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29 Aug 2025

Dear Healthcare Professionals,

FDA to recommend additional, earlier MRI monitoring for patients with Alzheimer's disease taking Leqembi (lecanemab)

Your attention is drawn to the following United States Food and Drug Administration's (FDA) announcement that earlier monitoring can potentially help identify patients experiencing brain swelling or fluid buildup and help inform treatment decision-making.

What Safety Concern Is FDA Announcing?

The FDA is recommending an additional, earlier magnetic resonance imaging (MRI) monitoring prior to the 3rd infusion for patients with Alzheimer's disease taking Leqembi (lecanemab). The earlier monitoring can identify individuals with amyloid-related imaging abnormalities with edema (ARIA-E), which is characterized by brain swelling or fluid buildup. ARIA-E is usually asymptomatic, although serious and life-threatening events, including seizure and status epilepticus, can occur and there have been deaths.

The Alzheimer's disease community has been aware of ARIA-E associated with Leqembi, and current prescribing information recommends MRI imaging before the 5th, 7th, and 14th infusions. However, after an in-depth analysis of this safety issue, the Agency has determined that an additional monitoring MRI prior to the 3rd infusion can potentially help identify ARIA-E events earlier.

ARIA-E can progress after initial detection on MRI. Identifying patients with ARIA-E can lead healthcare professionals, patients, and their families to delay or discontinue Leqembi treatment to potentially mitigate these serious and, in some cases, fatal events.

What Is FDA Doing?

We are requiring the prescribing information of Leqembi (lecanemab) to include an earlier monitoring MRI between the 2nd and 3rd infusion. This revised language will be in the monitoring schedule (Section

2.3) of the prescribing information. In the meantime, we want to bring public attention to this issue.

What Is Leqembi (lecanemab)?

Leqembi (lecanemab) is an amyloid beta-directed antibody that FDA approved in 2023 to slow the progression of Alzheimer's disease in patients with mild cognitive impairment or mild dementia stage of disease. Leqembi is an antibody infusion that removes beta-amyloid from the brain. Beta-amyloid is a protein fragment that plays an important role in the development of Alzheimer's disease by forming deposits in the brain called plaques and disturbing brain functioning.

Symptoms of dementia include the loss of memory, problem-solving, and ability to think clearly which can interfere with daily life. Alzheimer's disease is the most common type of dementia. It is a progressive, irreversible disease that typically affects people aged 60 or older. In 2020, there were approximately 6.9 million people living with Alzheimer's disease in the United States, and it is the 7th leading cause of death among U.S. adults.

What Should Patients and Caregivers Do?

Patients who have recently started Leqembi treatment should ask their healthcare professional about MRI monitoring for ARIA-E between the 2nd and 3rd infusion. Patients should contact their healthcare professional or go to the nearest hospital emergency room right away if they experience symptoms of ARIA-E, including headache, confusion, dizziness, vision changes, nausea, difficulty walking, or seizures. If patients do not have the ability to reach out to their healthcare professionals, their caregivers should do so on their behalf.

What Should Health Professionals Do?

Healthcare professionals should be aware of the new recommendations and perform monitoring MRIs on patients between the 2nd and 3rd Leqembi infusions. Healthcare professionals should advise patients (or their caregivers) to immediately contact them if they experience ARIA-E symptoms, such as headache, confusion, dizziness, vision changes, nausea, aphasia, weakness or seizure. In this case, healthcare professionals should order urgent MRIs.

If ARIA-E is diagnosed, healthcare professionals should discuss with patients and caregivers the potential need to delay or discontinue Leqembi treatment. Please refer to dose suspension criteria in the approved USPI in Section 2.3 Table 1. ARIA-E, with or without symptoms, can progress after initial detection on MRI.

What Did FDA Find?

During routine pharmacovigilance, FDA identified six deaths early in treatment, which prompted an in-depth analysis of serious and fatal outcomes related to ARIA-E before the 5th Leqembi infusion.

In the analysis, FDA identified 101 cases of serious ARIA-E (see Data Summary). Of these case reports, two (2%) occurred between the 2nd and 3rd infusion, 22 (22%) occurred between the 3rd and 4th infusion, 41 (40%) occurred between the 4th and 5th infusion, and 36 (36%) occurred after the 5th infusion.

In total, 24 cases of serious ARIA-E occurred before the 4th infusion, all of whom showed symptoms prompting an earlier unscheduled MRI for clinical assessment. This case review did not capture asymptomatic ARIA-E patients who were not identified until a later timepoint during the regularly scheduled MRIs, potentially underestimating the rate of ARIA-E earlier in the course of treatment.

Patients with ARIA-E can have symptom or imaging progression after initial detection on MRI. As such, it is important to detect these patients early, both with clinical assessment and MRI imaging, to determine whose treatment may need to be delayed or discontinued.

