Leqembi® (lecanemab) Authorized for Early Alzheimer's Disease in Great Britain

August 22, 2024

In Great Britain, lecanemab is indicated for the treatment of mild cognitive impairment and mild dementia due to Alzheimer's disease (AD) in adult patients that are apolipoprotein E ε4 (ApoE ε4) heterozygotes or non-carriers*[1]

Great Britain becomes the first country in Europe to authorize the medicine, which targets an underlying cause of AD[1]

TOKYO and CAMBRIDGE, Mass., August 22, 2024 – Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") and Biogen Inc. (Nasdaq: BIIB, Corporate headquarters: Cambridge, Massachusetts, CEO: Christopher A. Viehbacher, "Biogen") announced today that the humanized amyloid-beta (Aβ) monoclonal antibody "Leqembi®" (brand name, generic name: lecanemab) has been granted a Marketing Authorization by the Medicines and Healthcare products Regulatory Agency (MHRA) in Great Britain.[1] Lecanemab is indicated for the treatment of mild cognitive impairment (MCI) and mild dementia due to Alzheimer's disease (AD) in adult patients that are apolipoprotein E ε4 (ApoE ε4)* heterozygotes or non-carriers.[1] Lecanemab becomes the first treatment for early AD (MCI and mild dementia due to AD)[2] that targets an underlying cause of the disease, to be authorized in a country in Europe.[1]

Lecanemab selectively binds to Aβ aggregate species, with preferential activity for toxic Aβ protofibrils** (as well as fibrils, which are a major component of Aβ plaques).[2,3,4] It binds to these aggregate Aβ species to neutralize and clear them from the brain.[2,3,4]

The approval was primarily based on Phase 3 data from Eisai's global, placebo-controlled, double-blind, parallel-group, randomized Clarity AD clinical trial, in which the medicine met its primary endpoint (change from baseline in the Clinical Dementia Rating Sum of Boxes [CDR-SB]† at 18 months) and all key secondary endpoints with statistically significant results.[2] In the indicated population in Great Britain, the most common adverse reactions were infusion-related reaction, amyloid-related imaging abnormalities with hemorrhage (small spots of bleeding) (ARIA-H)‡, fall, headache and amyloid-related imaging abnormalities with cerebral edema (build-up of fluid) (ARIA-E)‡‡.[1]

In the United Kingdom, it is estimated that 982,000 people are living with dementia,[5] and AD is the cause in 60-70% of people with dementia.[6] These numbers are expected to rise, as the population ages.[5,6]

Eisai is working collaboratively with the National Institute for Health and Care Excellence (NICE), the Scottish Medicines Consortium (SMC) and the National Health Service (NHS) to make this medicine available to eligible people living with early AD as soon as possible.

Eisai serves as the lead for lecanemab's development and regulatory submissions globally with Eisai and Biogen co-commercializing and co-promoting the product and Eisai having final decision-making authority. In Great Britain, Eisai and Biogen will co-promote the medicine, with Eisai distributing the product as the Marketing Authorization holder.

*Apolipoprotein E is a protein involved in the metabolism of fats in humans. It is implicated in AD.

**Protofibrils are thought to be the most toxic Aβ species that contribute to brain damage in AD and play a major role in the cognitive decline of this progressive and devastating disease. Protofibrils can cause neuronal damage in the brain, which can subsequently adversely affect cognitive function through multiple mechanisms.[7] The mechanism by which this occurs has been reported not only by increasing the formation of insoluble Aβ plaques, but also by directly damaging signaling between neurons and other cells. It is believed that reducing protofibrils may reduce neuronal damage and cognitive impairment, potentially preventing the progression of AD.[8]

†CDR-SB is a commonly used diagnostic tool, which can help to stage dementia due to AD.[9] It is a global cognitive and functional scale that measures six domains of functioning, including memory, orientation, judgement and problem solving, community affairs, home and hobbies, and personal care.[9]

‡ARIA-H: amyloid-related imaging abnormalities with hemorrhage (microhemorrhages, and superficial siderosis).

‡‡ARIA-E: amyloid-related imaging abnormalities with oedema (edema/effusion).

More information can be found in the Summary of Product Characteristics and Patient Information leaflets which will be published on the MHRA Products website within 7 days of approval.

