FDA Grants Accelerated Approval for Alzheimer's Disease Treatment

Today, the U.S. Food and Drug Administration approved Leqembi (lecanemab-irmb) via the Accelerated Approval pathway for the treatment of Alzheimer's disease. Leqembi is the second of a new category of medications approved for Alzheimer's disease that target the fundamental pathophysiology of the disease. These medications represent an important advancement in the ongoing fight to effectively treat Alzheimer's disease.

"Alzheimer's disease immeasurably incapacitates the lives of those who suffer from it and has devastating effects on their loved ones," said Billy Dunn, M.D., director of the Office of Neuroscience in the FDA's Center for Drug Evaluation and Research. "This treatment option is the latest therapy to target and affect the underlying disease process of Alzheimer's, instead of only treating the symptoms of the disease."

Alzheimer's disease is an irreversible, progressive brain disorder affecting more than 6.5 million Americans that 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 amyloid beta plaques and neurofibrillary, or tau, tangles—that result in loss of neurons and their connections. These changes affect a person's ability to remember and think.

Leqembi was approved using the Accelerated Approval pathway, under which the FDA may approve drugs for serious conditions where there is an unmet medical need and a drug is shown to have an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit to patients. The results of a Phase 3 randomized, controlled clinical trial to confirm the drug's clinical benefit have recently been reported and the agency anticipates receiving the data soon.

Researchers evaluated Leqembi's efficacy in a double-blind, placebo-controlled, parallel-group, dose-finding study of 856 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 receiving the treatment had significant dose- and time-dependent reduction of amyloid beta plaque, with patients receiving the approved dose of lecanemab, 10 milligram/kilogram every two weeks, having a statistically significant reduction in brain amyloid plaque from baseline to Week 79 compared to the placebo arm, which had no reduction of amyloid beta plaque.

These results support the accelerated approval of Leqembi, which is based on the observed reduction of amyloid beta plaque, a marker of Alzheimer's disease. Amyloid beta plaque was quantified using positron emission tomography (PET) imaging to estimate the brain levels of amyloid beta plaque in a composite of brain regions expected to be widely affected by Alzheimer's disease pathology compared to a brain region expected to be spared of such pathology.

The prescribing information for Leqembi includes a warning for amyloid-related imaging abnormalities (ARIA), which are known to occur with antibodies of this class. ARIA usually does not have symptoms, although serious and life-threatening events rarely may occur. ARIA most commonly presents as temporary swelling in areas of the brain that usually resolves over time and may be accompanied by small spots of bleeding in or on the surface of the brain, though some people may have symptoms such as headache, confusion, dizziness, vision changes, nausea and seizure. Another warning for Leqembi is for a risk of infusion-related reactions, with symptoms such as flu-like symptoms, nausea, vomiting and changes in blood pressure. The most common side effects of Leqembi were infusion-related reactions, headache and ARIA.

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

The FDA granted this application Fast Track, Priority Review and Breakthrough Therapy designations.

The approval of Leqembi was granted to Eisai R&D Management Co., Ltd.

FDA News released Jan 06, 2023. www.fda.gov.

FDA Approves First Oral Treatment for Anemia

Caused by Chronic Kidney Disease for Adults on Dialysis

Today, the U.S. Food and Drug Administration approved Jesduvroq tablets (daprodustat) as the first oral treatment for anemia (decreased number of red blood cells) caused by chronic kidney disease for adults who have been receiving dialysis for at least four months. Jesduvroq is not approved for patients who are not on dialysis. Other FDA-approved treatments for this condition are injected into the blood or under the skin.

"With an oral drug option in addition to the FDA-approved injection options, adults with chronic kidney disease on dialysis now have multiple ways to treat their anemia," said Ann Farrell, M.D., director of the Division of Non-Malignant Hematology in the FDA's Center for Drug Evaluation and Research. "This approval demonstrates the FDA's commitment to helping bring a range of therapeutic options to patients with chronic diseases. Patients can consult with their healthcare providers to select the option that is most appropriate."

More than a half million adults in the U.S. have chronic kidney disease requiring dialysis (a treatment that filters the blood and removes excess fluid from the blood). Kidneys produce a hormone called erythropoietin, which signals the body to make red blood cells. In a person with chronic kidney disease on dialysis, the kidneys cannot produce enough erythropoietin, leading to reduced numbers of red blood cells.

Jesduvroq increases erythropoietin levels. The effectiveness of Jesduvroq was established in a randomized study of 2,964 adults receiving dialysis. In this study, adults received either oral Jesduvroq or injected recombinant human erythropoietin (a standard of care treatment for patients with anemia due to chronic kidney disease). Jesduvroq raised and maintained the hemoglobin (the protein in red blood cells that carries oxygen and is a common measure of anemia) within the target range of 10-11 grams/deciliter, similar to that of the recombinant human erythropoietin.

Jesduvroq has a boxed warning for an increased risk of thrombotic vascular (blood clotting) events including death, heart attack, stroke, and blood clots in the lungs, legs, or dialysis access site. Jesduvroq's warnings and precautions include a risk of hospitalization for heart failure, worsening increase of blood pressure, and stomach erosions and gastrointestinal bleeding.

