THE ROLE OF BBMs IN EARLY DETECTION OF AD PATHOLOGY

Recent advancements in Alzheimer's disease (AD) biomarker detection now enable the use of blood-based biomarker (BBM) tests to aid in clinical diagnosis[1–3]

Rachel is a real LEQEMBI patient.
People shown were compensated for their time, and information is accurate as of August 2025.

INDICATION

LEQEMBI® is indicated for the treatment of Alzheimer's disease (AD). Treatment with LEQEMBI should be initiated in patients with mild cognitive impairment (MCI) or mild dementia stage of disease, the population in which treatment was initiated in clinical trials.

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WARNING: AMYLOID-RELATED IMAGING ABNORMALITIES (ARIA)

- **Monoclonal antibodies directed against aggregated forms of beta amyloid, including LEQEMBI, can cause ARIA, characterized as ARIA with edema (ARIA-E) and ARIA with hemosiderin deposition (ARIA-H). Incidence and timing of ARIA vary among treatments. ARIA usually occurs early in treatment and is usually asymptomatic, although serious and life-threatening events, including seizure and status epilepticus, can occur. ARIA can be fatal. Serious intracerebral hemorrhages (ICH) >1 cm, some of which have been fatal, have been observed with this class of medications. Because ARIA-E can cause focal neurologic deficits that can mimic an ischemic stroke, consider whether such symptoms could be due to ARIA-E before giving thrombolytic therapy to a patient being treated with LEQEMBI.**
  - **Apolipoprotein E ε4 (ApoE ε4) Homozygotes: Patients who are ApoE ε4 homozygotes (~15% of patients with AD) treated with this class of medications have a higher incidence of ARIA, including symptomatic, serious, and severe radiographic ARIA, compared to heterozygotes and noncarriers. Testing for ApoE ε4 status should be performed prior to initiation of treatment to inform the risk of developing ARIA. Prior to testing, prescribers should discuss with patients the risk of ARIA across genotypes and the implications of genetic testing results. Prescribers should inform patients that if genotype testing is not performed, they can still be treated with LEQEMBI; however, it cannot be determined if they are ApoE ε4 homozygotes and at higher risk for ARIA.**
- **Consider the benefit of LEQEMBI for the treatment of AD and the potential risk of serious ARIA events when deciding to initiate treatment with LEQEMBI.**

Please see additional Select Safety Information throughout.
Please see full Prescribing Information for LEQEMBI, including Boxed WARNING.

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(lecanemab-irmb)

Why BBMs matter

BBMs:

- **BBM tests measure the presence of amyloid beta (Aβ) and phosphorylated tau (p-Tau)—hallmarks of AD pathology**[1,4,5]
- Can help identify patients with AD in the primary care or the specialized setting[1,2]
- May enable earlier and faster diagnoses as well as aid in risk assessment, prognosis, and patient management[1,2]
- **May be a more accessible and minimally invasive option for screening**[2]
  - These tools may be an option for patient populations living in geographic areas where access to medical care is limited[1,2]

Roles in confirming Aβ

- **Primary care physicians** performing BBMs at their checkups with appropriate patients may refer to your practice for further evaluation for cognitive decline and confirmation of Aβ
- The **specialist's role** is critical in evaluating, diagnosing, and developing an individualized patient treatment plan once Aβ is confirmed[1,2]
- Coordinated use of BBMs within your **health care system** may help cultivate an efficient diagnostic pathway with both PCPs and specialists playing a role[1]

CSF, cerebrospinal fluid; PCP, primary care provider; PET, positron emission tomography.

Before ordering a BBM test, a cognitive and/or functional assessment indicating mild cognitive impairment or dementia should be conducted[1,6,7]

BBMs are not intended as standalone diagnostic tests and should be integrated with patient/family history, brain imaging, routine laboratory tests, and other tests as appropriate[1,6,7]

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CONTRAINDICATION

Contraindicated in patients with serious hypersensitivity to lecanemab-irmb or to any of the excipients. Reactions have included angioedema and anaphylaxis.

