Category

Best Pharmaceutical Product

General Information

Company Name *

Eli Lilly and Company

Product/Solution Name *

Kisunla™ (donanemab-azbt)

Compound/Tech Name*

Donanemab

Trade Name *

Kisunla™

Corporate Name *

Eli Lilly and Company

Date of Approval *

2024-07-02

Indications *

Kisunla is an FDA-approved treatment for adults with early symptomatic Alzheimer's disease (AD), which includes mild cognitive impairment (MCI) or mild dementia stage of disease.

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475

Therapeutic Areas *

Alzheimer's disease, Neuroscience

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497

*Kindly clearly label your files with company name and asset name.

Background information and need for drug / device
(please be as specific as possible in your description; limit 500 words)

Alzheimer's disease is a fatal neurodegenerative disease, which first erodes memory and thinking skills and then associated abilities to function in daily life. Eventually Alzheimer's disease kills, but not before it slowly steals a person's identity. Alzheimer's disease is the seventh leading cause of death in

the United States, and of the top 10 causes of death, it is the only disease with an increasing mortality rate, and the only one that cannot currently be prevented or cured.1

In 2024, an estimated 6.9 million Americans aged 65 and older are living with Alzheimer's dementia. By 2060, this number is projected to more than double to approximately 14 million.1

Lilly has played an integral role in the development of a new class of drugs, amyloid targeting therapies, which have opened the door for disease modifying therapy for this disease for the first time in history. From this starting point, even more effective therapies, combination therapies, and most importantly prevention therapies may now be enabled.

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History of the development of the solution/product *
(please be as specific as possible in your description; 500 words)

For more than 35 years, Lilly scientists have been researching treatments to fight Alzheimer's disease (AD). We have invested more than $8 billion in research and development of potential Alzheimer's medicines and have enrolled more than 10,000 people in clinical trials. We have pioneered study designs and diagnostics that moved AD from a disease diagnosed based on symptoms to one based on brain pathology. We have created novel instruments to measure Alzheimer's disease in its earliest symptomatic stages, where new treatments can help the most. Kisunla results from more than three decades of perseverance, iterative development, collaborative research, and transparency.

Kisunla was first approved by the U.S. Food and Drug Administration (FDA) in 2024 for adults with early symptomatic Alzheimer's disease (AD), which includes people with mild cognitive impairment (MCI) as well as people with the mild dementia stage of AD, with confirmed amyloid pathology. Kisunla has since been approved by regulatory authorities in 12 other countries.

Approvals have been based on data from the TRAILBLAZER Phase 3 clinical trials. It is the first medicine to replicate positive results across multiple clinical trials. Trial participants were analyzed over 18 months in two groupings: one group that was less advanced in their disease (those with low to medium levels of tau protein) and the overall population, including participants with high tau levels. Using tau imaging to pathologically stage the disease was a first in developing amyloid therapies. Treatment with Kisunla significantly slowed clinical decline in both groups. Those people treated with Kisunla who were less advanced in their disease showed a significant slowing of decline of 35% compared with placebo on the integrated Alzheimer's Disease Rating Scale (iADRS), which measures memory, thinking, and daily functioning. The overall population's response to treatment was also statistically significant at 22%. Among the two groups analyzed, participants treated with Kisunla had up to a 39% lower risk of progressing to the next clinical stage of disease than those taking placebo.

Among the overall population of participants, Kisunla reduced amyloid plaques on average by 61% at 6 months, 80% at 12 months, and 84% at 18 months compared to the start of the study. One of the treatment goals of the study, novel across the field, was to remove amyloid plaques to minimal levels consistent with a visually negative scan using amyloid positron emission tomography (PET). If participants were confirmed to have reached these levels, they could complete treatment with

Kisunla and switch to placebo for the remainder of the study. In the overall population of people receiving Kisunla, 17% completed treatment at 6 months, 47% at 12 months, and 69% at 18 months based on an assessment of amyloid levels via an amyloid PET scan.

