LEQEMBI®
(lecanemab-irmb) 100 mg/mL
INJECTION FOR INTRAVENOUS USE

Get to know **Isaac**, a patient with **MCI due to AD**

HOW WILL YOU HELP **YOUR EARLY AD PATIENTS?**

The sooner MCI due to AD is diagnosed, the sooner you can intervene[1]

Hypothetical LEQEMBI patient.

AD=Alzheimer's disease; MCI=mild cognitive impairment.

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.

SELECT SAFETY INFORMATION: Boxed WARNING

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, rarely can occur. 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 and full Prescribing Information, including Boxed WARNING.

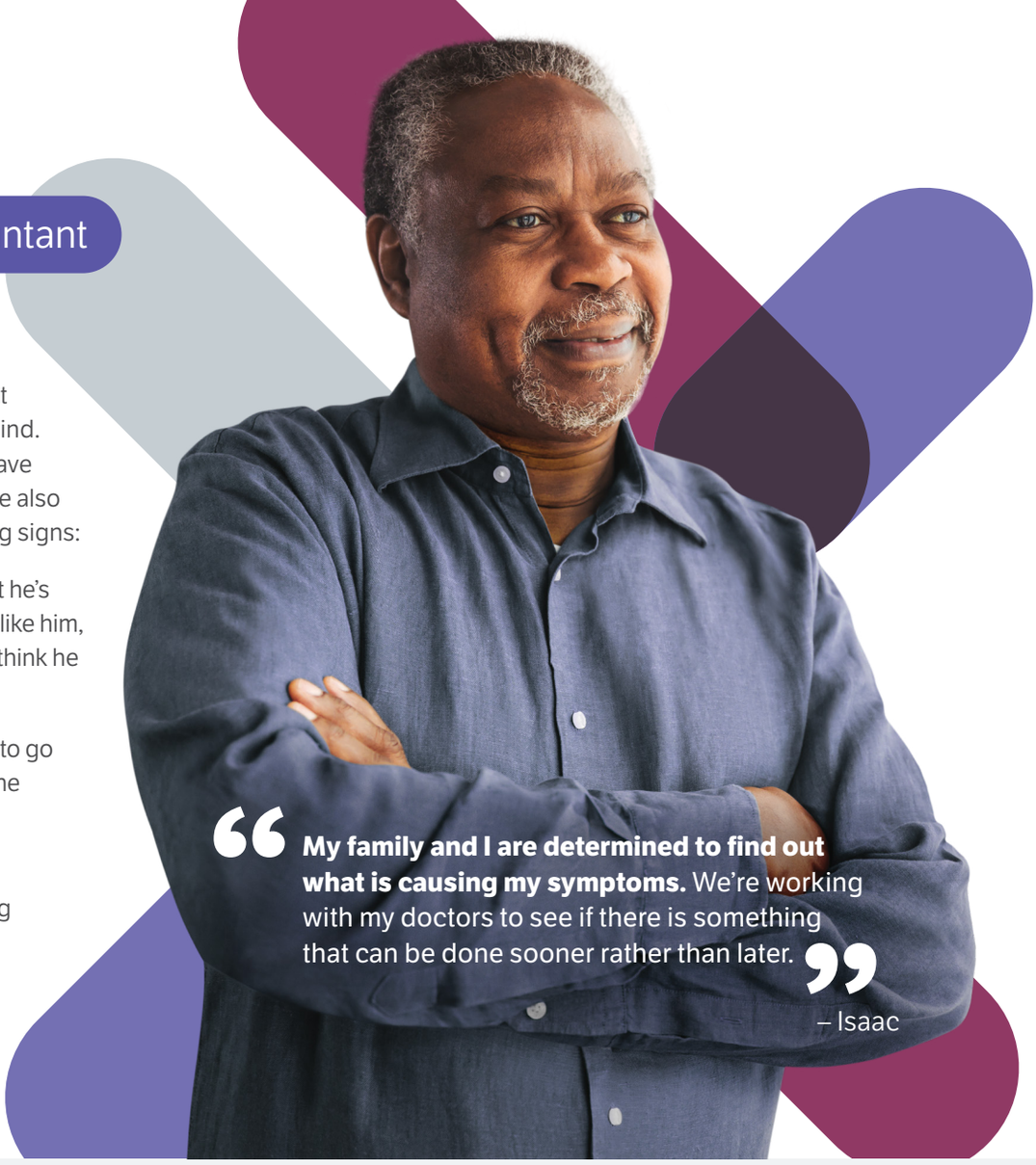
Meet Isaac, a retired accountant

Until recently, Isaac, **age 67**, has been dealing with **high blood pressure** that's controlled. But his **father's AD diagnosis** at age 76 has always been at the back of his mind. Isaac and his **wife (his primary support)**, have discussed some concerns, as his children are also beginning to notice some subtle but worrying signs:

"Isaac has always handled our finances. But he's made some basic mistakes, which is so unlike him, leading us to hire a separate accountant. I think he **may not be as sharp** as he used to be."

"He's always been that guy at family parties to go around and talk to each person. But lately he seems **less engaged** and sits quietly for long periods."

"We can sense he's **anxious** that something is causing his memory issues, and how it may affect those around him."



"**My family and I are determined to find out what is causing my symptoms.** We're working with my doctors to see if there is something that can be done sooner rather than later."