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Notes to Editors:

1. About lecanemab (Leqembi®)

Lecanemab is the result of a strategic research alliance between Eisai and BioArctic. It is a humanized immunoglobulin gamma 1 (IgG1) monoclonal antibody directed against aggregated soluble (protofibril) and insoluble forms of amyloid-beta (Aβ).[2,3]

Lecanemab's approval in Great Britain was primarily based on Phase 3 data from Eisai's global Clarity AD clinical trial, in which it met its primary endpoint and all key secondary endpoints with statistically significant results.[1,2] Clarity AD was a Phase 3 global, placebo-controlled, double-blind, parallel-group, randomized study in 1,795 patients with early AD (MCI or mild dementia due to AD, with confirmed presence of amyloid pathology), of which 1,521 were in the indicated population in the label in Great Britain (ApoE ε4 heterozygotes or non-carriers).[1] Of the total number of patients randomized 31% were non-carriers, 53% were heterozygotes and 16% were homozygotes.[1] The treatment group was administered lecanemab 10 mg/kg bi-weekly, with participants allocated in a 1:1 ratio to receive either placebo or lecanemab for 18 months.[1]

The primary endpoint was the global cognitive and functional scale, CDR-SB.[1] In the Clarity AD clinical trial, treatment with lecanemab, in the indicated population in Great Britain (ApoE ε4 heterozygotes or non-carriers), reduced clinical decline on CDR-SB by 33% at 18 months compared to placebo.[1] The mean CDR-SB score at baseline was approximately 3.2 in both groups.[1] The adjusted least-squares mean change from baseline at 18 months was 1.15 with lecanemab and 1.73 with placebo (difference, −0.58; 95% confidence interval [CI], −0.81 to −0.34; P<0.00001).[1] CDR-SB is a global cognitive and functional scale that measures six domains of functioning, including memory, orientation, judgement and problem solving, community affairs, home and hobbies, and personal care.[9]

In addition, the secondary endpoint from the AD Cooperative Study-Activities of Daily Living Scale for Mild Cognitive Impairment (ADCS-MCI-ADL), which measures information provided by people caring for patients with AD, noted 39% less decline compared to placebo at 18 months.[1] The adjusted mean change from baseline at 18 months in the ADCS-MCI-ADL score was −3.5 in the lecanemab group and −5.7 in the placebo group (difference, 2.2; 95% CI, 1.3 to 3.1; P<0.00001).[1] The ADCS-MCI-ADL assesses the ability of patients to function independently, including being able to dress, feed themselves and participate in community activities.

In the indicated population (ApoE ε4 heterozygotes or non-carriers), the most common adverse reactions were infusion-related reaction (26%), ARIA-H (13%), fall (11%), headache (11%) and ARIA-E (9%).[1]

Lecanemab is licensed in the U.S.,[x] Japan,[xi] China,[xii] South Korea,[xiii] Hong Kong,[xiv] Israel,[xv] the United Arab Emirates[xvi] and Great Britain[1] and marketed in the U.S., Japan and China. Eisai has also submitted applications for approval of lecanemab in 10 countries and regions, including the European Union.

2. About NHS, NICE and SMC

The NHS is a public healthcare system with the principle of providing free medical services to citizens. The NICE and the SMC are independent bodies that carry out assessments on the status of all newly licensed medicines, all new formulations of existing medicines and new indications for established products regarding their health benefits and price justification as advisory boards to the NHS about whether or not a newly licensed drug should be accepted for use under national health insurance.

3. About the Collaboration between Eisai and Biogen for AD

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.

4. About the Collaboration between Eisai and BioArctic for AD

Since 2005, Eisai and BioArctic have had a long-term collaboration regarding the development and commercialization of AD treatments. Eisai obtained the global rights to study, develop, manufacture and market lecanemab for the treatment of AD pursuant to an agreement with BioArctic in December 2007. The development and commercialization agreement on the antibody back-up was signed in May 2015.

5. About Eisai Co., Ltd.

Eisai's Corporate Concept is "to give first thought to patients and people in the daily living domain, and to increase the benefits that health care provides." Under this Concept (also known as *human health care* (*hhc*) Concept), we aim to effectively achieve social good in the form of relieving anxiety over health and reducing health disparities. With a global network of R&D facilities, manufacturing sites and marketing subsidiaries, we strive to create and deliver innovative products to target diseases with high unmet medical needs, with a particular focus in our strategic areas of Neurology and Oncology.

In addition, we demonstrate our commitment to the elimination of neglected tropical diseases (NTDs), which is a target (3.3) of the United Nations Sustainable Development Goals (SDGs), by working on various activities together with global partners.

For more information about Eisai, please visit www.eisai.com (for global headquarters: Eisai Co., Ltd.), and connect with us on X, LinkedIn and Facebook. The website and social media channels are intended for audiences outside of the UK and Europe. For audiences based in the UK and Europe, please visit www.eisai.eu and Eisai EMEA LinkedIn.

6. About Biogen

Founded in 1978, Biogen is a leading biotechnology company that pioneers innovative science to deliver new medicines to transform patient's lives

and to create value for shareholders and our communities. We apply deep understanding of human biology and leverage different modalities to advance first-in-class treatments or therapies that deliver superior outcomes. Our approach is to take bold risks, balanced with return on investment to deliver long-term growth.

The company routinely posts information that may be important to investors on its website at www.biogen.com. Follow Biogen on social media – Facebook, LinkedIn, X, YouTube.

