These appropriate use recommendations (AURs) are for the use of lecanemab for the treatment of early AD (ie, MCI due to AD or mild AD dementia) with con rmed brain amyloid pathology based on the clinical guidance developed by the Alzheimer's Disease and Related Disorders Therapeutics Working Group and the FDA Prescribing Information for lecanemab. This piece is part of an appropriate use toolkit independently developed by the Alzheimer's Association for HCPs who have decided to o er lecanemab for a patient meeting eligibility criteria. These AURs apply to lecanemab; other anti-amyloid monoclonal antibodies may have di erent management requirements. AURs speci c to the monoclonal antibody being considered should be referenced.

Review this section of the toolkit to learn more about eligibility criteria for lecanemab based on the CLARITY AD trial and the appropriate use recommendations.

Patient Eligibility Criteria

Lecanemab inclusion criteria from CLARITY AD and proposed in the AUR	
Eligibility Criteria Used in the CLARITY AD Pivotal Trial of Lecanemab	

Please see the lecanemab exclusion criteria (ie, criteria that render an individual ineligible) on the next page.

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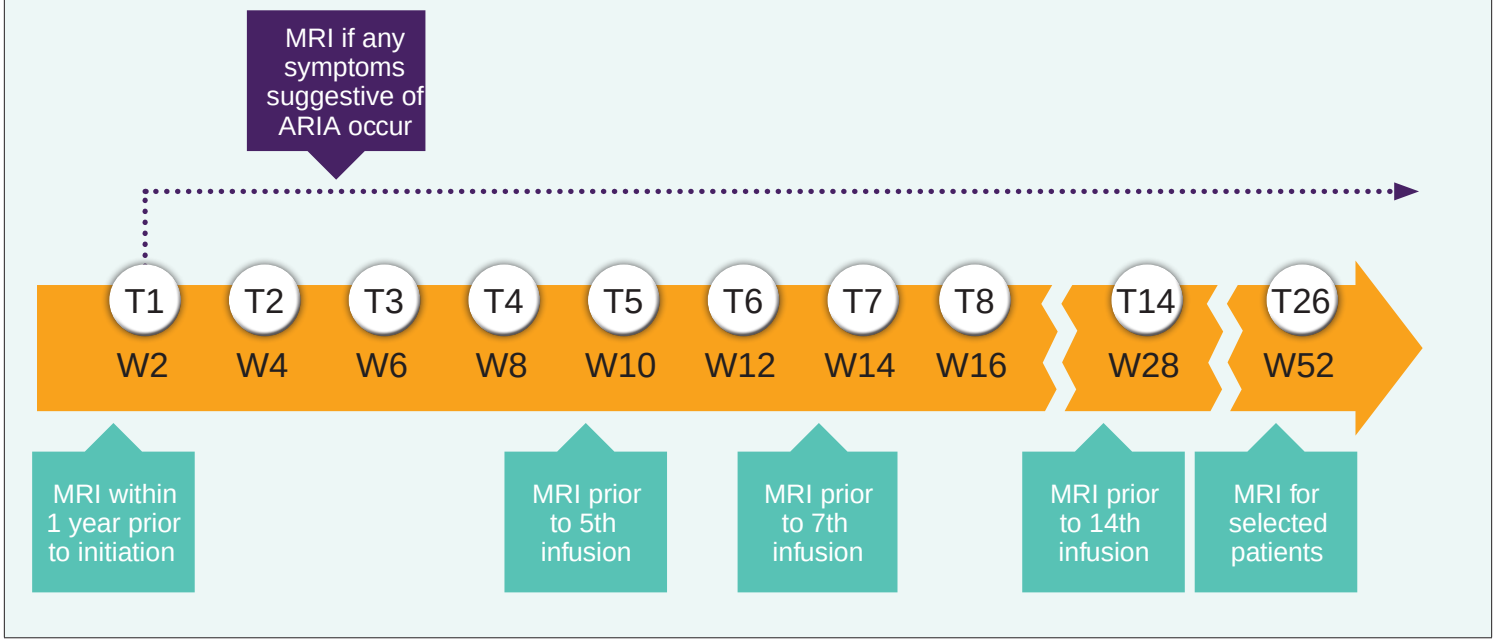
Review this section of the toolkit to learn more about the recommended safety MRI monitoring schedule for lecanemab and when supplementation with additional MRI scans may be appropriate.