– Isaac

Hypothetical LEQEMBI patient and quote.

Pathophysiological changes in the brain occur before and continue after symptoms onset.[2]

SELECT SAFETY INFORMATION (cont'd)

CONTRAINDICATION

LEQEMBI® is contraindicated in patients with serious hypersensitivity to lecanemab-irmb or to any of the excipients of LEQEMBI. 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.

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.

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Eager to pinpoint the cause of his symptoms, Isaac receives thorough evaluation by his care team

PCP work-up

- ✔ CBC with differential: **Normal**
- ✔ Chemistry panel: **Normal**
- ✔ Thyroid function: **Normal**
- ✔ Vitamin deficiencies: **None**
- ✔ Full blood panel: **Normal**
- ✔ MRI: **Ruled out non-AD causes of cognitive impairment**
- ! MMSE score: **26/30**
  MCI due to AD suspected

Neurologist work-up

1. Reassess for cognitive impairment

- ! Repeat MMSE: **26/30**
- ! MoCA score: **27/30**
- ! Neuropsychological testing: **Decline is supportive of MCI**

2. Differential diagnosis for AD

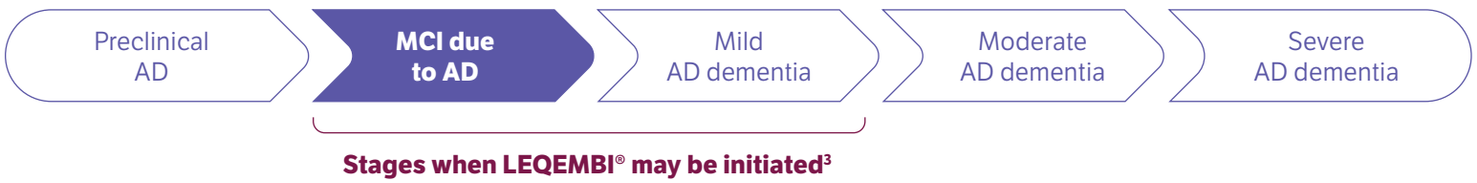
- ✔ Repeat blood workup
- ✔ Repeat MRI
- ✔ Review medications and comorbidities

3. Confirm diagnosis

- ! Aβ PET: **Positive**
  MCI due to AD confirmed

  Consider ApoE ε4 testing for anti-amyloid therapies

Where Isaac's diagnosis falls on the AD continuum[1]



The stages of AD depicted above in equal size are not necessarily equal in duration.[1]

Take proactive steps to diagnose AD at the earliest symptomatic stages.