Biogen Safe Harbor

This news release contains forward-looking statements, about the potential clinical effects of lecanemab; the potential benefits, safety and efficacy of lecanemab; potential regulatory discussions, submissions and approvals and the timing thereof; the treatment of Alzheimer's disease; the anticipated benefits and potential of Biogen's collaboration arrangements with Eisai; the potential of Biogen's commercial business and pipeline programs; including lecanemab; and risks and uncertainties associated with drug development and commercialization. These statements may be identified by words such as "aim," "anticipate," "believe," "could," "estimate," "expect," "forecast," "intend," "may," "plan," "possible," "potential," "will," "would" and other words and terms of similar meaning. Drug development and commercialization involve a high degree of risk, and only a small number of research and development programs result in commercialization of a product. Results in early-stage clinical studies may not be indicative of full results or results from later stage or larger scale clinical studies and do not ensure regulatory approval. You should not place undue reliance on these statements.

These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements, including without limitation unexpected concerns that may arise from additional data, analysis or results obtained during clinical studies; the occurrence of adverse safety events; risks of unexpected costs or delays; the risk of other unexpected hurdles; regulatory submissions may take longer or be more difficult to complete than expected; regulatory authorities may require additional information or further studies, or may fail or refuse to approve or may delay approval of Biogen's drug candidates; including lecanemab; actual timing and content of submissions to and decisions made by the regulatory authorities regarding lecanemab; uncertainty of success in the development and potential commercialization of the medicine; failure to protect and enforce Biogen's data, intellectual property and other proprietary rights and uncertainties relating to intellectual property claims and challenges; product liability claims; and third party collaboration risks, results of operations and financial condition. The foregoing sets forth many, but not all, of the factors that could cause actual results to differ from Biogen's expectations in any forward-looking statement. Investors should consider this cautionary statement as well as the risk factors identified in Biogen's most recent annual or quarterly report and in other reports Biogen has filed with the U.S. Securities and Exchange Commission. These statements speak only as of the date of this news release. Biogen does not undertake any obligation to publicly update any forward-looking statements.

References

[1] Lecanemab Great Britain Summary of Product Characteristics

[2] van Dyck, H., *et al*. Lecanemab in Early Alzheimer's Disease. *New England Journal of Medicine*. 2023;388:9-21. https://www.nejm.org/doi/full/10.1056/NEJMoa2212948.

[3] Johannesson, M., *et al.* Lecanemab demonstrates highly selective binding to Aβ protofibrils isolated from Alzheimer's disease brains. *Molecular and Cellular Neuroscience*. 2024;130:103949. https://doi.org/10.1016/j.mcn.2024.103949.

[4] Sehlin, D., *et al*. Large aggregates are the major soluble Aβ species in AD brain fractionated with density gradient ultracentrifugation. *PLoS One*. 2012;7(2):e32014. https://doi.org/10.1371/journal.pone.0032014.

[5] Alzheimer's Society. 2024. The economic impact of dementia. Available at: https://www.alzheimers.org.uk/about-us/policy-and-influencing/dementia-scale-impact-numbers. Last accessed: August 2024.

[6] World Health Organization. 2023. Dementia. Available at: https://www.who.int/news-room/fact-sheets/detail/dementia. Last accessed: August 2024

[7] Amin, L., Harris, D.A. Aβ receptors specifically recognize molecular features displayed by fibril ends and neurotoxic oligomers. *Nature Communications*. 2021;12:3451. doi:10.1038/s41467-021-23507-z.

[8] Ono, K., Tsuji, M. Protofibrils of Amyloid-β are Important Targets of a Disease-Modifying Approach for Alzheimer's Disease. *International Journal of Molecular Sciences*. 2020;21(3):952. doi: 10.3390/ijms21030952. PMID: 32023927; PMCID: PMC7037706.

[9] Morris, J.C. The Clinical Dementia Rating (CDR): current version and scoring rules. *Neurology*. 1993;43:2412-2414.

[10] U.S. Food and Drug Administration. 2023. FDA Converts Novel Alzheimer's Disease Treatment to Traditional Approval. Last accessed: August 2024.

[11] Reuters. 2023. Japan approves Alzheimer's treatment Leqembi by Eisai and Biogen. Last accessed: August 2024.

[12] The Pharma Letter. 2024. Brief - Alzheimer drug Leqembi now approved in China. Last accessed: August 2024.

[13] Pharmaceutical Technology. 2024. South Korea's MFDS approves Eisai-Biogen's LEQEMBI for Alzheimer's. Last accessed: August 2024.

[14] Pharmaceutical Technology. 2024. Hong Kong approves Leqembi for Alzheimer's treatment. Last accessed: August 2024.

[15] BioSpace. 2024. Leqembi approved for the treatment of Alzheimer's disease in Israel. Last accessed: August 2024.

[16] United Arab Emirates Ministry of Health & Prevention. 2024. Registered Medical Product Directory. Leqembi. Last accessed: August 2024.