PERSONALIZED MEDICINE COALITION

August 16, 2023

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

BY ELECTRONIC DELIVERY

Re: Proposed National Coverage Determination Reconsideration for Beta Amyloid Positron Emission Tomography in Dementia and Neurodegenerative Disease (CAG-00431R)

Dear Dr. Chin:

The Personalized Medicine Coalition (PMC), a multi-stakeholder group comprising more than 200 institutions from across the health care spectrum, thanks the Centers for Medicare & Medicaid Services (CMS) for the opportunity to comment on its *Proposed National Coverage Determination (NCD) Reconsideration for Beta Amyloid Positron Emission Tomography (PET) in Dementia and Neurodegenerative Disease*.[i] Beta amyloid PET imaging is a critical tool for diagnosing Alzheimer's disease (AD), ruling out a diagnosis of AD, and evaluating whether and how certain treatments may work for a patient. The emergence of new anti-amyloid treatments, some requiring multiple PET scans to inform an individual patient's treatment course, makes timely and appropriate access to this imaging tool essential for individuals living with AD and their families.

PMC supports CMS' proposals to remove the limit of one scan per lifetime and to end Coverage with Evidence Development (CED) for beta amyloid PET imaging for Medicare beneficiaries. This coverage approach is consistent with the evidence developed since NCD 220.6.20 was issued in September of 2013. Instead of finalizing its proposal to permit Medicare Administrative Contractors (MACs) to make coverage determinations independently, however, PMC urges CMS to keep a national coverage policy in place allowing more than one scan per lifetime without CED. We are concerned that in the absence of a national coverage policy, MACs and Medicare Advantage (MA) plans could develop inconsistent coverage policies that create new access barriers for Medicare beneficiaries.

PMC defines personalized medicine as an evolving field in which physicians use diagnostic tests to determine which medical treatments will work best for each patient or use medical interventions to alter molecular mechanisms that impact health. By combining data from diagnostic tests with an individual's medical history, circumstances, and values, health care providers can develop targeted treatment and prevention plans with their patients.

Personalized medicine is helping to shift the patient and provider experiences away from trial-and-error toward a more streamlined process for making clinical decisions, which will lead to improved patient outcomes, a reduction in unnecessary treatment costs, and better patient and provider satisfaction. PMC's members are leading the way in personalized medicine and recommend that patients who may benefit from this approach undergo appropriate testing and tailored treatment as soon as possible during their clinical experiences.

More than 6 million individuals are living with AD, which irreversibly degrades memory, cognitive function, and eventually motor function. AD is a primary cause of dementia in older Americans and, as CMS notes, it is one of the most burdensome diseases for the Medicare population. Abnormal levels of amyloid in the brain are one of the key pathologies found in patients with AD, and beta amyloid PET imaging is an essential tool for physicians in detecting the presence and level of amyloid plaques. Knowing amyloid status adds clarity for physicians managing the treatment of patients with suspected Alzheimer's disease by helping them reduce adverse events from inappropriate treatment, thus improving the chances of directing appropriate care.

Statement of Neutrality

Many of PMC's members will present their own responses to CMS' *Proposed National Coverage Determination Reconsideration for Beta Amyloid Positron Emission Tomography in Dementia and Neurodegenerative Disease* and will actively advocate for those positions. PMC's comments are designed to provide feedback so that the general concept of personalized medicine can advance, and are not intended to impact adversely the ability of individual PMC members, alone or in combination, to pursue separate comments with respect to the proposed decision.

1. PMC supports CMS' proposal to remove the coverage limit of one beta amyloid PET scan per patient.

In addition to confirming the presence of beta amyloid in the brains of patients who are being evaluated for AD prior to the initiation of anti-amyloid treatments or enrollment in anti-amyloid clinical trials, beta amyloid PET scans have become an important tool for monitoring a patient's response to anti-amyloid treatments and managing their treatment appropriately. Clinical trials for anti-amyloid treatments, for example, have utilized multiple beta amyloid PET scans to enroll patients and initiate amyloid targeting therapies, monitor reduction in beta amyloid levels during treatment, and potentially inform future decisions on treatment completion. In addition, while some patients with cognitive impairment may have a beta amyloid PET scan that does not indicate AD at one stage of their life, a repeat scan in future years could have a positive result as their disease progresses. CMS' current policy to cover only one beta amyloid PET scan per patient can constrain patients' choice of treatments and the appropriate management of anti-amyloid treatments.

PMC appreciates CMS' recognition in the proposed decision memo of the feedback it has received on how the use of beta amyloid PET scans has evolved to inform both treatment selection and treatment management and that its once in a lifetime limit is outdated and no longer clinically appropriate. We agree with CMS' proposal to remove the coverage limitation of one beta amyloid PET scan per patient. We believe this decision will improve patient access to

evolving personalized medicine approaches for initiating, monitoring and managing anti-amyloid treatments.

2. PMC supports CMS' proposal to end CED based on the available evidence.

For patients with progressive neurodegenerative diseases, timely access to beta amyloid PET scans is critical for providing patients with information regarding their disease and potential ways to manage and treat it. However, CMS' existing NCD only covers beta amyloid PET scans in the context of CED studies for the purposes of "excluding AD in narrowly defined and clinically difficult differential diagnoses" and to "enrich clinical trials seeking better treatments or prevention strategies for AD, by allowing for selection of patients on the basis of biological as well as clinical and epidemiological factors."[ii] Since access to PET is currently limited to sites participating in an approved study, Medicare's policy does not currently cover beta amyloid PET scans for patients who are unable to receive care at one of those sites. Thus, CMS' CED requirement limits beneficiaries' ability to access this important diagnostic tool.

