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Approval of the marketing authorisation for Kisunla (donanemab)

Re-examination leads to recommendation to approve

After re-examining its initial opinion, the European Medicines Agency has recommended approving the marketing authorisation for Kisunla for treating early Alzheimer's disease.

The Agency had initially refused the application for Kisunla on 27 March 2025. After a re-examination, on 24 July 2025 the Agency recommended granting a marketing authorisation for Kisunla in people who do not have a copy of the *ApoE4* gene (noncarriers) or people who have only one copy of the gene (heterozygotes).

The company that applied for authorisation is Eli Lilly Nederland B.V.

What is Kisunla and what is it to be used for?

Kisunla is a medicine for treating adults with mild cognitive impairment (memory and thinking problems) and mild dementia due to Alzheimer's disease (early Alzheimer's disease). It is for people who have only one or no copy of the *ApoE4* gene and who have amyloid beta plaques in the brain.

Kisunla contains the active substance donanemab and will be available as a solution for infusion (drip) into a vein.

How does Kisunla work?

The active substance in Kisunla, donanemab, is a monoclonal antibody (a type of protein) that attaches to a substance in the brain called amyloid beta. In people with Alzheimer's disease, the amyloid beta forms plaques, which can lead to problems with brain function. By attaching to amyloid beta, the medicine reduces the plaques in the brain and slows down the worsening of the disease.

What did the company present to support its application?

The company provided data from a study involving 1,736 patients with early Alzheimer's disease who had amyloid beta plaques in their brain and who received either Kisunla or placebo (a dummy treatment). The study included patients who had one or two copies of the *ApoE4* gene and those who were noncarriers. The main measure of effectiveness was a change in symptoms after 76 weeks, measured using the integrated Alzheimer's disease rating scale (iADRs). The iADRs measures how

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much the disease affects a patient's cognitive ability and functional ability (their ability to carry out daily tasks). Scores on the iADRs range from 0 to 144, with lower scores indicating worse cognitive and functional ability.

What were the main reasons for initially refusing the marketing authorisation?

During the initial evaluation, the Agency was concerned about amyloid related imaging abnormalities (ARIA), a side effect that occurs with monoclonal antibodies that target amyloid beta. ARIA is seen with brain imaging and involves swelling and potential bleeding in the brain. ARIA occurred in 36.8% of people who received Kisunla compared with 14.9% of people who received placebo. Although most cases did not involve symptoms, 1.6% of people treated with Kisunla experienced serious ARIA events, including some deaths.

In terms of effectiveness, the study showed that, overall, the iADRs score worsened by 11 points in patients who received Kisunla and 13 points in those given placebo. The results were similar in the noncarriers and people with only one copy of *ApoE4*.

The Agency noted at the time that the benefits of Kisunla were not large enough to outweigh the risks to patients due to ARIA. Therefore, the Agency's opinion was that the benefits of Kisunla did not outweigh its risks and recommended refusal of the marketing authorisation.

What happened during the re-examination?

During the re-examination, the Agency considered all the relevant data and new analyses presented by the company.

As was the case during the initial evaluation, the Agency also received feedback from patients and healthcare professionals who shared their experiences living with or treating the condition.

What were the conclusions of the re-examination?

The Agency considered safety data showing that 33.0% of those in the group of *ApoE4* noncarriers and people with just one copy of *ApoE4* had an ARIA while the rate in those with two copies of the gene was 55.9%. Furthermore, serious cases of ARIA occurred in 1.4% of noncarriers and people with just one copy of ApoE4 and 2.8% of those with two copies of the gene.

The Agency also considered the company's proposal for a different dosing regimen to reduce the risk of ARIA. This involved changing the way the initial doses are given by starting with a lower dose. The Agency also mandated additional measures to manage the risk, including more stringent rules for stopping treatment and excluding patients at risk.

Taking account of the new dosing regimen and the additional measures to reduce the risk of ARIA, the Agency's human medicines committee (CHMP) concluded that Kisunla's benefits outweigh its risks in noncarriers and people with just one copy of *ApoE4*.

Throughout the evaluation of Kisunla, the Agency considered the urgent needs of patients with Alzheimer's disease, including the need to slow down the disease in the early stages. The Agency also carefully considered views of patients, carers and healthcare professionals with direct experience with the disease as well as those of a scientific advisory group, which included experts in the field of neurology.