including [Boxed Warning](#) regarding ARIA, and [Medication Guide](#) for Kisunla.





KISUNLA IS A ONCE-MONTHLY TREATMENT,¹ WHICH MAY REDUCE PATIENT INFUSION BURDEN

INFUSION SCHEDULES AMONG TRADITIONALLY APPROVED ATTS OVER AN 18-MONTH TIME PERIOD^{1,2}



This graphic portrays only potential maximum dosing regimens per the products' approved labeling and is not intended to compare efficacy or safety.

Kisunla: Once-monthly infusion¹

- The recommended dosage of Kisunla is 700 mg every 4 weeks for 3 infusions, then 1400 mg every 4 weeks
- Administered as an IV infusion over ~30 minutes, followed by a minimum 30-minute observation period to monitor for infusion-related and hypersensitivity reactions

Leqembi® (lecanemab-irmb): Twice-monthly infusion²

- The recommended dosage of Leqembi is 10 mg/kg once every 2 weeks
- Administered as an IV infusion over ~60 minutes, followed by an observation period to monitor for infusion-related reactions

SELECT IMPORTANT SAFETY INFORMATION

Risk Factors for ARIA and Intracerebral Hemorrhages

- **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.

References: 1. Kisunla (donanemab-azbt). Prescribing Information. Lilly USA, LLC. 2. Leqembi (lecanemab-irmb). Prescribing Information. Eisai R&D Management Co., Ltd.

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





OVERVIEW OF DOSING & ADMINISTRATION CONSIDERATIONS FOR TRADITIONALLY APPROVED AMYLOID-TARGETING THERAPIES¹⁻⁵

	Kisunla™ (donanemab-azbt)	Leqembi® (lecanemab-irmb)
Indicated Population	MCI DUE TO AD OR MILD AD DEMENTIA WITH CONFIRMED AMYLOID PATHOLOGY	
Registrational Trial	<ul style="list-style-type: none"> TRAILBLAZER-ALZ 2 	<ul style="list-style-type: none"> Clarity AD
Dosing	Titration-based IV infusion <ul style="list-style-type: none"> Infusions 1, 2, and 3: 700 mg Infusion 4 and beyond: 1400 mg 	Weight-based IV infusion <ul style="list-style-type: none"> All infusions: 10 mg/kg
Frequency	Q4W	Q2W
Infusion Duration	30 minutes ^a	1 hour
MRI Monitoring for ARIA	MRIs before infusions 1, 2, 3, 4, and 7	MRIs before infusions 1, 5, 7, and 14
Treatment Period	<ul style="list-style-type: none"> Duration of study was ~18 months. Patients were eligible to switch to placebo based on a reduction of amyloid levels below predefined thresholds on PET imaging.^b 	<ul style="list-style-type: none"> Duration of study was 18 months with no eligibility to switch to placebo based on observed effects on amyloid imaging
Maximum No. of Infusions^c (~18 month study)		

This graphic is not intended to compare the efficacy and safety of products. Please review product labels, including Boxed Warnings.

^aPatients should be observed post-infusion for ≥30 minutes to evaluate for infusion reactions and hypersensitivity reactions.¹

^bIn TRAILBLAZER-ALZ 2, completion of active treatment was guided by amyloid PET levels measured at week 24, week 52, and week 76.¹ If amyloid plaque level was <11 Centiloids on any single PET scan or 11 to <25 Centiloids on 2 consecutive PET scans, subjects taking Kisunla were eligible to switch to placebo.² Amyloid PET values may increase after treatment with Kisunla is stopped. There are no data beyond the 76-week duration of the study to guide whether additional dosing with Kisunla may be needed for longer-term clinical benefit.¹

^cDosing may have been suspended in clinical studies based on protocol recommendations for severity and type of ARIA confirmed via MRI imaging.^{5,6}

SELECT IMPORTANT SAFETY INFORMATION

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

- 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.

Q2W=every 2 weeks.

References: 1. Kisunla (donanemab-azbt). Prescribing Information. Lilly USA, LLC. 2. Sims JR, Zimmer JA, Evans CD, et al; for TRAILBLAZER-ALZ 2 Investigators. Donanemab in early symptomatic Alzheimer disease: the TRAILBLAZER-ALZ 2 randomized clinical trial. *JAMA*. 2023;330(6):512-527. 3. Leqembi (lecanemab-irmb). Prescribing Information. Eisai R&D Management Co., Ltd. 4. van Dyck CH, Swanson CJ, Aisen P, et al. Lecanemab in early Alzheimer's disease. *N Engl J Med*. 2023;388(1):9-21. doi:10.1056/NEJMoa2212948 5. van Dyck CH, Swanson CJ, Aisen P, et al. Supplement BAN2401-G000-301 Clinical Study Protocols. Lecanemab in early Alzheimer's disease. *N Engl J Med*. 2023;388(1):9-21. doi:10.1056/NEJMoa2212948 6. Sims JR, Zimmer JA, Evans CD, et al; for TRAILBLAZER-ALZ 2 Investigators. Supplement 1: I5T-MC-AACI Clinical Study Protocols. Donanemab in early symptomatic Alzheimer disease: the TRAILBLAZER-ALZ 2 randomized clinical trial. *JAMA*. 2023;330(6):512-527.

