

LEQEMBI[®]

(lecanemab-irmb)

Diagnostic Workup Checklist

INDICATION

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

SELECT SAFETY INFORMATION

WARNING: AMYLOID RELATED IMAGING ABNORMALITIES (ARIA)

Monoclonal antibodies directed against aggregated forms of amyloid beta, including LEQEMBI, can cause amyloid related imaging abnormalities (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 rarely can occur. Serious intracerebral hemorrhages >1 cm, some of which have been fatal, have been observed in patients treated with this class of medications.

- **Apolipoprotein E ε4 (ApoE ε4) Homozygotes:** Patients who are ApoE ε4 homozygotes (approximately 15% of Alzheimer's disease patients) treated with this class of medications, including LEQEMBI, 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 Alzheimer's disease and potential risk of serious adverse events associated with ARIA when deciding to initiate treatment with LEQEMBI.



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

Patient's Name

Date of Birth

LEQEMBI Diagnostic Workup Checklist

This document is intended to help health care providers determine the appropriateness of LEQEMBI therapy and document clinical decision making. For complete information, refer to the full Prescribing Information.

This content is intended for health care providers only for informational purposes and does not substitute for sound medical judgment or clinical decision making in the context of medical treatment.

DIAGNOSIS

 Mild cognitive impairment stage of Alzheimer's disease

 Mild dementia stage of Alzheimer's disease

CONFIRMATION OF COGNITIVE IMPAIRMENT*

DATE PERFORMED

 AD8 Score
 Mini-Cog™ Score
 MMSE Score
 SLUMS Score
 MoCA Score
 Other Score

NOTES

CONFIRMATION OF FUNCTIONAL IMPAIRMENT*

DATE PERFORMED

 FAQ Score
 CDR-SB Score
 FAST Score
 Other Score

NOTES

Checklist continues on following page

*This is not a comprehensive list of cognitive or functional assessment tools.

AD8=The 8-item Informant Interview to Differentiate Aging and Dementia; CDR-SB=Clinical Dementia Rating-Sum of Boxes; FAQ=Functional Activities Questionnaire; FAST=Functional Assessment Staging Tool; GPCOG=General Practitioner Assessment of Cognition; MIS=Memory Impairment Screen; MMSE=Mini-Mental Status Examination; MoCA=Montreal Cognitive Assessment; SLUMS=Saint Louis University Mental Status Examination.

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.



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Patient's Name

Date of Birth

CONFIRMATION OF BETA-AMYLOID (A β) PATHOLOGY

DATE PERFORMED

 Beta-amyloid PET Scan

RESULT

 CSF AnalysisRESULT t-tau p-tau p-tau: A β ratio Other

RESULT

RECOMMENDED APOE ϵ 4 TEST

DATE PERFORMED

 NOT PERFORMED Positive Homozygous Heterozygous Negative**BASELINE MONITORING FOR AMYLOID RELATED IMAGING ABNORMALITIES (ARIA)**RECENT BASELINE BRAIN MRI PRIOR TO INITIATING TREATMENT¹

DATE PERFORMED

ARIA Type and Radiographic Severity

 ARIA-E Mild Moderate Severe Negative ARIA-H microhemorrhage Mild Moderate Severe Negative ARIA-H superficial siderosis Mild Moderate Severe Negative

NOTES

¹In addition to the baseline MRI required prior to initiating treatment, 3 additional MRI's are required to be completed before the 5th, 7th, and 14th infusions. ARIA-E=ARIA with edema; ARIA-H=ARIA with hemosiderin deposition; CSF=cerebrospinal fluid; PET=positron emission tomography.

SELECT SAFETY INFORMATION (cont'd)**WARNINGS AND PRECAUTIONS****AMYLOID RELATED IMAGING ABNORMALITIES**

LEQEMBI can cause ARIA-E and ARIA-H. ARIA-E can be observed on MRI as brain edema or sulcal effusions, and ARIA-H as microhemorrhage and superficial siderosis. ARIA can occur spontaneously in patients with Alzheimer's disease. ARIA-H associated with monoclonal antibodies directed against aggregated forms of beta amyloid generally occurs in association with an occurrence of ARIA-E. ARIA-H and ARIA-E can occur together.

