May 15, 2026

National Government Services Medical Policy Unit
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Submitted electronically via: NGSDraftLCDComments@anthem.com

Subject: Molecular Pathology Procedures (DL35000)

Dear Medical Policy Unit,

On behalf of the Association for Molecular Pathology (AMP), The American College of Medical Genetics and Genomics (ACMG) and the College of American Pathologists (CAP), thank you for the opportunity to comment on the draft Local Coverage Determination (dLCD) entitled: Molecular Pathology Procedures.

AMP is an international medical and professional association representing approximately 3,100 physicians, doctoral scientists, and medical laboratory scientists (technologists) who perform or are involved with laboratory testing based on knowledge derived from molecular biology, genetics, and genomics. Membership includes professionals from academic medicine, hospital-based and private clinical laboratories, government, and the in vitro diagnostics industry.

The CAP is the world's largest organization of board-certified pathologists and leading provider of laboratory accreditation and proficiency testing programs. The CAP serves patients, pathologists, and the public by fostering and advocating excellence in the practice of pathology and laboratory medicine worldwide.

Founded in 1991, the American College of Medical Genetics and Genomics (ACMG) is a prominent authority in the field of medical genetics and genomics and the only nationally recognized medical professional organization solely dedicated to improving health through the practice of medical genetics and genomics. The only medical specialty society in the US that represents the full spectrum of medical genetics disciplines in a single organization, the ACMG provides education, resources, and a voice for more than 2,500 clinical and laboratory geneticists, genetic counselors, and other healthcare professionals. ACMG's mission is to improve health through the clinical and laboratory practice of medical genetics as well as through advocacy, education and clinical research, and to guide the safe and effective integration of genetics and genomics into all of medicine and healthcare, resulting in improved personal and public health.

AMP, ACMG, and CAP members are highly involved in the development, validation, and interpretation of molecular diagnostic tests, including clinically actionable genetic tests that guide therapeutic decision-making and help ensure the safe use of treatments in patients with Alzheimer's disease. AMP and CAP support the proposal to remove APOE from the list of Tier 2 non-covered codes/gene

combinations. APOE genotyping is FDA-recommended, guideline-endorsed, supported by phase 3 trial evidence, and alters management of a CMS-covered drug, establishing clear medical necessity for reimbursement. As such, **AMP, ACMG, and CAP urge NGS to explicitly cover APOE testing for pre-treatment risk stratification before anti-amyloid monoclonal antibody therapy**.

APOE genotyping for patients with diagnosed Alzheimer's disease who are being considered for anti-amyloid therapies is clinically actionable and directly informs treatment decisions, satisfying Medicare's "reasonable and necessary" standard under §1862(a)(1)(A). As NGS has been made aware, the prescribing information for lecanemab states that APOE ε4 testing should be performed prior to initiation of therapy to inform risk discussions related to amyloid-related imaging abnormalities (ARIA), the primary safety concern associated with this class of therapies.[1] APOE ε4 status is the strongest known predictor of ARIA risk, with significantly elevated rates observed in ε4 carriers, particularly homozygotes.[2,3,4] In this context, APOE genotyping is not screening or exploratory testing; it is a necessary component of safe and appropriate use of a CMS-covered therapy.

APOE genotyping directly informs clinical decision-making through treatment selection (e.g., whether to initiate anti-amyloid therapy), risk stratification and informed consent discussions, and monitoring strategies for ARIA complications. For example, patients with an APOE ε4/ε4 genotype face substantially increased ARIA risk and may require alternative treatment approaches or enhanced monitoring protocols, while non-carriers may proceed under standard monitoring. Our members report that APOE results are routinely incorporated into treatment decisions and patient counseling for individuals with Alzheimer's disease.[5] This demonstrates that APOE genotyping has immediate and meaningful implications for patient management, rather than speculative or long-term predictive value.

