Category

Best Pharmaceutical Product

General Information

Company Name *

Eisai Inc. and Biogen Inc.

Product/Solution Name *

LEQEMBI®

Compound/Tech Name*

lecanemab-irmb

Trade Name *

LEQEMBI®

Corporate Name *

LEQEMBI®

Date of Approval *

2023-07-06

Indications *

LEQEMBI® is indicated for the treatment of Alzheimer's disease, specifically, for patients with mild cognitive impairment (MCI) or mild dementia stage of disease, the population in which treatment was initiated in clinical trials. Complete prescribing information linked here.

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462

Therapeutic Areas *

Alzheimer's disease (AD)

words remaining :

497

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

Attached Files:

- LEQEMBI Prescribing Information.pdf

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

LEQEMBI® (lecanemab-irmb) is the first traditionally approved treatment shown to reduce the rate of disease progression and to slow cognitive and functional decline in adults with mild cognitive impairment (MCI) or mild dementia state of Alzheimer's disease (AD). LEQEMBI targets and clears protofibrils, the most neurotoxic form of amyloid β (Aβ) that continuously accumulates, and removes the existing plaques to treat this progressive, chronic disease. The FDA approved LEQEMBI under the accelerated approval pathway on January 6, 2023, and received traditional approval on July 6, 2023.

Following inconclusive data from clinical studies of early agents targeting Aβ, researchers shifted efforts on antibodies targeting soluble, aggregated forms of the protein. This approach was based on the observation that the pathogenic Artic Alzheimer mutation causes high levels of protofibrils to form, and these protofibrils are believed to be present in all cases of AD. Clinical research was pursued to determine if reducing Aβ protofibrils could reduce neuronal toxicity and potentially improve other synaptic dysfunction, inflammatory changes, and neuronal loss. A Phase 1 study demonstrated lecanemab, a humanized immunoglobulin gamma 1 (IgG1) monoclonal antibody directed against aggregated soluble (protofibrils) and insoluble forms of Aβ was well-tolerated and informed the selection of dose and dose regimens in the subsequent Phase 2b study.

The 18-month Phase 2 proof-of-concept study employed an innovative Bayesian design for efficient subject allocation to the most effective dose(s) in the trial. In this study lecanemab did not meet the 12-month primary endpoint. However, prespecified 18-month analyses showed reduction in Aβ and a reduction of clinical decline across several clinical and biomarker endpoints- paving the way for the robust Phase 3 Clarity AD trial.

Eisai's global Clarity AD clinical trial was an 18-month, multicenter, double-blind, Phase 3 clinical trial in patients with mild cognitive impairment or mild dementia due to AD with confirmed presence of amyloid. In this global confirmatory study, lecanemab, reduced markers of amyloid in early AD and resulted in moderately less decline on measures of cognition and function than placebo at 18 months - demonstrating the ability to slow disease progression in early AD. Results were published in New England Journal of Medicine (in uploaded documents).

AD has become a critical issue for society and healthcare systems. It's a progressive, fatal disease that greatly impacts the people living with it, their loved ones and care partners, and society. LEQEMBI demonstrated clinically meaningful slowing of cognitive and functional decline, helping patients in a group generalizable to U.S. Medicare beneficiaries, including a mix of racial and ethnic groups, patients with common comorbid conditions and/or concomitant medications and patients with mild cognitive impairment due to AD or mild AD, remain in earlier stages of AD for a longer period.

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Attached Files:

- FDA Grants Accelerated Approval for Alzheimers Disease Treatment FDA.pdf
- Lecanemab in Early Alzheimers Disease New England Journal of Medicine.pdf
- LEQEMBI Prescribing Information .pdf

- A randomized doubleblind phase 2b proofofconcept clinical trial in early Alzheimers disease with lecanemab an antiA protofibril antibody Alzheimers Research Therapy Full Text.pdf

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

The accelerated approval of LEQEMBI (lecanemab-irmb) was based on Phase 2 data from a randomized, double-blind, standalone, proof-of-concept dose-ranging study in AD. This indication was approved under accelerated approval based on a reduction in Aβ plaques observed in patients treated with LEQEMBI. The accelerated approval pathway expedites development of drugs to address unmet medical needs based on a surrogate endpoint, thereby potentially allowing for earlier patient access to treatment.

The traditional approval of LEQEMBI was based on Phase 3 data from Eisai's global Clarity AD clinical trial, in which LEQEMBI met its primary endpoint and all key secondary endpoints with statistically significant results and confirmed the clinical benefit of LEQEMBI. Clarity AD was the first completed Phase 3 trial to demonstrate the ability of a treatment to reduce the rate of disease progression and to slow cognitive and functional decline in adults with AD.