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





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 preparation¹
- Inspect the content of the vial for particulate matter and discoloration prior to preparation. Kisunla solution is clear to opalescent, colorless to slightly yellow to slightly brown. Discard if discolored or foreign particles are observed¹
- 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 dose¹
 - 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 vial¹
- 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 immediately¹
- Administer the diluted infusion solution via IV infusion over approximately 30 minutes¹
 - 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 indicated¹
- Flush the line with 0.9% sodium chloride injection at the end of the infusion¹
- Plan to observe the patient post-infusion for a minimum of 30 minutes to evaluate for any infusion-related or hypersensitivity reactions¹

For more information on preparing Kisunla for infusion, visit [kisunla.lilly.com](https://www.kisunla.lilly.com)

SELECT IMPORTANT SAFETY INFORMATION

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

- 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.

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

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



KEY TAKEAWAYS

Please see 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



KISUNLA CAN MAKE A DIFFERENCE FOR PATIENTS WITH EARLY SYMPTOMATIC AD¹

AS MEASURED AT 76 WEEKS IN TRAILBLAZER-ALZ 2^{1,2}

KEY KISUNLA TAKEAWAYS^{1,2}



Significant slowing of cognitive and functional decline by up to 35%



37% reduced risk of progressing to the next stage of AD



Potential to stop dosing upon removal of amyloid plaques to minimal levels*



Once-monthly 30-minute infusion

- Kisunla, like other AβTAs, can cause ARIA, which is usually asymptomatic, though rarely serious and life-threatening events can occur
- The most common adverse reactions reported in ≥5% of patients treated with Kisunla and ≥2% higher than placebo: ARIA-H microhemorrhage (25% vs 11%), ARIA-E (24% vs 2%), ARIA-H superficial siderosis (15% vs 3%), headache (13% vs 10%), and IRRs (9% vs 0.5%)

You can now impact the course of AD¹

- Identify appropriate amyloid-positive patients with early symptomatic AD
- Consider initiating treatment with Kisunla

*In the Phase 3 clinical trial, dosing was continued or stopped in response to observed effects on amyloid PET 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

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.

References: 1. Kisunla (donanemab-azbt). Prescribing Information. Lilly USA, LLC. 2. Withington CG, Turner RS. Amyloid-related imaging abnormalities with anti-amyloid antibodies for the treatment of dementia due to Alzheimer's disease. *Front Neurol.* 2022;13:862369. doi:10.3389/fneur.2022.862369

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





CENTERS FOR MEDICARE & MEDICAID SERVICES (CMS) COVERS KISUNLA UNDER COVERAGE WITH EVIDENCE DEVELOPMENT (CED)^{1,2}

NATIONAL COVERAGE DETERMINATION (NCD) ON MONOCLONAL ANTIBODIES DIRECTED AGAINST AMYLOID FOR THE TREATMENT OF AD (200.3)

CMS provides coverage for¹:

- Patients who have a clinical diagnosis of MCI due to AD or mild AD dementia, both with confirmed presence of amyloid beta pathology consistent with AD

Coverage criteria—drugs in class that receive traditional FDA approval¹:

- Patient must be enrolled in Medicare
- Patients must have a diagnosis of MCI due to AD or mild AD dementia, with documented evidence of beta-amyloid plaques in the brain
- Physician must participate in a qualifying registry* with an appropriate clinical team and follow-up care[†]

Note: Medicare removed the NCD for beta amyloid PET in 2023.³

*For more information on qualifying registries, visit <https://www.cms.gov/medicare/coverage/coverage-evidence-development/monoclonal-antibodies-directed-against-amyloid-treatment-alzheimers-disease-ad>

[†]Prescribing clinicians or their staff shall submit at first baseline treatment via the dedicated CMS CED data submission portal and every 6 months for up to 24 months (5 total assessments).⁴

SELECT IMPORTANT SAFETY INFORMATION

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

- 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.

References: 1. CMS.gov. Monoclonal antibodies directed against amyloid for the treatment of Alzheimer’s disease (CAG-00460N). Accessed February 20, 2024. <https://www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=N&ncaid=305> 2. CMS.gov. Monoclonal antibodies directed against amyloid for the treatment of Alzheimer’s Disease (AD). Accessed February 20, 2024. <https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?ncid=375&ncdver=1> 3. CMS.gov. CMS Manual System. Beta amyloid positron emission tomography in dementia and neurodegenerative disease. NCA CAG-00431R Decision Sheet. Accessed October 20, 2023. <https://www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=N&ncaid=308> 4. CMS.gov. Monoclonal antibodies directed against amyloid for the treatment of Alzheimer’s Disease (AD). Accessed February 20, 2024. <https://www.cms.gov/medicare/coverage/coverage-evidence-development/monoclonal-antibodies-directed-against-amyloid-treatment-alzheimers-disease-ad>

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





IMPORTANT SAFETY INFORMATION INCLUDING WARNINGS

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.

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





IMPORTANT SAFETY INFORMATION INCLUDING WARNINGS (CONT'D)

Amyloid-Related Imaging Abnormalities (ARIA)

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

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

Incidence of ARIA

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

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

Incidence of ICH

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

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





IMPORTANT SAFETY INFORMATION INCLUDING WARNINGS (CONT'D)

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

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.

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



IMPORTANT SAFETY INFORMATION INCLUDING WARNINGS (CONT'D)

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

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.

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





IMPORTANT SAFETY INFORMATION INCLUDING WARNINGS (CONT'D)

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

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.

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





IMPORTANT SAFETY INFORMATION INCLUDING WARNINGS (CONT'D)

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 $\geq 5\%$ of patients treated with Kisunla (n=853) and $\geq 2\%$ 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 see full [Prescribing Information](#), including [Boxed Warning](#) regarding ARIA, and [Medication Guide](#) for Kisunla.

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