WARNINGS AND PRECAUTIONS

AMYLOID-RELATED IMAGING ABNORMALITIES

Medications in this class, including LEQEMBI, can cause ARIA-E, which can be observed on MRI as brain edema or sulcal effusions, and ARIA-H, which includes microhemorrhage and superficial siderosis. ARIA can occur spontaneously in patients with AD, particularly in patients with MRI findings suggestive of cerebral amyloid angiopathy (CAA), such as pretreatment microhemorrhage or superficial siderosis. ARIA-H generally occurs with ARIA-E. Reported ARIA symptoms may include headache, confusion, visual changes, dizziness, nausea, and gait difficulty. Focal neurologic deficits may also occur. Symptoms usually resolve over time.

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Triage or confirmation

Sensitivity and specificity criteria can help determine whether a BBM test is suitable for triage or confirmation[6]

How to Interpret: Target profiles of BBMs for specialists based on Alzheimer's Association Clinical Practice Guidelines

	Triage[6] (To determine if a patient is negative for amyloid pathology or if further evaluation by PET or CSF is necessary)	**Confirmation**[1,2,6] (Alternative to amyloid PET or CSF as a diagnostic test to confirm brain amyloid pathology)
Results	**Positive test** results indicate a high likelihood of amyloid pathology but require confirmation via amyloid PET or CSF testing **Negative test** results indicate amyloid pathology is unlikely and reduce the number of individuals requiring PET or CSF follow-up	**Positive test** results identify the presence of Aβ pathology; if performed in primary care, patient should be referred to a specialist for disease management **Negative test** results rule out Aβ pathology
Desired characteristics	High sensitivity ≥90% sensitivity and ≥75-85% specificity can be used as a triaging test	High specificity and sensitivity ≥90% sensitivity and specificity can serve as a substitute for amyloid PET imaging or CSF AD biomarker testing in patients with cognitive impairment presenting to specialized care for memory disorders
Benefits	Prioritizes patients for further evaluation with PET and CSF to confirm amyloid pathology	Could reduce the need for PET/CSF, and allows for timelier diagnosis

The Alzheimer's Association Clinical Practice Guidelines suggest that a BBM test should not be obtained before a comprehensive clinical evaluation by a health care professional, and test results should always be interpreted within clinical context.[8]

Review the Alzheimer's Association Clinical Practice guidelines for use of BBMs

Eisai does not endorse or recommend any specific BBM test. This link to external guidelines is provided for educational purposes only and is independent of Eisai. Eisai is not responsible for the content of third-party websites.

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Available BBM tests

BBMs can aid in the clinical diagnosis of AD and can help confirm eligibility for patients to start anti-amyloid therapy such as LEQEMBI®[2]

Commercially distributed assays, including an FDA-cleared test option, may be available at the following labs[3]

Lab	Available Test(s)	Lab	Available Test(s)	Lab	Available Test(s)
Quest		Mayo Clinic		Labcorp	

Information provided for educational purposes only. This list is not an endorsement or recommendation by Eisai of any laboratory or test.

Reach out to your local lab provider for help in determining which test(s) may be most appropriate.

This information is current as of August 25, 2025, but may change as more BBMs become available.

If there is a question about the blood test satisfying payer coverage requirements before initiating any therapeutic agent, please reach out to the specific payer for that determination.

Learn more about specific BBMs on the CEOi Alzheimer's disease blood test performance database

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WARNINGS AND PRECAUTIONS (cont'd)

AMYLOID-RELATED IMAGING ABNORMALITIES (cont'd)

Incidence of ARIA

Symptomatic ARIA occurred in 3% and serious ARIA symptoms in 0.7% with LEQEMBI. Clinical ARIA symptoms resolved in 79% of patients during the period of observation. ARIA, including asymptomatic radiographic events, was observed: LEQEMBI, 21%; placebo, 9%. ARIA-E was observed: LEQEMBI, 13%; placebo, 2%. ARIA-H was observed: LEQEMBI, 17%; placebo, 9%. No increase in isolated ARIA-H was observed for LEQEMBI vs placebo.

Incidence of ICH

ICH >1 cm in diameter was reported in 0.7% with LEQEMBI vs 0.1% with placebo. Fatal events of ICH in patients taking LEQEMBI have been observed.

