LECANEMAB APPROPRIATE USE RECOMMENDATIONS

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 confirmed 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 offer lecanemab for a patient meeting eligibility criteria. These AURs apply to lecanemab; other anti-amyloid monoclonal antibodies may have different management requirements. AURs specific 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

ALZHEIMER'S® ASSOCIATION

Lecanemab inclusion criteria from CLARITY AD and proposed in the AUR	
Eligibility Criteria Used in the CLARITY AD Pivotal Trial of Lecanemab	**Eligibility Criteria for Lecanemab Treatment From the AUR**
Inclusion Criteria (ie, required criteria for an individual to be considered)	
Diagnosis of MCI or mild AD dementia	Clinical diagnosis of MCI or mild AD dementia[a]
Objective impairment in episodic memory as indicated by at least 1 standard deviation below age-adjusted mean in the WMS-IV LMII	Clinical diagnosis of MCI or mild AD dementia[a]
Positive biomarker for brain amyloid pathology	Positive amyloid PET or CSF studies indicative of AD
50-90 years of age	Physician judgement used for patients outside the 50-90 year age range
MMSE score >22 at screening and baseline and <30 at screening and baseline	MMSE 22-30 or other cognitive screening instrument with a score compatible with early AD
BMI >17 and <35 at screening	Physician judgement used for patients at the extremes of BMI
If receiving an acetylcholinesterase inhibitor (donepezil, rivastigmine, galantamine) or memantine or both must be on a stable dose for at least 12 weeks prior to baseline	Patients may be on cognitive enhancing agents (donepezil, rivastigmine, galantamine, or memantine) for AD; patients may not be on aducanumab
Unless otherwise stated, participants must have been on stable doses of all other (that is, non-AD-related) permitted concomitant medications for at least 4 weeks prior to baseline	Patients may be on standard of care for other medical illnesses (see below for specifics regarding anticoagulation)
Have an identified study partner	Have a care partner or family member(s) who can ensure that the patient has the support needed to be treated with lecanemab
Provide written informed consent	Patients, care partners, and appropriate family members should understand the requirements for lecanemab therapy and the potential benefit and potential harm of treatment

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

AD, Alzheimer's disease; AUR, appropriate use recommendations; BMI, body mass index; CSF, cerebrospinal fluid; HCP, healthcare provider; MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination; PET, positron emission tomography; WMS-IV LMII, Wechsler Memory Scale IV-Logical Memory (subscale) II.

[a]MCI due to AD (intermediate likelihood) diagnostic criteria include cognitive concerns by the patient, knowledgeable informant, or the physician; objective impairment in one or more cognitive domains including memory, executive function, attention, language, and visuospatial skills; generally preserved activities of daily living; no dementia; and positive AD biomarker. Dementia diagnostic criteria include cognitive or behavioral impairment involving a minimum of 2 of the following domains: memory, executive function, visuospatial function, language, or behavior; cognitive impairment detected and diagnosed through a combination of (1) history-taking from the patient and a knowledgeable informant and (2) an objective cognitive assessment; symptoms interfere with the ability to function at work or perform usual activities; decline from previous levels of functioning; and symptoms are not explained by delirium or major psychiatric disorder. MMSE score of 22-30 is used to define MCI and mild AD dementia.

Cummings J, Apostolova L, Rabinovici GD, et al. Lecanemab: appropriate use recommendations. *J Prev Alzheimers Dis.* 2023;10(3):362-377. doi:10.14283/jpad.2023.30

Please scan or click below to view the full Prescribing Information for lecanemab

Please scan or click below to view the lecanemab appropriate use recommendations publication

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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 (cont'd)

