July 13, 2022

Joseph Hutter, M.D.
Coverage and Analysis Group
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244

Dear Dr. Hutter:

The Society of Nuclear Medicine and Molecular Imaging (SNMMI), the American Geriatrics Society (AGS), the American Academy of Neurology (AAN) appreciate that CMS has initiated a reconsideration of the national coverage determination (NCD) on beta amyloid positron emission tomography (PET) in dementia and neurodegenerative disease (NCD 220.6.20). This NCD limits coverage of beta amyloid PET scans to CMS-approved clinical trials that meet the requirements for Coverage under Evidence Development (CED) and limits the number of beta amyloid PET scans covered per patient to one per lifetime. This means that if a patient had a negative beta amyloid PET scan when enrolled in a trial in 2015, no additional PET scans will be covered by Medicare even though seven years have elapsed, and the patient's beta amyloid status may have changed.

We continue to believe that this NCD inappropriately limits coverage of beta amyloid PET for Medicare beneficiaries, including beneficiaries who may be candidates for monoclonal antibodies (mAbs) directed against amyloid for the treatment of Alzheimer's Disease (AD) under the recently finalized mAbs NCD. Furthermore, in order for a PET scan to be covered by Medicare for a patient seeking to participate in a mAb trial, the patient has to enroll in the trial even though the scan may be negative, showing that the patient is not in fact a candidate for mAb therapy. In our view it puts an inappropriate administrative burden on patients and trial sponsors to require patients to enroll in a clinical trial in order to determine whether they are eligible to participate in that trial.

As we have recommended to CMS in the past, we continue to believe that NCD 220.6.20 should be retired in its entirety. Retirement of the 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.

There is robust literature demonstrating that beta amyloid PET supports 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.[1] 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 ($p < 0.0001$).[2] 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.

However, if this NCD is not retired, we urge CMS to remove the limitation covering only one beta amyloid PET scan per patient per lifetime. All patients in the Phase 2 and 3 clinical trials for aducanumab and other late phase mAbs were required to have a positive beta amyloid PET scan before entering the trial and received additional scans during the trials. The additional scans were used (1) to assess impact on cerebral amyloid plaque content, and (2) to determine whether to continue therapy. In the phase 2 trial of donanemab, amyloid plaque levels were evaluated using PET at 24, 52, and 76 weeks, with an increasing percentage of patients in the donanemab group having amyloid-negative status over time. The authors report that approximately 27.4% and 54.7% of participants in the donanemab group had sufficient lowering of the amyloid plaque level to switch to placebo infusion at 28 and 56 weeks, respectively.[3]

Restriction to one PET scan per lifetime will negatively impact participation in trials under the mAbs NCD and may negatively impact care by not providing physicians the information they need to make appropriate treatment decisions (e.g., to stop monoclonal antibody therapy, which could lead to unwanted toxicity and no benefit to the patient). 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 situation raises major health equity issues and may limit the participation in trials of low-income beneficiaries. It also creates considerable administrative and financial complications for trial sponsors.

We are not aware of any clinical evidence supporting any limit on the number of beta amyloid PET scans whether the number is one or any other number. As stated above, there is no evidence to suggest that an outdated scan can provide the diagnostic information needed to determine whether a patient is currently a candidate for mAb therapy or whether mAb therapy should be discontinued. Central nervous system beta amyloid status can change over time and ongoing clinical trials for monoclonal antibodies have used the results of post treatment beta amyloid PET to inform a decision to discontinue mAb therapy.

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[1] 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.

[2] 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.

[3] Mintun MA, Lo A, Evans C, et al. Donanemab in Early Alzheimer's Disease. N ENGL J MED 2021: 384 (18): 1691 - 1704.

Furthermore, we note that there is no coverage limitation on the number of covered blood or cerebrospinal fluid (CSF) tests for identifying beta amyloid status nor is there any limitation requiring those tests be performed in a clinical trial - even though blood and CSF testing have not been authorized by the FDA for that indication. In fact, beta amyloid PET is the only FDA authorized test for detecting beta amyloid in the central nervous system. If CMS does not retire or revise NCD 220.6.20, this inequitable coverage of beta amyloid PET as compared to the other modalities for identifying beta amyloid would continue.

We urge CMS to retire NCD 220.6.20. If CMS declines to do so, then the NCD should be revised to provide for coverage of beta amyloid PET at the discretion of the treating physician with no limitation on the number of scans covered per patient per lifetime.

We look forward to continuing to work with CMS on establishing appropriate coverage for diagnostic and therapeutic services for AD patients.

Sincerely,

Society of Nuclear Medicine and Molecular Imaging

American Geriatrics Society

American Academy of Neurology