FDA approves updated label for Lilly's Kisunla (donanemab-azbt) with new dosing in early symptomatic Alzheimer's disease

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The newly recommended dosing schedule significantly lowered ARIA-E rates compared to the original dosing schedule, adding to the established safety profile of the treatment

INDIANAPOLIS, July 9, 2025 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) announced today that the U.S. Food and Drug Administration (FDA) has approved a label update with a new recommended titration dosing schedule for Kisunla (donanemab-azbt), Lilly's once-monthly amyloid-targeting therapy for adults with early symptomatic Alzheimer's disease (AD), which includes people with mild cognitive impairment (MCI) as well as people in the mild dementia stage of AD, with confirmed amyloid pathology.[1,2] In the TRAILBLAZER-ALZ 6 study, the modified titration schedule significantly lowered the incidence of amyloid-related imaging abnormalities with edema/effusion (ARIA-E) versus the original dosing schedule at 24 and 52 weeks, while still achieving similar levels of amyloid plaque removal and P-tau217 reduction.

"We are confident that this label update for Kisunla will significantly aid healthcare professionals in evaluating appropriate treatment options for their patients," stated Brandy Matthews, MD, FAAN, Lilly's Vice President of Global & US Medical Affairs for Alzheimer's Disease. "This update underscores our unwavering commitment to patient safety and the advancement of Alzheimer's disease treatment by potentially mitigating the risk of ARIA-E."

The new recommended dosing regimen involves a more gradual titration, and the TRAILBLAZER-ALZ 6 study significantly lowered the incidence of ARIA-E by 41% at 24 weeks and by 35% at 52 weeks versus the original dosing schedule. ARIA-E is a side effect of amyloid plaque-targeting therapies, including Kisunla. ARIA-E is usually asymptomatic, although serious and fatal events can occur. The new dosing recommendation differs from the original dosing by shifting a single vial from the first dose to the third dose, delivering the same amount of Kisunla by week 24. This resulted in lower rates of ARIA-E without compromising Kisunla's ability to reduce amyloid plaque or Kisunla's once-monthly dosing with the potential for limited-duration treatment based on amyloid plaque removal to minimal levels.[3-6]

Key findings from the TRAILBLAZER-ALZ 6 study, which supports this label update, included:

- The primary endpoint of the study was the proportion of participants with any occurrence of ARIA-E by week 24. The results showed the incidence of ARIA-E was 14% in patients receiving the modified titration compared with 24% for those receiving the original dosing regimen, a 41% lower relative risk.[7] At week 52, the incidence of ARIA-E was 16% in patients receiving the modified titration compared with 25% for those receiving the original dosing regimen, a 35% lower relative risk.
- Including asymptomatic radiographic events at week 52, ARIA, ARIA-E, and ARIA-H were observed in 29%, 16%, and 25% of patients receiving the modified titration dosing. ARIA-E and ARIA-H are different types of amyloid-related imaging abnormalities (ARIA). ARIA with edema is characterized as ARIA-E and ARIA with hemosiderin deposition is characterized as ARIA-H.
- Patients on the modified titration experienced a reduction of amyloid plaque and P-tau217 comparable to patients receiving the original dosing regimen. As observed using amyloid PET at the primary endpoint of 24 weeks, amyloid plaque levels in patients on the modified titration of donanemab in TRAILBLAZER-ALZ 6 were reduced on average 67% from baseline compared to 69% for patients on the original dosing regimen.[7,8]
- No new adverse reactions were identified in this study, although higher rates of hypersensitivity reactions and infusion-related reactions were observed.

"This updated dosing strategy is a meaningful advancement for patients and their care teams," said Elly Lee, MD, Chief Medical Officer and Principal Investigator, Irvine Center for Clinical Research. "By significantly reducing the risk of ARIA-E, we can offer patients and care teams greater confidence in the safety of Kisunla while preserving its ability to reduce amyloid."