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WARNINGS AND PRECAUTIONS (cont'd)

AMYLOID-RELATED IMAGING ABNORMALITIES (cont'd)

Risk Factors of ARIA and ICH

ApoE ε4 Carrier Status

Of the patients taking LEQEMBI, 16% were ApoE ε4 homozygotes, 53% were heterozygotes, and 31% were noncarriers. With LEQEMBI, ARIA was higher in ApoE ε4 homozygotes (LEQEMBI: 45%; placebo: 22%) than in heterozygotes (LEQEMBI: 19%; placebo: 9%) and noncarriers (LEQEMBI: 13%; placebo: 4%). Symptomatic ARIA-E occurred in 9% of ApoE ε4 homozygotes vs 2% of heterozygotes and 1% of noncarriers. Serious ARIA events occurred in 3% of ApoE ε4 homozygotes and in ~1% of heterozygotes and noncarriers. The recommendations on management of ARIA do not differ between ApoE ε4 carriers and noncarriers.

Radiographic Findings of CAA

Neuroimaging findings that may indicate CAA include evidence of prior ICH, cerebral microhemorrhage, and cortical superficial siderosis. CAA has an increased risk for ICH. The presence of an ApoE ε4 allele is also associated with CAA.

The baseline presence of at least 2 microhemorrhages or the presence of at least 1 area of superficial siderosis on MRI, which may be suggestive of CAA, have been identified as risk factors for ARIA. Patients were excluded from Clarity AD for the presence of >4 microhemorrhages and additional findings suggestive of CAA (prior cerebral hemorrhage >1 cm in greatest diameter, superficial siderosis, vasogenic edema) or other lesions (aneurysm, vascular malformation) that could potentially increase the risk of ICH.

Concomitant Antithrombotic or Thrombolytic Medication

In Clarity AD, baseline use of antithrombotic medication (aspirin, other antiplatelets, or anticoagulants) was allowed if the patient was on a stable dose. Most exposures were to aspirin. Antithrombotic medications did not increase the risk of ARIA with LEQEMBI. The incidence of ICH: 0.9% in patients taking LEQEMBI with a concomitant antithrombotic medication vs 0.6% with no antithrombotic and 2.5% in patients taking LEQEMBI with an anticoagulant alone or with antiplatelet medication such as aspirin vs none in patients receiving placebo.

Fatal cerebral hemorrhage has occurred in 1 patient taking an anti-amyloid monoclonal antibody in the setting of focal neurologic symptoms of ARIA and the use of a thrombolytic agent.

Additional caution should be exercised when considering the administration of antithrombotics or a thrombolytic agent (e.g., tissue plasminogen activator) to a patient already being treated with LEQEMBI. Because ARIA-E can cause focal neurologic deficits that can mimic an ischemic stroke, treating clinicians should consider whether such symptoms could be due to ARIA-E before giving thrombolytic therapy in a patient being treated with LEQEMBI.

Caution should be exercised when considering the use of LEQEMBI in patients with factors that indicate an increased risk for ICH and, in particular, patients who need to be on anticoagulant therapy or patients with findings on MRI that are suggestive of CAA.

Radiographic Severity With LEQEMBI

Most ARIA-E radiographic events occurred within the first 7 doses, although ARIA can occur at any time, and patients can have >1 episode. Maximum radiographic severity of ARIA-E with LEQEMBI was mild in 4%, moderate in 7%, and severe in 1% of patients. Resolution on MRI occurred in 52% of ARIA-E patients by 12 weeks, 81% by 17 weeks, and 100% overall after detection. Maximum radiographic severity of ARIA-H microhemorrhage with LEQEMBI was mild in 9%, moderate in 2%, and severe in 3% of patients; superficial siderosis was mild in 4%, moderate in 1%, and severe in 0.4% of patients. With LEQEMBI, the rate of severe radiographic ARIA-E was highest in ApoE ε4 homozygotes (5%) vs heterozygotes (0.4%) or noncarriers (0%). With LEQEMBI, the rate of severe radiographic ARIA-H was highest in ApoE ε4 homozygotes (13.5%) vs heterozygotes (2.1%) or noncarriers (1.1%).

Monitoring and Dose Management Guidelines

Baseline brain MRI and periodic monitoring with MRI are recommended. Enhanced clinical vigilance for ARIA is recommended during the first 14 weeks of treatment. Depending on ARIA-E and ARIA-H clinical symptoms and radiographic severity, use clinical judgment when considering whether to continue dosing or to temporarily or permanently discontinue LEQEMBI. If a patient experiences ARIA symptoms, clinical evaluation should be performed, including MRI if indicated. If ARIA is observed on MRI, careful clinical evaluation should be performed prior to continuing treatment.

