FOR UNITED KINGDOM CONSUMER AND EUROPEAN AND UNITED KINGDOM TRADE AND MEDICAL MEDIA

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

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 authorise the medicine, which targets an underlying cause of AD[1]

Authorisation based on data from the global Phase 3 trial, Clarity AD, which demonstrated that lecanemab slowed disease progression vs placebo at 18 months[1,2]

Eisai is working collaboratively with health technology assessment bodies and the National Health Service to support access for eligible patients

HATFIELD, HERTFORDSHIRE, UNITED KINGDOM (UK), and MAIDENHEAD, UK, 22 August, 2024 – Eisai Europe Ltd. and Biogen International GmbH have announced today that Leqembi® (lecanemab) has been granted a Marketing Authorisation (MA) by the Medicines and Healthcare products Regulatory Agency (MHRA) in Great Britain. 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] Great Britain is the eighth country in the world to grant MA, making lecanemab the first monoclonal antibody therapy for early AD (MCI and mild dementia due to AD)[2] that targets amyloid-beta (Aβ) to be authorised in a country in Europe.[1]

The medicine was awarded an Innovative Licensing and Access Pathway (ILAP) passport by the MHRA in February 2023,[3] as there is a significant unmet patient need for treatments that alter an underlying cause of the disease for people living with early AD.[4] Lecanemab is a humanised Aβ monoclonal antibody that 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).[1,2,5,6] It binds to these aggregate Aβ species to neutralise and clear them from the brain.[1,2,5,6]

The approval was primarily based on Phase 3 data from Eisai's global, placebo-controlled, double-blind, parallel-group, randomised 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 haemorrhage (small spots of bleeding) (ARIA-H)‡, fall, headache and amyloid-related imaging abnormalities with cerebral oedema (build-up of fluid) (ARIA-E)‡‡.[1,2]

"Today signals a significant moment for the AD community. We are now one step closer to eligible people in Great Britain receiving a much-needed new treatment option that can slow disease progression, as demonstrated through clinical trials, by targeting an underlying cause of Alzheimer's disease for the first time," said Gary Hendler, Regional Chairman and CEO, Eisai EMEA, Senior Vice President & Global Corporate Officer, Eisai Co. Ltd, Tokyo. "This could mean maintaining independence and the ability to continue daily activities and hobbies for as long as possible. We are proud that 40 years of AD research has led to this important milestone."

"The authorisation of lecanemab in Great Britain marks a significant step forward in the pursuit of innovation for AD," said Wolfram Schmidt, President, Head of Europe, Biogen. "We remain steadfast in our mission to further AD research and bring treatment options to patients."

In the UK, it is estimated that 982,000 people are living with dementia,[7] and AD is the cause in 60-70% of people with dementia.[8] These numbers are expected to rise, as the population ages.[7,8] People living with AD can experience loss of cognition, memory and independence, as well as psychological symptoms such as depression and anxiety.[9] For care partners, witnessing the changes in their loved ones can be difficult and providing round-the-clock care can impact their own emotional well-being, employment and finances. [7,9]

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

Eisai serves as the lead of lecanemab development and regulatory submissions globally with both Eisai and Biogen co-commercialising 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 MA 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.[10] The mechanism by which this occurs has been reported not only by increasing the formation of insoluble Aβ plaques, but also by directly damaging signalling between neurons and other cells. It is believed that reducing protofibrils may reduce neuronal damage and cognitive impairment, potentially preventing the progression of AD.[11]

†CDR-SB is a commonly used diagnostic tool, which can help to stage dementia due to AD.[12] 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.[12]

‡ARIA-H: amyloid-related imaging abnormalities with haemorrhage (cerebral microhaemorrhages and superficial siderosis).

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

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Notes to editors:

1. About lecanemab

Lecanemab is the result of a strategic research alliance between Eisai and BioArctic. It is a humanised immunoglobulin gamma 1 (IgG1) monoclonal antibody directed against aggregated soluble (protofibril) and insoluble forms of amyloid-beta (Aβ).[2,5] The medicine is authorised in the U.S.,[13] Japan,[14] China,[15] South Korea,[16] Hong Kong,[17] Israel,[18] the United Arab Emirates[19] 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.