The U.S. FDA approved Kisunla in July 2024 based on the TRAILBLAZER-ALZ 2 Phase 3 clinical trial data. The study demonstrated that Kisunla significantly slowed cognitive and functional decline in patients who were less pathologically advanced in their disease by up to 35% and by 22% in the overall study population compared to placebo at 18 months.[9] Kisunla reduced the risk of progressing to the next clinical stage of disease by 37% over the same period.[3] Cognitive and functional decline was characterized by more severe memory and thinking problems, more trouble with daily activities, and a greater need for help from caregivers.[3,10]

Please see the INDICATION AND SAFETY SUMMARY WITH WARNINGS below.

Lilly Support Services for Kisunla is dedicated to assisting patients throughout their treatment journey with Kisunla. This free program provides essential services, including coverage determination assistance, care coordination, nurse navigator support, and personalized resources. For more information about Lilly Support Services and Kisunla, visit www.kisunla.lilly.com or call 1-800-LillyRx (1-800-545-5979).

About Kisunla™ (donanemab)
Kisunla™ (donanemab-azbt) (pronounced kih-SUHN-lah) is an amyloid-targeting therapy for people with mild cognitive impairment (MCI) as well as people with mild dementia stage of early symptomatic Alzheimer's disease, with confirmed amyloid pathology. Kisunla (donanemab-azbt) injection for intravenous use is available as a 350 mg/20 mL single-dose vial. Kisunla can cause serious side effects, including amyloid-related imaging abnormalities, or ARIA, and infusion-related reactions.

About TRAILBLAZER-ALZ 6 study and the TRAILBLAZER-ALZ program
TRAILBLAZER-ALZ 6 (NCT05738486) is a Phase 3b, multicenter, randomized, double-blind study to investigate different dosing regimens and their effect on ARIA-E in adults with early symptomatic Alzheimer's disease. The trial enrolled 843 participants ages 60-85 selected based on cognitive assessments in conjunction with amyloid plaque imaging by PET scan.[7] These study results were published in *Alzheimer's and Dementia*.

About TRAILBLAZER-ALZ 2 study
TRAILBLAZER-ALZ 2 (NCT04437511) is a Phase 3, randomized, double-blind, placebo-controlled study to evaluate the safety and efficacy of donanemab in participants with early symptomatic Alzheimer's disease (MCI or mild dementia due to Alzheimer's disease) with the presence of confirmed Alzheimer's disease neuropathology. The trial enrolled 1,736 participants, across 8 countries, selected based on cognitive assessments in conjunction with evidence of Alzheimer's disease pathology. The Phase 3 TRAILBLAZER-ALZ 2 study results were published in the *Journal of the American Medical Association* (JAMA).

Lilly continues to study donanemab in multiple clinical trials, including TRAILBLAZER-ALZ 3, evaluating the potential to reduce the risk of progression to symptomatic AD in participants with preclinical AD; and TRAILBLAZER-ALZ 5, a registration trial for early symptomatic AD currently enrolling in China, Korea, Taiwan, and other geographies.

INDICATION AND SAFETY SUMMARY WITH WARNINGS

Kisunla™ (kih-SUHN-lah)s used to treat adults with early symptomatic Alzheimer's disease (AD), which includes mild cognitive impairment (MCI) or mild dementia stage of disease.

Warnings - Kisunla can cause Amyloid-Related Imaging Abnormalities or "ARIA." This is a common side effect that does not usually cause any symptoms, but serious symptoms can occur. ARIA can be fatal. ARIA is most commonly seen as temporary swelling in an area or areas of the brain that usually goes away over time. Some people may also have spots of bleeding on the surface of or in the brain and infrequently, larger areas of bleeding in the brain can occur. Although most people do not have symptoms, some people have headaches, dizziness, nausea, difficulty walking, confusion, vision changes and seizures.

Some people have a genetic risk factor (homozygous apolipoprotein E ε4 gene carriers) that may cause an increased risk for ARIA. Talk to your healthcare provider about testing to see if you have this risk factor.

You may be at higher risk of developing bleeding in the brain if you take medicines to reduce blood clots from forming (antithrombotic medicines) while receiving Kisunla. **Talk to your healthcare provider to see if you are on any medicines that increase this risk.**

Your healthcare provider will do magnetic resonance imaging (MRI) brain scans before and during your treatment with Kisunla to check you for ARIA.