Jesduvroq is not approved for patients with anemia due to chronic kidney disease who are not on dialysis because its safety has not been established in that population.

The most common side effects of Jesduvroq include high blood pressure, thrombotic vascular events, abdominal pain, dizziness and allergic reactions.

Patients should not use Jesduvroq if they also take certain drugs that cause increased levels of Jesduvroq or if they have uncontrolled high blood pressure.

The FDA granted the approval to GlaxoSmithKline LLC.

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FDA Approves First Over-the-Counter Naloxone Nasal Spray

Agency Continues to Take Critical Steps to Reduce Drug Overdose Deaths Being Driven Primarily by Illicit Opioids

Today, the U.S. Food and Drug Administration approved Narcan, 4 milligram (mg) naloxone hydrochloride nasal spray for over-the-counter (OTC), nonprescription, use – the first naloxone product approved for use without a prescription. Naloxone is a medication that rapidly reverses the effects of opioid overdose and is the standard treatment for opioid overdose. Today's action paves the way for the life-saving medication to reverse an opioid overdose to be sold directly to consumers in places like drug stores, convenience stores, grocery stores and gas stations, as well as online.

The timeline for availability and price of this OTC product is determined by the manufacturer. The FDA will work with all stakeholders to help facilitate the continued availability of naloxone nasal spray products during the time needed to implement the Narcan switch from prescription to OTC status, which may take months. Other formulations and dosages of naloxone will remain available by prescription only.

Drug overdose persists as a major public health issue in the United States, with more than 101,750 reported fatal overdoses occurring in the 12-month

period ending in October 2022, primarily driven by synthetic opioids like illicit fentanyl.

"The FDA remains committed to addressing the evolving complexities of the overdose crisis. As part of this work, the agency has used its regulatory authority to facilitate greater access to naloxone by encouraging the development of and approving an over-the-counter naloxone product to address the dire public health need," said FDA Commissioner Robert M. Califf, M.D. "Today's approval of OTC naloxone nasal spray will help improve access to naloxone, increase the number of locations where it's available and help reduce opioid overdose deaths throughout the country. We encourage the manufacturer to make accessibility to the product a priority by making it available as soon as possible and at an affordable price."

Narcan nasal spray was first approved by the FDA in 2015 as a prescription drug. In accordance with a process to change the status of a drug from prescription to nonprescription, the manufacturer provided data demonstrating that the drug is safe and effective for use as directed in its proposed labeling. The manufacturer also showed that consumers can understand how to use the drug safely and effectively without the supervision of a healthcare professional. The application to approve Narcan nasal spray for OTC use was granted priority review status and was the subject of an advisory committee meeting in February 2023, where committee members voted unanimously to recommend it be approved for marketing without a prescription.

The approval of OTC Narcan nasal spray will require a change in the labeling for the currently approved 4 mg generic naloxone nasal spray products that rely on Narcan as their reference listed drug product. Manufacturers of these products will be required to submit a supplement to their applications to effectively switch their products to OTC status. The approval may also affect the status of other brand-name naloxone nasal spray products of 4 mg or less, but determinations will be made on a case-by-case basis and the FDA may contact other firms as needed.

The use of Narcan nasal spray in individuals who are opioid dependent may result in severe opioid withdrawal characterized by body aches, diarrhea, increased heart rate (tachycardia), fever, runny nose, sneezing, goose bumps, sweating, yawning, nausea or vomiting, nervousness, restlessness or irritability, shivering or trembling, abdominal cramps, weakness and increased blood pressure.

"Naloxone is a critical tool in addressing opioid overdoses and today's approval underscores the extensive efforts the agency has undertaken to combat the overdose crisis," said Patrizia Cavazzoni, M.D., director of the FDA's Center for Drug Evaluation and Research. "The FDA is working with our federal partners to help ensure continued access to all forms of naloxone during the transition of this product from prescription status to nonprescription/OTC status. Further, we will work with any sponsor seeking to market a nonprescription naloxone product, including through an Rx to OTC switch, and encourage manufacturers to contact the agency as early as possible to initiate discussions."

The FDA has taken a series of measures to help facilitate access to naloxone products. In November 2022, the agency announced its preliminary assessment that certain naloxone products, such as the one ultimately approved today, have the potential to be safe and effective for over-the-counter use and encouraged sponsors to submit applications for approval of OTC naloxone products. The agency previously announced in 2019 that it had designed, tested, and validated a model naloxone Drug Facts Label (DFL) with easy-to-understand pictograms on how to use the drug to encourage manufacturers to pursue approval of OTC naloxone products. The model DFL was used to support the approved application along with the results of a simulated use Human Factors validation study designed to assess whether all the components of the product with which a user would interact could be used safely and effectively as intended.

Through the FDA Overdose Prevention Framework, the agency remains focused on responding to all facets of substance use, misuse, substance use disorders, overdose and death in the U.S. The framework's priorities include: supporting primary prevention by eliminating unnecessary initial prescription drug exposure and inappropriate prolonged prescribing; encouraging harm reduction through innovation and education; advancing development of evidence-based treatments for substance use disorders; and protecting the public from unapproved, diverted or counterfeit drugs presenting overdose risks.

The FDA granted the OTC approval of Narcan to Emergent BioSolutions.

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Source: FDA