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 ARIA rates among *APOE4* carriers and recommendations for *APOE* testing prior to initiating lecanemab.

Apolipoprotein E (APOE) Genetic Testing

ALZHEIMER'S ASSOCIATION

APOE in humans has 3 alleles: *APOE ε3* (*APOE3*), *APOE ε2* (*APOE2*), and *APOE ε4* (*APOE4*). The *APOE4* genotype is present in ~20% to 25% of the population and increases the risk of clinical AD in a dose-dependent manner. There is a significant interaction with sex, with female *APOE4* carriers at higher risk for AD than males, particularly at younger ages. People who are *APOE4* heterozygotes possess 1 copy of the allele, while those who are homozygotes possess 2 copies of the allele. In the CLARITY AD trial, 53% of patients were heterozygous for *APOE4* and 16% were homozygous for *APOE4*.

Amyloid-related imaging abnormalities (ARIA) is a common side effect of treatment with amyloid-lowering monoclonal antibodies. Two types of ARIA can occur: ARIA-E with edema and ARIA-H with hemorrhagic changes. Risk for ARIA, symptomatic ARIA, and recurrent ARIA is higher among *APOE4* carriers (especially homozygotes). *APOE4* carriers are also at increased risk for cerebral amyloid angiopathy-related inflammation/amyloid beta-related angiitis (CAA-ri/ABRA), a risk factor for ARIA.

ARIA rates reported for the CLARITY AD trial of lecanemab

	***APOE4* Noncarrier Lecanemab (N=278)**	***APOE4* Heterozygote Lecanemab (N=479)**	***APOE4* Homozygote Lecanemab (N=141)**
ARIA-E	5.4%	10.9%	32.6%
Symptomatic ARIA-E	1.4%	1.7%	9.2%
Serious event with ARIA-E	0.7%	0.4%	2.1%
Total ARIA-H (Concurrent & Isolated)	11.9%	14.0%	39.0%

Given the increased risk for ARIA in *APOE4* carriers, *APOE* genotyping is recommended for all consenting patients being considered for lecanemab therapy before initiating treatment. The *APOE* gene produces the APOE protein, and some laboratory tests are able to determine *APOE* status by assessing the patient's proteotype. Information regarding the patient's *APOE* status will inform risk discussions and help guide safety considerations. Genotyping of a treatment candidate that reveals the patient to be an *APOE4* gene carrier has implications for all first-degree relatives, as they might share the genetic risk. Counseling regarding genotyping and its ramifications has an important role in appropriate treatment discussions.

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

AD, Alzheimer's disease; *APOE*, apolipoprotein E; *APOE4*, apolipoprotein ε4 allele; ARIA, amyloid-related imaging abnormalities; ARIA-E, ARIA with edema; ARIA-H, ARIA with hemorrhagic changes; HCP, healthcare provider; MCI, mild cognitive impairment.

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