The Clarity AD trial included patients similar to Isaac, who has MCI, the earliest symptomatic AD stage[1,4]

Patient baseline characteristics in Clarity AD:

- Median age: **73 (range 50-90 years)[4]**
- ≥2 comorbid conditions*: **63.7% of patients[4]**
- Mean MMSE score: **25.5/30 (range 22-30)[4,5]**

Clarity AD: 18-month, global, placebo-controlled, double-blind, parallel-group, randomized clinical trial of 1795 patients with MCI due to AD (n=528/859) or mild AD dementia (n=331/859) with confirmed Aβ pathology. Patients were randomized 1:1 to receive IV infusions of LEQEMBI 10 mg/kg or placebo once every 2 weeks.[1,5]

*Including hypertension, hyperlipidemia, ischemic heart disease, diabetes, and obesity.[4]

Aβ=amyloid beta; CBC=complete blood count; IV=intravenous; MMSE=Mini-Mental State Examination; MoCA=Montreal Cognitive Assessment; MRI=magnetic resonance imaging; PCP=primary care provider; PET=positron emission tomography.

SELECT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

AMYLOID-RELATED IMAGING ABNORMALITIES (cont'd)

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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Explore available resources to start LEQEMBI®

Support for your patients and your office

Help patients start and stay on treatment

- Appointment tracker
- Patient brochure
- Infusion guide

Equip your office with tailored resources

- Dosing calculator
- Diagnostic workup checklist
- Specialty distributor guide
- Diagnosis to infusion brochure

Navigate access to treatment

- Enrollment form
- Health insurance brochure
- Coding quick reference guide
- Request an ARM tool
- Sample letters

Get to know the LEQEMBI Infusion Center Locator Tool*

*This tool is developed, hosted and maintained by NICA, an organization independent from Eisai. Eisai does not control or validate the content on the NICA Infusion Center Locator website. By making this link available, Eisai is not endorsing or recommending any particular infusion provider. The list of infusion providers searchable in the Locator is not comprehensive. Other infusion providers may be available to patients. An infusion site that would like to request to be added to the NICA Infusion Center Locator may contact NICA. When using the NICA Infusion Center Locator, it is the responsibility of the referring prescriber and/or patient to contact the site directly for any site-specific questions, including to confirm whether a site offers the prescribed medication, accepts the patient's insurance, and has schedule availability.

ARM=Access & Reimbursement Manager; NICA=National Infusion Center Association.

LEQEMBI was studied in the earliest stages of symptomatic AD.[1]

SELECT SAFETY INFORMATION (cont'd)

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.

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The first step was to **catch AD early**

THE NEXT STEP IS TO TREAT

Patients like Isaac **depend on you to intervene**

Hypothetical LEQEMBI patient and caregiver.

Help Isaac take action against AD. Start LEQEMBI® today.

> The progressive nature of AD warrants proactive collaboration between the PCP and neurologist to **detect and diagnose AD patients earlier**. Equally important is identifying which patients may be appropriate for **LEQEMBI**.
>
> – Isaac's neurologist

Hypothetical quote and actor portrayal.

SELECT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

AMYLOID-RELATED IMAGING ABNORMALITIES (cont'd)

Risk Factors of ARIA and ICH (cont'd)

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.

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Start your appropriate patients on LEQEMBI® today

Learn how LEQEMBI can help

SELECT SAFETY INFORMATION (cont'd)
WARNINGS AND PRECAUTIONS (cont'd)
AMYLOID-RELATED IMAGING ABNORMALITIES (cont'd)
Risk Factors of ARIA and ICH (cont'd)

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.

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.
- In the event of an IRR, 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 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%).

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

References: 1. Alzheimer's Association. 2024 Alzheimer's disease facts and figures. *Alzheimers Dement*. 2024;20(5):1-149. **2.** Bateman RJ, Xiong C, Benzinger TLS, et al. Clinical and biomarker changes in dominantly inherited Alzheimer's disease. *N Engl J Med*. 2012;367(9):795-804. **3.** LEQEMBI (lecanemab-irmb) injection, for intravenous use [package insert]. Nutley, NJ: Eisai Inc. **4.** Iwatsubo T, Irizarry M, van Dyck C, Sabbagh M, Bateman RJ, Cohen S. Clarity AD: a phase 3 placebo-controlled, double-blind, parallel-group, 18-month study evaluating lecanemab in early Alzheimer's disease. Presented at: CTAD Conference; November 29-December 2, 2022; San Francisco, CA. **5.** van Dyck CH, Swanson CJ, Aisen P, et al. Lecanemab in early Alzheimer's disease. *N Engl J Med*. 2023;388(1):9-21.

Eisai

Biogen.

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