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Rachel is a real LEQEMBI patient and Doug is her care partner. People shown were compensated for their time, and information is accurate as of August 2025.

BBMs may enable earlier and faster diagnosis for appropriate patients[2]

Visit the LEQEMBI® website

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WARNINGS AND PRECAUTIONS (cont'd)

HYPERSENSITIVITY REACTIONS

Hypersensitivity reactions, including angioedema, bronchospasm, and anaphylaxis, have occurred with LEQEMBI. Promptly discontinue the infusion upon the first observation of any signs or symptoms consistent with a hypersensitivity reaction and initiate appropriate therapy.

INFUSION-RELATED REACTIONS (IRRs)

IRRs were observed—LEQEMBI: 26%; placebo: 7%—and most cases with LEQEMBI (75%) occurred with the first infusion. IRRs were mostly mild (69%) or moderate (28%). Symptoms included fever and flu-like symptoms (chills, generalized aches, feeling shaky, and joint pain), nausea, vomiting, hypotension, hypertension, and oxygen desaturation.

IRRs can occur during or after the completion of infusion. In the event of an IRR during the infusion, the infusion rate may be reduced or discontinued, and appropriate therapy initiated as clinically indicated. Consider prophylactic treatment prior to future infusions with antihistamines, acetaminophen, nonsteroidal anti-inflammatory drugs, or corticosteroids.

ADVERSE REACTIONS

- The most common adverse reactions reported in ≥5% with LEQEMBI infusion every 2 weeks and ≥2% higher than placebo were IRRs (LEQEMBI: 26%; placebo: 7%), ARIA-H (LEQEMBI: 14%; placebo: 8%), ARIA-E (LEQEMBI: 13%; placebo: 2%), headache (LEQEMBI: 11%; placebo: 8%), superficial siderosis of central nervous system (LEQEMBI: 6%; placebo: 3%), rash (LEQEMBI: 6%; placebo: 4%), and nausea/vomiting (LEQEMBI: 6%; placebo: 4%)
- Safety profile of LEQEMBI IQLIK for maintenance treatment was similar to LEQEMBI infusion. Patients who received LEQEMBI IQLIK experienced localized and systemic (less frequent) injection-related reactions (mild to moderate in severity)

LEQEMBI (lecanemab-irmb) is available:

- Intravenous infusion: 100 mg/mL
- Subcutaneous injection: 200 mg/mL

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References: 1. Angioni D, Delrieu J, Hansson O, et al. Blood biomarkers from research use to clinical practice: what must be done? A report from the EU/US CTAD task force. *J Prev Alzheimers Dis*. 2022;9(4):569-579. **2.** Hampel H, Hu Y, Cummings J, et al. Blood-based biomarkers for Alzheimer's disease: current state and future use in a transformed global healthcare landscape. *Neuron*. 2023;111(18):2781-2799. **3.** US Food and Drug Administration. FDA clears first blood test used in diagnosing Alzheimer's disease. Accessed August 1, 2025. https://www.fda.gov/news-events/press-announcements/fda-clears-first-blood-test-used-diagnosing-alzheimers-disease **4.** Beason-Held LL, Goh JO, An Y, et al. Changes in brain function occur years before the onset of cognitive impairment. *J Neurosci*. 2013;33(46):18008-18014. **5.** Alzheimer's Association. 2025 Alzheimer's disease facts and figures. *Alzheimers Dement*. 2025;21:e70235. doi:10.1002/alz.70235 **6.** Schindler SE, Galasko D, Pereira AC, et al. Acceptable performance of blood biomarker tests of amyloid pathology-recommendations from the Global CEO Initiative on Alzheimer's Disease. *Nat Rev Neurol*. 2024;20(7):426-439. **7.** Porsteinsson AP, Isaacson RS, Knox S, Sabbagh MN, Rubino I. Diagnosis of early Alzheimer's disease: clinical practice in 2021. *J Prev Alzheimers Dis*. 2021;8(3):371-386. **8**. Palmqvist S, Whitson HE, Allen LA, et al. Alzheimer's Association Clinical Practice Guideline on the use of blood-based biomarkers in the diagnostic workup of suspected Alzheimer's disease within specialized care settings. *Alzheimers Dement*. 2025;21:1-17. doi:10.1002/alz.70535

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