Knowing that these medicines have the greatest potential benefit when people are treated earlier in their disease, Lilly is working hard in partnership with others to improve detection and diagnosis for people with Alzheimer's disease who urgently need effective treatment options.

Kisunla can cause amyloid-related imaging abnormalities (ARIA), which is a potential side effect with amyloid plaque-targeting therapies that does not usually cause symptoms. It can be detected via magnetic resonance imaging (MRI) scans and, when it does occur, may present as temporary swelling in an area or areas of the brain, which usually resolves over time, or as small spots of bleeding in or on the brain's surface. Infrequently, larger areas of bleeding in the brain can occur. ARIA can be serious, and life-threatening events can occur. Kisunla can also cause certain types of allergic reactions, some of which may be serious and life-threatening, that typically occur during infusion or within 30 minutes post-infusion.

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Why this drug or device is innovative, the broad implications for future research, and/or how it will improve the human condition *

Development of this drug involved a number of major innovations for Alzheimer's disease:

• First clinical trial to show a significant slowing of decline on pre-specified primary clinical endpoint.
• Approved by regulatory authorities in 13 different countries across the world.
• First therapy to replicate significant slowing of cognitive and functional decline on the prespecified primary endpoint in two clinical trials, with Phase 2 and Phase 3 primary outcome results nearly identical.
• Used amyloid imaging to identify patients to treat. This was enabled by Lilly introducing the first FDA-approved amyloid imaging agent in 20125 and being the first to enroll a clinical trial based predominantly on amyloid PET for inclusion, now standard across the field.
• Used amyloid imaging to stop treatment - this enabled approximately half of participants to finish dosing within 1 year, a new paradigm for treating Alzheimer's disease with limited-duration therapy, which can result in lower treatment costs and fewer infusions.
• Used tau imaging to stratify patients and predict response to therapy. Lilly was the first to enroll a clinical trial based on tau imaging, using the first FDA-approved tau imaging agent Lilly brought to market. Lilly discovered for the first time that patients at earliest stage of disease, based on both tau pathology and clinical symptoms, had even greater benefit, with 60% slowing of decline compared to placebo. This important observation gives confidence to prevention strategies in Alzheimer's disease
• Largest effect size in an Alzheimer's disease trial, correlated with most significant removal of amyloid plaques seen to date.
• Largest safety database for this new class of amyloid-plaque targeting therapies, allowing more detailed characterization of safety risks and mitigations

These results clearly demonstrate the urgent need to diagnose and treat Alzheimer's disease sooner than we do today, when treatments with the potential to delay disease progression can have the biggest potential impact. Earlier diagnosis and treatment of patients with early symptomatic Alzheimer's disease have the potential to meaningfully slow disease progression, giving patients invaluable time to maintain their independence for longer.

Lilly continues to study donanemab in multiple clinical trials, including TRAILBLAZER-ALZ 3, which is focused on preventing symptomatic Alzheimer's disease in participants with preclinical Alzheimer's disease and TRAILBLAZER-ALZ 6, which is focused on expanding our understanding of ARIA through novel MRI sequences, blood-based biomarkers, and different dosing regimens of donanemab.

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Please provide appropriate references (PubMed, Abstract, Website) *

1. Alzheimer's Association. 2024 Alzheimer's Disease Facts and Figures. Alzheimers Dement 2024;20(5):1-146.
2. Eli Lilly. Lilly's Kisunla™ (donanemab-azbt) Approved by the FDA for the Treatment of Early Symptomatic Alzheimer's Disease. July 2, 2024. https://investor.lilly.com/news-releases/news-release-details/lillys-kisunlatm-donanemab-azbt-approved-fda-treatment-early.
3. Mintun MA, Lo AC, Duggan Evans C, et al. Donanemab in Early Alzheimer's Disease. N Engl J Med. 2021;384(18):1691-1704. doi:10.1056/NEJMoa2100708.
4. 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. doi:10.1001/jama.2023.13239.
5. Amyvid (Florbetapir F 18 Injection). Prescribing Information. Lilly USA, LLC.

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