ARIA usually occurs early in treatment and is usually asymptomatic, although serious and life-threatening events, including seizure and status epilepticus, rarely can occur. Reported symptoms associated with ARIA may include headache, confusion, visual changes, dizziness, nausea, and gait difficulty. Focal neurologic deficits may also occur. Symptoms associated with ARIA usually resolve over time.



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SELECT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

AMYLOID RELATED IMAGING ABNORMALITIES (cont'd)

ARIA Monitoring and Dose Management Guidelines

Obtain recent baseline brain magnetic resonance imaging (MRI) prior to initiating treatment with LEQEMBI. Obtain an MRI prior to the 5th, 7th and 14th infusions.

Recommendations for dosing in patients with ARIA-E and ARIA-H depend on clinical symptoms and radiographic severity. Depending on ARIA severity, use clinical judgment in considering whether to continue dosing, temporarily discontinue treatment, or permanently discontinue LEQEMBI.

Enhanced clinical vigilance for ARIA is recommended during the first 14 weeks of treatment with LEQEMBI. If a patient experiences symptoms suggestive of ARIA, 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.

There is no experience in patients who continued dosing through symptomatic ARIA-E or through asymptomatic, but radiographically severe, ARIA-E. There is limited experience in patients who continued dosing through asymptomatic but radiographically mild to moderate ARIA-E. There are limited data in dosing patients who experienced recurrent ARIA-E.

Incidence of ARIA

In Study 2, symptomatic ARIA occurred in 3% (29/898) of LEQEMBI-treated patients. Serious symptoms associated with ARIA were reported in 0.7% (6/898) of patients treated with LEQEMBI. Clinical symptoms associated with ARIA resolved in 79% (23/29) of patients during the period of observation.

Including asymptomatic radiographic events, ARIA was observed in LEQEMBI: 21% (191/898); placebo: 9% (84/897). ARIA-E was observed in LEQEMBI: 13% (113/898); placebo: 2% (15/897). ARIA-H was observed in LEQEMBI: 17% (152/898); placebo: 9% (80/897). There was no increase in isolated ARIA-H for LEQEMBI vs placebo.

ApoE ε4 Carrier Status and Risk of ARIA

In Study 2, 16% (141/898) of patients in the LEQEMBI arm were ApoE ε4 homozygotes, 53% (479/898) were heterozygotes, and 31% (278/898) were noncarriers.

The incidence of ARIA was higher in ApoE ε4 homozygotes (LEQEMBI: 45%; placebo: 22%) than in heterozygotes (LEQEMBI: 19%; placebo: 9%) and noncarriers (LEQEMBI: 13%; placebo: 4%). Among patients treated with LEQEMBI, symptomatic ARIA-E occurred in 9% of ApoE ε4 homozygotes compared with 2% of heterozygotes and 1% of noncarriers. Serious events of ARIA occurred in 3% of ApoE ε4 homozygotes, and approximately 1% of heterozygotes and noncarriers.

The recommendations on management of ARIA do not differ between ApoE ε4 carriers and noncarriers.

Radiographic Findings

The majority of ARIA-E radiographic events occurred early in treatment (within the first 7 doses), although ARIA can occur at any time and patients can have more than 1 episode. The maximum radiographic severity of ARIA-E in patients treated with LEQEMBI was mild in 4% (37/898), moderate in 7% (66/898), and severe in 1% (9/898). Resolution on MRI occurred in 52% of ARIA-E patients by 12 weeks, 81% by 17 weeks, and 100% overall after detection. The maximum radiographic severity of ARIA-H microhemorrhage in LEQEMBI-treated patients was mild in 9% (79/898), moderate in 2% (19/898), and severe in 3% (28/898) of patients; superficial siderosis was mild in 4% (38/898), moderate in 1% (8/898), and severe in 0.4% (4/898). Among LEQEMBI-treated patients, the rate of severe radiographic ARIA-E was highest in ApoE ε4 homozygotes 5% (7/141), compared to heterozygotes 0.4% (2/479) or noncarriers 0% (0/278). Among LEQEMBI-treated patients, the rate of severe radiographic ARIA-H was highest in ApoE ε4 homozygotes 13.5% (19/141), compared to heterozygotes 2.1% (10/479) or noncarriers 1.1% (3/278).



