AMERICAN ACADEMY OF NEUROLOGY®

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August 8, 2023

Tamara Syrek Jensen, JD
Director, Coverage and Analysis Group
Center for Clinical Standards and Quality
Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244

RE: Beta Amyloid Positron Emission Tomography in Dementia and Neurodegenerative Disease [CAG-00431R]

Dear Ms. Syrek Jensen

The American Academy of Neurology (AAN) is the world's largest neurology specialty society representing more than 40,000 neurologists and clinical neuroscience professionals. The AAN is dedicated to promoting the highest quality patient-centered neurologic care. A neurologist is a physician with specialized training in diagnosing, treating, and managing disorders of the brain and nervous system. These disorders affect one in six people and include conditions such as multiple sclerosis (MS), Alzheimer's disease, Parkinson's disease, stroke, migraine, epilepsy, traumatic brain injury, ALS, and spinal muscular atrophy.

The AAN appreciates that the Centers for Medicare and Medicaid Services (CMS) has proposed the retirement of the national coverage determination (NCD) for beta-amyloid positron emission tomography (PET) in dementia and neurodegenerative disease (NCD 220.6.20). The AAN believes it is appropriate that this NCD be retired given the recent FDA approval of monoclonal antibodies (mAbs) products directed against amyloid for the treatment of Alzheimer's disease (AD). We strongly urge the agency to finalize this proposal expeditiously. The AAN, along with the American Geriatric Society (AGS) and the Society for Nuclear Medicine and Molecular Imaging (SNMMI)[1], sent a letter to the administrator in 2021 recommending that this NCD be retired in order to expand access for patients that may be candidates for mAbs, as detection of amyloid presence is a critical tool for neurologists when considering the use of these therapies. Retirement of this NCD would mean that beta-amyloid PET would be covered at the discretion of Part A/B Medicare Administrative Contractors (MACs) just like every other PET scan, including Tau PET, furnished for non-oncologic indications.

[1] AAN AGS and SNMMI joint comments on National Coverage Analysis (NCA) for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease

The AAN requests that CMS clarify that, along with removing limitations on the reimbursement of these scans, the radiopharmaceuticals required to complete them will also regain covered status. The AAN believes this should be explicitly clarified in the final policy to ensure that the MACs are advised the radio pharmaceutical is an essential requisite injected medication for every study, and needs to be covered, as without coverage there cannot be a PET scan.

There is robust literature demonstrating that beta-amyloid PET influences clinical decision-making. In the IDEAS Study which included 11,409 participants with mild cognitive impairment (MCI) or dementia of uncertain cause, ninety days after beta-amyloid PET, patient care plans changed (compared with the pre-PET plan) in 60.2% of patients initially characterized as having MCI and 63.5% of patients initially characterized as having dementia of unknown cause.[2] Similarly, Pontecorvo et al. found that immediate notification of beta-amyloid PET findings was associated with a change in patient management, particularly changes in AD medication. The information provided by the scan had a significant impact on prescribing patterns in that acetylcholinesterase inhibitors were prescribed to 67% of the amyloid-positive and 27% of the amyloid-negative subjects in the information group compared with 56 and 43%, respectively, in the control group ($p < 0.0001$).[3] Based on the evidence demonstrating the clinical utility of amyloid PET, CMS should retire NCD 220.6.20 and allow coverage at contractor discretion for beta-amyloid PET, similar to coverage for other non-oncologic PET indications.

While the AAN understands that CMS has an interest in controlling costs and protecting program integrity, we believe beta-amyloid PET scans are a vital diagnostic tool and deference should be appropriately shown to the judgment of the treating clinician. Restriction to one PET scan per lifetime is likely to negatively impact participation in Coverage with Evidence Development requirements under the NCD for mAbs directed against amyloid for the treatment of Alzheimer's disease.[4] The AAN also believes that current restrictions on beta-amyloid PET scans may negatively impact care by limiting the information that physicians need to make appropriate treatment decisions, including whether to stop monoclonal antibody therapy. If Medicare coverage is limited to one scan per patient, the additional PET scans furnished under the mAb CED requirements will not be covered, and those costs will have to be borne by the trial sponsors or directly by beneficiaries. With multiple products now approved by the FDA, requiring confirmation of amyloid pathology

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[2] Rabinovici GD, Gatsonis C, Apgar C, et al. Association of Amyloid Positron Emission Tomography With Subsequent Change in Clinical Management Among Medicare Beneficiaries With Mild Cognitive Impairment or Dementia. JAMA. 2019 04 02;321(13):1286-94. doi: https://dx.doi.org/10.1001/jama.2019.2000. PMID: 30938796.

[3] Pontecorvo MJ, Siderowf A, Dubois B, et al. Effectiveness of Florbetapir PET Imaging in Changing Patient Management. Dement Geriatr Cogn Disord. 2017;44(3-4):129-43. doi: https://dx.doi.org/10.1159/000478007. PMID: 28787712

[4] Monoclonal Antibodies Directed against Amyloid for the Treatment of Alzheimer's Disease, 7 Apr. 2022, www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=N&ncaid=305&fromTracking=Y&.

prior to initiating treatment[5][6] and a clearly demonstrated interest on the part of CMS of better understanding the safety and efficacy of these products, pre-existing policy is no longer necessary.

Additionally, the AAN notes that limiting amyloid PET scans to one per lifetime raises major health equity issues and may limit CED participation for low-income beneficiaries. Doing so would also run counter to CMS' stated goal of generating data that is generalizable to the broader Medicare population.[7] Furthermore, the AAN believes there may be circumstances in which the clinician believes an additional scan is warranted. Such circumstances include but are not limited to, technical issues with tracer, movement artifact, development of new cognitive symptoms, or the initial scan being done when the patient is not symptomatic. Additionally, given the approval and growing availability of mAbs for the treatment of AD, further amyloid testing may be reasonable and necessary for ensuring optimal care for patients, especially if a treatment were to be approved with a "treat to clear" regimen wherein confirmation of cleared amyloid could serve to reduce or end the course of treatment which will benefit patients clinically and economically.

The AAN would like to reiterate our gratitude to CMS for heeding our recommendations and our approval of this proposed retirement. Coverage of these scans, and the agents required for them, will assist our members in diagnosing and treating their patients. If you have any questions regarding these comments or seek further input, please contact Matt Kerschner, Director, Regulatory Affairs and Policy at mkerschner@aan.com or Max Linder, Senior Government Relations Manager at mlinder@aan.com.

Sincerely,

Carlayne E. Jackson, MD, FAAN
President, American Academy of Neurology

[5] Leqembi (lecanemab) [FDA Label] Food and Drug Administration website. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761269s001lbl.pdf Revised 07/2023
[6] Aduhelm (aducanumab) [FDA Label] Food and Drug Administration website. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/761178s005lbl.pdf Revised 04/2022
[7] Monoclonal Antibodies Directed against Amyloid for the Treatment of Alzheimer's Disease, 7 Apr. 2022, www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=N&ncaid=305&fromTracking=Y&.