You should carry information that you are receiving Kisunla, which can cause ARIA, and that ARIA symptoms can look like stroke symptoms. **Call your healthcare provider or go to the nearest hospital emergency room right away if you have any of the symptoms listed above.**

There are registries that collect information on treatments for Alzheimer's disease. Your healthcare provider can help you become enrolled in these registries.

Warnings - Kisunla can cause serious allergic and infusion-related reactions. Do not receive Kisunla if you have serious allergic reactions to donanemab-azbt or any of the ingredients in Kisunla. Symptoms may include swelling of the face, lips, mouth, or eyelids, problems breathing, hives, chills, irritation of skin, nausea, vomiting, sweating, headache, or chest pain. You will be monitored for at least 30 minutes after you receive Kisunla for any reaction. **Tell your healthcare provider right away if you have these symptoms or any reaction during or after a Kisunla infusion.**

Other common side effects

- Headache

Tell your healthcare provider right away if you have any side effects. These are not all of the possible side effects of Kisunla. **You can report side effects at 1-800-FDA-1088 or www.fda.gov/medwatch**.

Before you receive Kisunla, tell your healthcare provider:

- About all medicines you take, including prescription and over-the-counter medicines, as well as vitamins and herbal supplements. Especially tell your healthcare provider if you have medicines to reduce blood clots from forming (antithrombotic medicines, including aspirin).
- About all of your medical conditions including if you are pregnant, breastfeeding, or plan to become pregnant or breastfeed. Kisunla has not been studied in people who were pregnant or breastfeeding. It is not known if Kisunla could harm your unborn or breastfeeding baby.

How to receive Kisunla
Kisunla is a prescription medicine given through an intravenous (IV) infusion using a needle inserted into a vein in your arm. Kisunla is given once every 4 weeks. Each infusion will last about 30 minutes.

Learn more
For more information about Kisunla, call 1-800-LillyRx (1-800-545-5979) or go to **kisunla.lilly.com**.

This summary provides basic information about Kisunla. It does not include all information known about this medicine. Read the information given to you about Kisunla. This information does not take the place of talking with your healthcare provider. Be sure to talk to your healthcare provider about Kisunla. Your healthcare provider is the best person to help you decide if Kisunla is right for you.

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Please see full Prescribing Information including boxed warning for ARIA and Medication Guide for Kisunla.

About Lilly
Lilly is a medicine company turning science into healing to make life better for people around the world. We've been pioneering life-changing discoveries for nearly 150 years, and today our medicines help tens of millions of people across the globe. Harnessing the power of biotechnology, chemistry and genetic medicine, our scientists are urgently advancing new discoveries to solve some of the world's most significant health challenges: redefining diabetes care; treating obesity and curtailing its most devastating long-term effects; advancing the fight against Alzheimer's disease; providing solutions to some of the most debilitating immune system disorders; and transforming the most difficult-to-treat cancers into manageable diseases. With each step toward a healthier world, we're motivated by one thing: making life better for millions more people. That includes delivering innovative clinical trials that reflect the diversity of our world and working to ensure our medicines are accessible and affordable. To learn more, visit Lilly.com and Lilly.com/news, or follow us on Facebook, Instagram and LinkedIn. P-LLY

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Cautionary Statement Regarding Forward-Looking Statements
This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about Kisunla (donanemab-azbt) as a treatment for people with early symptomatic Alzheimer's disease, Kisunla dosing regimens and the prevalence of ARIA-E, and future readouts, presentations, and other milestones relating to Kisunla and reflects Lilly's current beliefs and expectations. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of drug research, development, and commercialization. Among other things, there is no guarantee that planned or ongoing studies will be completed as planned, that future study results will be consistent with study findings to date, that Kisunla will receive additional regulatory approvals or that Kisunla will be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's Form 10-K and Form 10-Q filings with the United States Securities and Exchange Commission. Except as required by law, Lilly undertakes no duty to update forward-looking statements to reflect events after the date of this release.

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