Data Summary

During routine pharmacovigilance, FDA identified six fatal cases of amyloid related imaging abnormalities with edema (ARIA-E) early in treatment. These fatalities prompted an in-depth analysis of serious and fatal outcomes of ARIA-E occurring prior to the 5th infusion of Leqembi (lecanemab). This analysis included data from FDA Adverse Event Reporting System (FAERS) reports, literature, and information requested from the applicant.

In the in-depth analysis, FDA identified 101 cases of serious ARIA-E in FAERS. Of these case reports, two (2%) occurred between the 2nd and 3rd infusions, 22 (22%) occurred between the 3rd and 4th infusions, 41 (40%) occurred between the 4th and 5th infusions, and 36 (36%) occurred after the 5th infusion.

In total, 24 cases of serious ARIA-E occurred before the 4th infusion. All 24 patients diagnosed with ARIA-E before the 4th infusion showed symptoms, which prompted an earlier unscheduled MRI for clinical assessment. This case review does not capture asymptomatic patients who may have had ARIA before the 3rd infusion but were not identified until a later timepoint during the regularly scheduled MRIs, potentially underestimating the rate of ARIA-E earlier in the course.

FDA also completed a review of the six fatal cases. Of the six fatalities identified in the original review, only one was initially asymptomatic and identified on the first monitoring MRI (i.e., prior to the 5th infusion). The remaining five developed symptoms within 0-8 days of their most recent infusion prompting urgent MRIs. Four of these cases developed symptoms after the 3rd infusion, and the last case developed symptoms after the 4th infusion. The four fatalities that occurred shortly following the 3rd infusion suggest a developing process that was likely already present at the time of the infusion, given the severity of symptoms and relatively rapid onset after the 3rd infusion. Earlier identification of ARIA-E may lead to a delay or discontinuation of Leqembi treatment to potentially mitigate serious and, in some cases, fatal events.

What Is My or My Loved One's Risk?

All medicines may have side effects even when used correctly as prescribed. Patients may be at higher risk of ARIA-E due to specific genetic factors or other underlying medical conditions. However, people respond differently to medicines. As a result, we cannot determine the exact likelihood of someone experiencing ARIA-E or other side effects from taking Leqembi. Talk to your healthcare professional(s) if you have questions or concerns about this medication's risks.

Facts about Leqembi

- Leqembi (lecanemab) is an amyloid beta-directed antibody that FDA approved in 2023 to slow disease progression in patients with Alzheimer's diseases. It is indicated for patients with mild cognitive impairment or mild dementia stage of disease.
- It is an antibody infusion that removes beta-amyloid from the brain.
- The recommended dosage is 10 mg/kg that must be diluted then administered as an intravenous infusion over approximately one hour, once every two weeks.
- The most common reactions include infusion-related reactions, ARIA-H, ARIA-E, and headache.
- Leqembi can lead to serious and potentially fatal symptoms of amyloid related imaging abnormalities with edema (ARIA-E) (i.e., brain swelling or fluid buildup).
- ARIA-E may present as headache, confusion, dizziness, vision changes, nausea, aphasia, weakness, or seizure. However, many patients do not have symptoms.
- To identify patients experiencing ARIA-E, FDA now recommends MRI imaging before the 3rd, 5th, 7th, and 14th infusions. Patients should also obtain a recent MRI (within one year before starting treatment) for a baseline comparison.

Please refer to the following website in FDA for details:
https://www.fda.gov/drugs/drug-safety-and-availability/fda-recommend-additional-earlier-mri-monitoring-patients-alzheimers-disease-taking-leqembi-lecanemab

In Hong Kong, Leqembi Concentrate For Solution For Infusion 200mg/2ml (HK-68289) and Leqembi Concentrate For Solution For Infusion 500mg/5ml (HK-68290) are pharmaceutical products containing lecanemab registered by Eisai (Hong Kong) Company Limited. Both products are prescription-only medicines. So far, the Department of Health (DH) has not received any case of adverse drug reaction with regard to lecanemab. In light of the above FDA's announcement, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board of Hong Kong.

Please note that this letter serves as a means for the DH to communicate important new safety information about registered pharmaceutical products with healthcare professionals in Hong Kong and is not intended to serve as guidelines or to replace professional clinical judgement. Healthcare professionals are advised to balance the risk of possible adverse effects against the benefit of treatment.

Please report any adverse events caused by drugs to the Clinical Trials and Pharmacovigilance Unit of the DH (tel. no.: 2319 2920, fax: 2319 6319 or email: adr@dh.gov.hk). For details, please refer to the website at Drug Office under "ADR Reporting": http://www.drugoffice.gov.hk/adr.html. You may wish to visit the Drug Office's website for subscription and browsing of "Drug News" which is a monthly digest of drug safety news and information issued by Drug Office.

Yours faithfully,

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(Vincent CHIANG)
for Assistant Director (Drug)