AMERICAN ACADEMY OF NEUROLOGY®

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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 38,000 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 initiated a reconsideration 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 has received renewed focus following the coverage determination process for monoclonal antibodies (mAbs) directed against amyloid for the treatment of Alzheimer's disease (AD).

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. The AAN is reiterating this request, as we continue to believe that NCD 220.6.20 should be retired in its entirety. Retirement would mean that beta-amyloid PET would be covered at the

[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

discretion of Part A/B Medicare Administrative Contractors (MACs) just like every other PET scan, including Tau PET, furnished for non-oncologic indications.

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.

If the existing NCD is not retired in its entirety, the AAN believes that this reconsideration provides an opportunity to modify current coverage with evidence development (CED) requirements for these scans, to remove the restriction on the number of scans that will be covered. The AAN is not aware of any clinical evidence supporting a specific numeric limit on the use of beta-amyloid PET scans. 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 clinical judgment. Restriction to one PET scan per lifetime is likely to negatively impact participation in trials under the NCD for mAbs directed against amyloid for the treatment of Alzheimer's disease. 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 (e.g., to stop monoclonal antibody therapy). If Medicare coverage is limited to one scan per patient, the additional PET scans furnished during the trials will not be covered and those costs will have to be borne by the trial sponsors or beneficiaries. This limitation raises major health equity issues and may limit trial participation for low-income beneficiaries. Furthermore, the AAN believes that 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, the AAN wants to take this opportunity to reiterate our gratitude for the prudent decision-making this year regarding the final NCD for aducanumab and other mAbs

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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.

directed against amyloid for the treatment of Alzheimer's Disease. The final NCD demonstrated an understanding of both current limitations and the great potential impact of these novel therapies on patients living with AD. We were grateful to have been able to engage with CMS multiple times throughout the process and appreciate that several changes were made to the final NCD in alignment with our recommendations. These include modification so that trials are not solely limited to the hospital outpatient setting, a commitment from CMS to quickly reconsider the NCD if a mAb product has answered the CED questions with quality evidence, and deference to CED investigators in determining key elements of study design.

We are eager to offer that same support to CMS as this reconsideration moves forward in order to establish appropriate coverage for diagnostic and therapeutic services for AD patients. If you have any questions regarding these comments or seek further input, please contact Matt Kerschner, Director, Regulatory Affairs at mkerschner@aan.com or Max Linder, Government Relations Manager at mlinder@aan.com.

Sincerely,

Orly Avitzur, MD, MBA, FAAN

President, American Academy of Neurology