

FDA NEWS RELEASE

FDA Converts Novel Alzheimer's Disease Treatment to Traditional Approval

Action Follows Confirmatory Trial to Verify Clinical Benefit

For Immediate Release:

July 06, 2023

Today, the U.S. Food and Drug Administration converted Leqembi (<https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&AppNo=761269>) (lecanemab-irmb), indicated to treat adult patients with Alzheimer's Disease, to traditional approval following a determination that a confirmatory trial verified clinical benefit. Leqembi is the first amyloid beta-directed antibody to be converted from an accelerated approval to a traditional approval for the treatment of Alzheimer's disease. The drug works by reducing amyloid plaques that form in the brain, a defining pathophysiological feature of the disease.

Leqembi was approved in January under the Accelerated Approval pathway (<https://www.fda.gov/news-events/press-announcements/fda-grants-accelerated-approval-alzheimers-disease-treatment>). This pathway allows the FDA to approve drugs for serious conditions where there is an unmet medical need, based on clinical data demonstrating the drug's effect on a surrogate endpoint—in the case of Leqembi, reducing amyloid plaques in the brain—that is reasonably likely to predict a clinical benefit to patients. As a postmarketing requirement of the accelerated approval, the FDA required the applicant to conduct a clinical trial, often referred to as a confirmatory study, to verify the anticipated clinical benefit of Leqembi. Efficacy of Leqembi was evaluated using the results of Study 301 (CLARITY AD), a Phase 3 randomized, controlled clinical trial.

“Today's action is the first verification that a drug targeting the underlying disease process of Alzheimer's disease has shown clinical benefit in this devastating disease,” said Teresa Buracchio, acting director of the Office of Neuroscience in the FDA's Center for Drug Evaluation and Research. **“This confirmatory study verified that it is a safe and effective treatment for patients with Alzheimer's disease.”**

Alzheimer's disease (<https://www.fda.gov/consumers/minority-health-and-health-equity-resources/alzheimers-disease>) is an irreversible, progressive brain disorder affecting more than

6.5 million Americans. The disease slowly destroys memory and thinking skills and eventually, the ability to carry out simple tasks. While the specific causes of Alzheimer's are not fully known, it is characterized by changes in the brain—including the formation of amyloid beta plaques and neurofibrillary, or tau, tangles—that result in loss of neurons and their connections.

Study 301 was a multicenter, randomized, double-blind, placebo-controlled, parallel-group study that enrolled 1,795 patients with Alzheimer's disease. Treatment was initiated in patients with mild cognitive impairment or mild dementia stage of disease and confirmed presence of amyloid beta pathology. Patients were randomized in a 1:1 ratio to receive placebo or Leqembi at a dose of 10 milligrams (mg)/kilograms (kg), once every two weeks. Leqembi demonstrated a statistically significant and clinically meaningful reduction of decline from baseline to 18 months on the primary endpoint, the Clinical Dementia Rating Scale Sum of Boxes score, compared to placebo. Statistically significant differences between treatment groups were also demonstrated on all secondary endpoints, which included the Alzheimer's Disease Assessment Scale Cognitive Subscale 14, and the Alzheimer's Disease Cooperative Study-Activities of Daily Living Scale for Mild Cognitive Impairment.

On June 9 (<https://www.fda.gov/advisory-committees/advisory-committee-calendar/updated-information-june-9-2023-meeting-peripheral-and-central-nervous-system-drugs-advisory>), the FDA convened the Peripheral and Central Nervous System Drugs Advisory Committee to discuss whether Study 301 provided evidence of clinical benefit of Leqembi for the treatment of Alzheimer's disease. All committee members voted affirmatively that the results of the study verified the clinical benefit of Leqembi for the indicated use.

The most common side effects of Leqembi were headache, infusion-related reactions and amyloid-related imaging abnormalities (ARIA), a side effect known to occur with the class of antibodies targeting amyloid. ARIA most commonly presents as temporary swelling in areas of the brain seen on imaging studies that usually resolves over time and may be accompanied by small spots of bleeding in or on the surface of the brain. Although ARIA is often not associated with any symptoms, symptoms can occur and include headache, confusion, dizziness, vision changes and nausea. ARIA can also infrequently present with serious and life-threatening brain edema that can be associated with seizures and other severe neurological symptoms. Intracerebral hemorrhages can occur in patients treated with this class of medications and can be fatal. A boxed warning is included in the prescribing information to alert patients and caregivers to the potential risks associated with ARIA.

Patients treated with Leqembi who are homozygous for the ApoE ϵ 4 allele have a higher incidence of ARIA, including symptomatic, serious and severe ARIA, compared to heterozygotes and noncarriers. The prescribing information states that testing for ApoE ϵ 4 status should be performed before starting treatment with Leqembi to inform the risk of developing ARIA.

Use of anticoagulant medication was associated with an increased number of intracerebral hemorrhages in patients taking Leqembi compared to placebo. The prescribing information recommends caution when considering use of Leqembi in patients taking anticoagulants or with other risk factors for intracerebral hemorrhage.

Leqembi is contraindicated in patients with serious hypersensitivity to lecanemab-irmb or to any of its inactive ingredients. Adverse reactions may include angioedema (swelling) and anaphylaxis (allergic reaction).

Leqembi should be initiated in patients with mild cognitive impairment or mild dementia stage of Alzheimer's disease, the population in which treatment was studied in clinical trials. The labeling states that there are no safety or effectiveness data on initiating treatment at earlier or later stages of the disease than were studied.

The approval of Leqembi was granted to Eisai Inc.

Related Information

- [Alzheimer's Disease \(https://www.fda.gov/consumers/minority-health-and-health-equity-resources/alzheimers-disease\)](https://www.fda.gov/consumers/minority-health-and-health-equity-resources/alzheimers-disease)
- [Frequently Asked Questions about the FDA Drug Approval Process \(https://www.fda.gov/drugs/special-features/frequently-asked-questions-about-fda-drug-approval-process\)](https://www.fda.gov/drugs/special-features/frequently-asked-questions-about-fda-drug-approval-process)
- [June 9, 2023 Peripheral and Central Nervous System Drugs Advisory Committee Meeting \(https://www.fda.gov/advisory-committees/advisory-committee-calendar/updated-information-june-9-2023-meeting-peripheral-and-central-nervous-system-drugs-advisory\)](https://www.fda.gov/advisory-committees/advisory-committee-calendar/updated-information-june-9-2023-meeting-peripheral-and-central-nervous-system-drugs-advisory)

###

The FDA, an agency within the U.S. Department of Health and Human Services, protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products.

Inquiries

Media:

✉ [April Grant \(mailto:april.grant@fda.hhs.gov\)](mailto:april.grant@fda.hhs.gov)

☎ 202-657-8179

Consumer:

📞 888-INFO-FDA

🔗 [More Press Announcements \(/news-events/newsroom/press-announcements\)](/news-events/newsroom/press-announcements)