ARIA Monitoring

ALZHEIMER'S ASSOCIATION

MRI monitoring for lecanemab



LECANEMAB APPROPRIATE USE RECOMMENDATIONS

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Review this section of the toolkit to learn more about the radiographi9Biorrt, accompanyroms,Band when lecanemab discontinuation may be appropriate.

Descrrption of mild, mode/MCidadte,Band severe /MCidaddiog/MCidadphic ARIA (from the Prescrr

ARIA Type	Rity		
	Mild	Mode/MCidadte	Severe
ARIA-E	FLAIR hyperintensity con ned to sulcusBand/or cortex/subcortex white matter in 1 location <5 cm	FLAIR hyperintensity 5 to 10 cm in sreatest dimension, or more than 1 site of involvement, each measuring <10 cm	FLAIR hyperintensity >10 cm with

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Review this section of the toolkit to learn more about the incidence, grading, and management of infusion reactions with lecanemab.

Incidence

Usually occur during the rst 2 treatments and seen during the infusion or up to several hours after the infusion.
In the CLARITY AD phase 3 trial of lecanemab, infusion reactions occurred in 26.4% of participants on lecanemab.

Infusion reaction symptoms

Fever, chills, headache, rash, nausea, vomiting, abdominal discomfort, and elevated blood pressure. Infusion reactions typically resolve within 24 hours and can usually be managed at home.

Grading of infusion reactions

Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Mild transient reaction; infusion interruption not indicated; intervention not indicated	Infusion interruption but responds promptly to symptomatic treatment (eg, antihistamines, acetaminophen, NSAIDs, narcotics, IV uids); prophylactic medication indicated for <24 hours	Prolonged recurrence of symptoms following initial improvement; hospitalization may be indicated for clinical sequelae (eg, poorly controlled hypertension)	Life-threatening consequences; urgent intervention indicated (may require pressor or ventilatory support)	Death

Managing reactions

- For mild to moderate skin hypersensitivity reactions, diphenhydramine or a topical corticosteroid cream can be used

Grade 2 Infusion Reactions

- Interrupt lecanemab
- Treat with diphenhydramine and acetaminophen every 4-6 hours until symptoms fully resolve
- 30 minutes before the next infusion after a reaction, pretreatment with oral diphenhydramine (25 mg-50 mg) and oral acetaminophen (650 mg-1000 mg) should occur
  - If this is ine ective, low-dose oral dexamethasone (0.75 mg) or oral methylprednisolone (80 mg) for management of elevated blood pressure can be given 6 hours prior to infusions
- A prophylactic regimen should be used until the patient is asymptomatic for 2-4 infusions
- If a new reaction occurs, oral diphenhydramine (25 mg-50 mg) and oral acetaminophen (650 mg-1000 mg) can be given every 4-6 hours

Grade 3 or Higher Infusion Reactions

- Discontinue lecanemab
- Significant symptoms can be treated with oral dexamethasone Ö X Ú { ¬ ƒ P - K o Á í " P - K ü × or oral methylprednisolone (80 mg twice daily for 2-3 days)

AD, Alzheimer's disease; HCP, healthcare provider; IV, intravenous; MCI, mild cognitive impairment; NSAID, nonsteroidal anti-inflammatory.

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Review this section of the toolkit to learn more about recommended resources for the safe and e ective use of lecanemab and management of serious or severe ARIA.

Resources needed by a clinician or medical center for the safe and e ective use of lecanemab

- Clinician skilled in the assessment of cognition to identify individuals with MCI or mild dementia due to AD
- MRI available for baseline assessment of cerebrovascular pathology and for monitoring of amyloid-related imaging abnormalities (ARIA)
- Radiologists, neurologists, or other clinicians expert in the identi cation and interpretation of cerebrovascular lesions and ARIA
- Amyloid positron emission tomography or lumbar puncture capability to determine the amyloid status of treatment candidates
- Radiologists, nuclear medicine specialists, neurologists, or other specialists skilled in the interpretation of amyloid imaging or neurologist, radiologists, or other clinicians skilled in the conduct of lumbar puncture
- Apolipoprotein E genotyping resources
- Genetic expertise to counsel patients on the implications of apolipoprotein E genotyping
- Expertise in communicating with patients and care partners regarding anticipated bene ts, potential harm, and requirements for administration and monitoring while on lecanemab
- Infusion settings that can be made available every 2 weeks to patients receiving therapy
- Knowledgeable sta at infusion sites capable of recognizing and managing infusion reactions