Further, the use of APOE genotyping in this clinical context is supported by major professional societies. The American Academy of Neurology recommends offering APOE ε4 testing prior to initiation of anti-amyloid monoclonal antibody therapy and the American Academy of Family Physicians similarly recommends APOE testing for patients being considered for amyloid-targeting therapies.[6,7] These recommendations establish APOE testing as part of the standard of care for managing patients eligible for these therapies.

Explicit Medicare coverage of APOE genotyping in this setting aligns with National Government Services' policy on pharmacogenomic testing (L39995), as APOE testing predicts risk of serious adverse events and directly informs the use of a covered therapy. APOE testing is analogous to other tests routinely covered by Medicare that guide the safe use of therapeutics, including HLA-B*5701* testing prior to abacavir therapy and DPYD testing prior to fluoropyrimidine therapy. Because Medicare covers lecanemab under

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1 U.S. Food and Drug Administration. *LEQEMBI (lecanemab) prescribing information.* Updated January 23, 2026.

2 Jeong SY, Suh CH, Lim JS, et al. Incidence of Amyloid-Related Imaging Abnormalities in Phase III Clinical Trials of Anti-Amyloid-β Immunotherapy: An Updated Meta-Analysis. *Neurology.* 2025;104(8):e213483.

3 Zimmer JA, Ardayfio P, Wang H, et al. Amyloid-Related Imaging Abnormalities With Donanemab in Early Symptomatic Alzheimer Disease. *JAMA Neurol.* 2025;82(5):461–469.

4 Loomis SJ, Miller R, Castrillo-Viguera C, et al. Genome-Wide Association Studies of ARIA From the Aducanumab Phase 3 Studies. *Neurology.* 2024;102(3):e207919.

5 Ritchie, Marina et al. "Apolipoprotein E Genetic Testing in a New Age of Alzheimer Disease Clinical Practice." Neurology. Clinical practice vol. 14,2 (2024): e200230. doi:10.1212/CPJ.0000000000200230

6 Ramanan VK, Armstrong MJ, Choudhury P, et al. Antiamyloid Monoclonal Antibody Therapy for Alzheimer Disease: Emerging Issues in Neurology. *Neurology.* 2023;101(19):842–852.

7 Arias JJ, Tyler AM, Douglas MP, Phillips KA. Private Payer Coverage Policies for ApoE-e4 Genetic Testing. *Genet Med.* 2021;23(4):614–620.

Part B, the associated pharmacogenomic testing used to ensure safe administration meets the same standard for coverage.[8,9,10]

In conclusion, to ensure appropriate patient access, AMP, ACMG, and CAP recommend that the final LCD be revised to explicitly cover APOE genotyping for patients who are being considered for anti-amyloid monoclonal antibody therapy. Simply removing APOE from the list of non-covered codes may lead to variability in coverage and access and put patients at significant risk, which is unwarranted given the state of the clinical evidence supporting testing. Affirmative coverage language is necessary to reflect current clinical practice, align with FDA labeling and guideline recommendations, and ensure safe and effective use of covered therapies.

AMP, ACMG, and CAP appreciate the opportunity to provide input on this dLCD and would welcome continued engagement with the contractor on this important issue. Please contact Samantha Pettersen, Public Policy Manager at Spettersen@amp.org or Nonda Wilson, Economic Affairs Manager at nwilson@cap.org if we can be of further assistance.

Sincerely,

Association for Molecular Pathology
American College of Medical Genetics and Genomics
College of American Pathologists

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[8] Daval CJR, Kesselheim AS. Authority of Medicare to Limit Coverage of FDA-Approved Products. *JAMA Intern Med.* 2023;183(9):999–1004.

[9] Zhou FF, Essien UR, Souza JM, et al. Disparities in Early Lecanemab Uptake Among US Medicare Beneficiaries. *JAMA Netw Open.* 2025;8(5).

[10] Klein EG, Schroeder K, Wessels AM, et al. Donanemab Data and Coverage With Evidence Development. *Alzheimers Dement.* 2024;20(4):3127–3140.