Lecanemab's approval was primarily based on Phase 3 data from Eisai's global Clarity AD clinical trial, in which the medicine 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, randomised 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 for Great Britain (ApoE ε4 heterozygotes or non-carriers).[1] Of the total number of patients randomised 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 −0.35; P<0.00001) in the indicated population.[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.[12]

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]

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.

▼: This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See https://yellowcard.mhra.gov.uk/ for how to report side effects.

2. About the Collaboration between Eisai and Biogen for AD

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

3. About the Collaboration between Eisai and BioArctic for AD

Since 2005, Eisai and BioArctic have had a long-term collaboration regarding the development and commercialisation 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 commercialisation agreement on the antibody back-up was signed in May 2015.

4. About Eisai EMEA Neurology

At Eisai, we give our first thought to patients, their care partners and to society, and to increase the benefits health care provides them – we call this *human health care* (*hhc*). We focus beyond the realm of health to the value we bring to society. Through the power of collaboration and by using insights to guide our work, we can make a meaningful contribution to people and society, and to improve outcomes and services for all.

In EMEA, we are the European hub of Tokyo-based Eisai Co. Ltd., forming part of a multinational team working across a global network of R&D facilities, manufacturing sites and marketing subsidiaries.

Our collective passion and dedication to patient care is the driving force behind our efforts to discover and develop innovative medicines in a variety of therapeutic areas where a high unmet medical need remains, including oncology and neurology.

Our mission is clear; we strive to make a significant long-lasting contribution to society in an ethical, compliant, and sustainable way by embodying *human health care* in everything we do.

For more information about Eisai in the EMEA region please visit www.eisai.eu.

5. 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 with aspirations 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.

Biogen routinely post information that may be important to investors on its website.

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 AD; the anticipated benefits and potential of Biogen's collaboration arrangements with Eisai; the potential of Biogen's commercial business and pipeline programmes; including lecanemab; and risks and uncertainties associated with drug development and commercialisation. 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 commercialisation involve a high degree of risk, and only a small number of research and development programmes result in commercialisation 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 commercialisation 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] Eisai. Internal correspondence with MHRA. 17 February 2023.
[4] Gov.UK. 2023. Guidance: Innovative Licensing and Access Pathway. Available at: https://www.gov.uk/guidance/innovative-licensing-and-access-pathway. Last accessed: August 2024.
[5] 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.
[6] 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.
[7] 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.
[8] World Health Organization. 2023. Dementia. Available at: https://www.who.int/news-room/fact-sheets/detail/dementia. Last accessed: August 2024.
[9] Koca, E., Taşkapilioğlu, Ö., Bakar, M. Caregiver Burden in Different Stages of Alzheimer's Disease. *Archives of Neuropsychiatry.* 2017;54(1):82-86.
[10] 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.
[11] 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.
[12] Morris, J.C. The Clinical Dementia Rating (CDR): current version and scoring rules. *Neurology*. 1993;43:2412-2414.
[13] U.S. Food and Drug Administration. 2023. FDA Converts Novel Alzheimer's Disease Treatment to Traditional Approval. Last accessed: August 2024.
[14] Reuters. 2023. Japan approves Alzheimer's treatment Leqembi by Eisai and Biogen. Last accessed: August 2024.
[15] The Pharma Letter. 2024. Brief - Alzheimer drug Leqembi now approved in China. Last accessed: August 2024.
[16] Pharmaceutical Technology. 2024. South Korea's MFDS approves Eisai-Biogen's LEQEMBI for Alzheimer's. Last accessed: August 2024.
[17] Pharmaceutical Technology. 2024. Hong Kong approves Leqembi for Alzheimer's treatment. Last accessed: August 2024.
[18] BioSpace. 2024. Leqembi approved for the treatment of Alzheimer's disease in Israel. Last accessed: August 2024.
[19] United Arab Emirates Ministry of Health & Prevention. 2024. Registered Medical Product Directory. Leqembi. Last accessed: August 2024.