The primary endpoint of the Clarity AD trial was the global cognitive and functional scale, Clinical Dementia Rating Sum of Boxes (CDR-SB). LEQEMBI treatment reduced clinical decline on CDR-SB by 27% at 18 months compared to placebo. CDR-SB is accepted by the FDA as a primary outcome assessment for studies in AD intended to demonstrate substantial evidence of effectiveness. Additionally, the secondary endpoint of AD Cooperative Study-Activities of Daily Living Scale for Mild Cognitive Impairment (ADCS MCI-ADL), as measured by people caring for patients with AD, noted a statistically significant benefit of 37% compared to placebo at 18 months. This scale measures the ability of patients to function independently, including being able to dress, feed themselves and participate in community activities.

Eligibility criteria for Clarity AD allowed patients with a broad range of comorbidities/comedications, thus demonstrating LEQEMBI'S clinically meaningful slowing of cognitive and functional decline, helping patients in a group generalizable to U.S. Medicare beneficiaries, including a mix of racial and ethnic groups, patients with common comorbid conditions and/or concomitant medications and patients with mild cognitive impairment (MCI) due to AD or mild AD, remain in earlier stages of AD for a longer period of time.

In the large, global Clarity AD clinical trial, LEQEMBI met its primary endpoint and all key secondary endpoints with statistically significant results, confirming the clinical benefit of LEQEMBI.

For background, Eisai and Biogen have been collaborating on the joint development and commercialization of AD treatments since 2014. Eisai serves as the lead of lecanemab development and regulatory submissions globally with both companies co-commercializing and co-promoting the product and Eisai having final decision-making authority.

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Attached Files:

- EISAI PRESENTS FULL RESULTS OF LECANEMAB PHASE 3 CONFIRMATORY CLARITY AD STUDY FOR EARLY ALZHEIMERS DISEASE AT CLINICAL TRIALS ON ALZHEIMERS DISEASE CTAD CONFERENCE.pdf
- clarityctadpresentation.pdf

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

As the first anti-amyloid treatment for Alzheimer's disease with traditional approval, LEQEMBI opened a new era in the treatment of AD spurring renewed interest and enthusiasm in research of this devastating disease.

Eisai's global Clarity AD clinical trial was the first completed, confirmatory Phase 3 study to demonstrate an association between amyloid clearance and a reduction in cognitive and functional decline. LEQEMBI treatment reduced clinical decline on CDR-SB by 27% at 18 months compared to placebo. Additionally, the secondary endpoint of AD Cooperative Study-Activities of Daily Living Scale for Mild Cognitive Impairment (ADCS MCI-ADL), as measured by people caring for patients with AD, noted a statistically significant benefit of 37%. This measures patients' ability to function independently, including being able to dress, feed themselves and participate in community activities.

Eligibility criteria for Clarity AD positioned the study to demonstrate LEQEMBI'S clinically meaningful slowing of cognitive and functional decline in a patient group generalizable to U.S. Medicare beneficiaries, including a mix of racial and ethnic groups, patients with common comorbid conditions and/or concomitant medications and patients with mild cognitive impairment (MCI) due to AD or mild AD.

This clinical advance was a significant step forward in the treatment of AD as it's the first completed Phase 3 trial to demonstrate the ability of an investigational (at the time) treatment to reduce the rate of disease progression and to slow cognitive and functional decline in adults with AD, providing more time for patients in earlier stages of disease, when they are most functional.

New therapeutic agents that act on the AD disease pathology are needed as there have been minimal clinical advancements in the last 25 years. The treatment goals for patients with early AD are to have sustained effects on cognitive function, activities of daily living and psychiatric symptoms, to maintain independence longer by slowing progression of the disease and to improve or maintain quality of life.

Clarity AD was the first completed Phase 3 study to demonstrate an association between amyloid clearance and a reduction cognitive and functional decline. In Clarity AD, LEQEMBI demonstrated consistent results across scales of cognition and function and subgroups (race, ethnicity, comorbidities). The convergence of evidence across cognition and function, disease progression, health related quality of life, and caregiver burden demonstrate that LEQEMBI treatment may provide meaningful benefits to patients, their care partners, physicians and society.

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Attached Files:

- LEQEUS2375 LEQEMBI ClarityAD Fact Sheet July 2023 Update.pdf

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

1.) https://pubmed.ncbi.nlm.nih.gov/37874099/
2.) https://pubmed.ncbi.nlm.nih.gov/37357276/\
3.) https://www.nejm.org/doi/full/10.1056/NEJMoa2212948

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