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SELECT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

AMYLOID RELATED IMAGING ABNORMALITIES (cont'd)

Intracerebral Hemorrhage

Intracerebral hemorrhage >1 cm in diameter was reported in 0.7% (6/898) of patients in Study 2 after treatment with LEQEMBI compared to 0.1% (1/897) on placebo. Fatal events of intracerebral hemorrhage in patients taking LEQEMBI have been reported.

Concomitant Antithrombotic Medication:

In Study 2, baseline use of antithrombotic medication (aspirin, other antiplatelets, or anticoagulants) was allowed if the patient was on a stable dose. The majority of exposures to antithrombotic medications were to aspirin. Antithrombotic medications did not increase the risk of ARIA with LEQEMBI. The incidence of intracerebral hemorrhage was 0.9% (3/328 patients) in patients taking LEQEMBI with a concomitant antithrombotic medication at the time of the event compared to 0.6% (3/545 patients) in those who did not receive an antithrombotic. Patients taking LEQEMBI with an anticoagulant alone or combined with an antiplatelet medication or aspirin had an incidence of intracerebral hemorrhage of 2.5% (2/79 patients) compared to none in patients who received placebo.

Because intracerebral hemorrhages >1 cm in diameter have been observed in patients taking LEQEMBI, additional caution should be exercised when considering the administration of anticoagulants or a thrombolytic agent (e.g., tissue plasminogen activator) to a patient already being treated with LEQEMBI.

Other Risk Factors for Intracerebral Hemorrhage:

Patients were excluded from enrollment in Study 2 for findings on neuroimaging that indicated an increased risk for intracerebral hemorrhage. These included findings suggestive of cerebral amyloid angiopathy (prior cerebral hemorrhage >1 cm in greatest diameter, >4 microhemorrhages, superficial siderosis, vasogenic edema) or other lesions (aneurysm, vascular malformation) that could potentially increase the risk of intracerebral hemorrhage. The presence of an ApoE ε4 allele is also associated with cerebral amyloid angiopathy, which has an increased risk for intracerebral hemorrhage. Caution should be exercised when considering the use of LEQEMBI in patients with factors that indicate an increased risk for intracerebral hemorrhage and in particular for patients who need to be on anticoagulant therapy.

HYPERSENSITIVITY REACTIONS

Hypersensitivity reactions, including angioedema, bronchospasm, and anaphylaxis, have occurred in LEQEMBI-treated patients. 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

In Study 2, infusion-related reactions were observed in LEQEMBI: 26% (237/898); placebo: 7% (66/897), and the majority of cases in LEQEMBI-treated patients (75%, 178/237) occurred with the first infusion. Infusion-related reactions were mostly mild (69%) or moderate (28%) in severity. Infusion-related reactions resulted in discontinuations in 1% (12/898) of LEQEMBI-treated patients. Symptoms of infusion-related reactions 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 infusion-related reaction, the infusion rate may be reduced, or the infusion may be discontinued, and appropriate therapy initiated as clinically indicated. Prophylactic treatment with antihistamines, acetaminophen, nonsteroidal anti-inflammatory drugs, or corticosteroids prior to future infusions may be considered.

ADVERSE REACTIONS

In Study 2, the most common adverse reaction leading to discontinuation of LEQEMBI was ARIA-H microhemorrhages that led to discontinuation in 2% (15/898) of patients treated with LEQEMBI compared to <1% (1/897) of patients on placebo.

In Study 2, the most common adverse reactions reported in ≥5% of patients treated with LEQEMBI (N=898) and ≥2% higher than placebo (N=897) were infusion-related reactions (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%).

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