ALZHEIMER'S ASSOCIATION

Lecanemab exclusion criteria from CLARITY AD and proposed in the AUR[1]	
Eligibility Criteria Used in the CLARITY AD Pivotal Trial of Lecanemab	**Eligibility Criteria for Lecanemab Treatment From the AUR**
Exclusion Criteria (ie, criteria that render an individual ineligible)	
Any neurological condition that may be contributing to cognitive impairment above and beyond that caused by the participant's AD	Any medical, neurologic, or psychiatric condition that may be contributing to the cognitive impairment or any non-AD MCI or dementia
More than 4 microhemorrhages (defined as 10 mm or less at the greatest diameter); a single macrohemorrhage >10 mm at greatest diameter; an area of superficial siderosis; evidence of vasogenic edema; multiple lacunar infarcts or stroke involving a major vascular territory; severe small vessel; or other major intracranial pathology	More than 4 microhemorrhages (defined as 10 mm or less at the greatest diameter); a single macrohemorrhage >10 mm at greatest diameter; an area of superficial siderosis; evidence of vasogenic edema; more than 2 lacunar infarcts or stroke involving a major vascular territory; severe subcortical hyperintensities consistent with a Fazekas score of 3; evidence of ABRA; CAA-ri; or other major intracranial pathology that may cause cognitive impairment
Evidence of other clinically significant lesions on brain MRI at screening that could indicate a dementia diagnosis other than AD	MRI evidence of a non-AD dementia
History of TIA, stroke, or seizures within 12 months of screening	Recent history (within 12 months) of stroke or TIAs or any history of seizures
Any psychiatric diagnosis or symptoms (example, hallucinations, major depression, or delusions) that could interfere with study procedures in the participant	Mental illness (eg, psychosis) that interferes with comprehension of the requirements, potential benefit, and potential harms of treatment and are considered by the physician to render the patient unable to comply with management requirements
GDS score >8 at screening	Major depression that will interfere with comprehension of the requirements, potential benefit, and potential harms of treatment; patients for whom disclosure of a positive biomarker may trigger suicidal ideation. Patients with less severe depression or whose depression resolves may be treatment candidates
Any immunological disease that is not adequately controlled, or which requires treatment with immunoglobulins, systemic monoclonal antibodies (or derivatives of monoclonal antibodies), systemic immunosuppressants, or plasmapheresis during the study	Any history of immunologic disease (eg, lupus erythematosus, rheumatoid arthritis, Crohn's disease) or systemic treatment with immunosuppressants, immunoglobulins, or monoclonal antibodies or their derivatives
Participants with a bleeding disorder that is not adequately controlled (including a platelet count <50,000 or INR >1.5 for participants who are not on anticoagulant treatment, eg, warfarin)	Patients with a bleeding disorder that is not under adequate control (including a platelet count <50,000 or INR >1.5 for participants who are not on an anticoagulant)
Participants who are on anticoagulant therapy should have their anticoagulant status optimized and be on a stable dose for 4 weeks before screening	Patients on anticoagulants (coumadin, dabigatran, edoxaban, rivaroxaban, apixaban, betrixaban, or heparin) should not receive lecanemab; tPA should not be administered to individuals on lecanemab
Any other medical conditions (example, cardiac, respiratory, gastrointestinal, renal disease) which are not stably and adequately controlled, or which could affect the participant's safety or interfere with the study assessments	Unstable medical conditions that may affect or be affected by lecanemab therapy

Patients on experimental therapy were excluded from the CLARITY AD trial. Patients and their care partners should discuss with the leadership of a clinical trial of potential interest whether ongoing treatment with lecanemab is compatible with trial eligibility.[2]

ABRA, amyloid beta-related angiitis; AD, Alzheimer's disease; AUR, appropriate use recommendations; CAA-ri, cerebral amyloid angiopathy-related inflammation; GDS, Geriatric Depression Scale; HCP, healthcare provider; INR, international normalized ratio; MCI, mild cognitive impairment; MRI, magnetic resonance imaging; PET, positron emission tomography; TIA, transient ischemic attack; tPA, tissue plasminogen activator.

1. Cummings J, Apostolova L, Rabinovici GD, et al. Lecanemab: appropriate use recommendations. *J Prev Alzheimers Dis.* 2023;10(3):362-377. doi:10.14283/jpad.2023.30 **2.** Clinicaltrials.gov. https://www.clinicaltrials.gov/study/NCT03887455#participation-criteria. Accessed January 24, 2024.