In the decade since CMS finalized its existing NCD requiring additional evidence development, more than 30 academic manuscripts involving over 1,000 individual researchers have been generated demonstrating the benefits of beta amyloid PET imaging, with benefits including altered clinical management, changed patient diagnoses, and improved provider confidence.[iii] Notably, this includes results of the Imaging Dementia – Evidence for Amyloid Scanning (IDEAS) study that was developed and conducted in response to CMS' CED requirements for beta amyloid PET scans to assess the association between amyloid PET and subsequent changes in clinical management for Medicare beneficiaries with mild cognitive impairment (MCI) or dementia. The IDEAS study included 11,409 participants initially characterized as having MCI or dementia of uncertain cause. Ninety days after beta amyloid PET imaging, patient care plans changed in 60.2 percent of patients initially characterized as having MCI and 63.5 percent of patients initially characterized as having dementia of unknown cause. In some cases, changes to care plans helped patients avoid unnecessary additional testing such as neuropsychological testing, other imaging tests, and cerebrospinal fluid analysis.[iv] An aggregated analysis of other studies found that beta amyloid PET scans contribute to a change in diagnosis for approximately 30 percent of patients and increased diagnostic confidence in approximately 60 percent of patients.[v] No new CED studies have been approved since 2016. In fact, a limited extension of the original IDEAS study for underserved populations, the New IDEAS study, lacks trial sites in 18 states,[vi] and as CMS notes, is not active and has not been completed due to enrollment issues.

We appreciate CMS' acknowledgement in its proposed decision memo that a number of relevant clinical studies have been conducted and new evidence has been developed outside the context of CMS' CED requirement, specifically in the development of evidence for new anti-amyloid treatments. We support CMS' determination that separate CED studies on beta amyloid PET scans are no longer needed. Furthermore, we appreciate CMS' recognition that the use of beta amyloid PET scanning has changed and has become more individualized with the emergence of new treatments. We believe removing CED requirements will help expand access to care for patients who may benefit from a beta amyloid PET scan, but who also face geographical, institutional and other barriers to equitable participation in such clinical studies.

3. PMC urges CMS to keep a National Coverage Determination in place, without a one-time scan limit and without CED.

PMC shares CMS' interest in reducing the burden placed on providers and patients by the agency's existing test limitation and CED requirements. However, CMS proposes to remove its national coverage policy and allow local MACs to make coverage determinations regarding beta amyloid PET imaging, to include covering more than one scan per patient's lifetime and use within or outside the context of a CMS approved study. As noted above, PMC is concerned that in the absence of a national coverage policy, MACs and MA plans could develop inconsistent coverage policies, such as by imposing varying utilization management controls in the face of increased utilization, that create new barriers and inequities in access to this important diagnostic tool.

To fully optimize Medicare beneficiaries' access to beta amyloid PET scans that enable personalized medicine approaches to managing and treating a patient's disease, PMC encourages CMS to keep a National Coverage Determination (NCD) in place clarifying that beta amyloid PET scanning is "reasonable and necessary" without a one-time scan limit and without CED as conditions for coverage. If CMS chooses to move forward with removing its existing NCD, PMC encourages CMS to work with MACs and MA plans to ensure consistent coverage policies emerge in the absence of a national coverage policy.

PMC appreciates your commitment to ensuring that beneficiaries with dementia, Alzheimer's and other neurodegenerative diseases have access to the diagnostic and imaging tools needed to address their medical needs. We look forward to working with you and your colleagues at CMS to ensure the Medicare program fosters patient access to personalized medicine and the technologies enabling this approach to care. If you have any questions about PMC's comments, please contact me at 202-499-0986 or cbens@personalizedmedicinecoalition.org, or David Davenport, PMC's Manager of Public and Science Policy, at ddavenport@personalizedmedicinecoalition.org or 804-291-8572.

Sincerely,

Cynthia A. Bens
Senior Vice President, Public Policy

[i] Centers for Medicare & Medicaid Services. *Proposed National Coverage Determination Reconsideration for Beta Amyloid Positron Emission Tomography in Dementia and Neurodegenerative Disease (CAG-00431R).* July 17, 2023. https://www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=Y&NCAId=308. (Accessed August 10, 2023.)

[ii] Centers for Medicare & Medicaid Services. *Beta Amyloid Positron Tomography in Dementia and Neurodegenerative Disease (NCD 220.6.20)*. September 27, 2013. https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?ncdid=356&ncdver=1. (Accessed August 10, 2023.)

[iii] Partnership to Fight Chronic Diseases. *Amyloid Beta PET Scans: By the Numbers*. https://www.fightchronicdisease.org/sites/default/files/PFCD%20PET%20By%20The%20Numbers%20%281%29.pdf (Accessed August 10, 2023.)
[iv] Gil D. Rabinovici et al. "Association of Amyloid Positron Emission Tomography With Subsequent Change in Clinical Management Among Medicare Beneficiaries With Mild Cognitive Impairment or Dementia." *JAMA*. April 2, 2019. Vol. 321(13):1286–1294. https://pubmed.ncbi.nlm.nih.gov/30938796/. (Accessed August 10, 2023.)
[v] Enrico R. Fantoni et al. "A Systematic Review and Aggregated Analysis on the Impact of Amyloid PET Brain Imaging on the Diagnosis, Diagnostic Confidence, and Management of Patients being Evaluated for Alzheimer's Disease." *J Alzheimers Dis*. 2018. Vol. 63(2):783-796. https://pubmed.ncbi.nlm.nih.gov/29689725/. (Accessed August 10, 2023.)
[vi] The New IDEAS Study. *Find a Site by State*. https://www.ideas-study.org/Find-a-Site/Site-Locator-by-State. (Accessed August 15, 2023.)