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August 8, 2023

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Attention: CAG-00431R
Mail Stop C4–26–05
7500 Security Boulevard
Baltimore, MD 21244–1850

Re: Beta Amyloid Positron Emission Tomography in Dementia and Neurodegenerative Disease (CAG-00431R)

Dear Administrator Brooks-LaSure:

The Medical Imaging Technology Alliance (MITA) is writing in support of the Centers for Medicare & Medicaid Services' (CMS) Proposed Decision Memorandum to end Coverage with Evidence Development (CED) requirements and remove the one lifetime limit for Beta Amyloid Positron Emission Tomography (PET) in dementia and neurodegenerative disease. MITA believes the published clinical evidence and scientific data over the past decade warrant national coverage of amyloid imaging for Medicare beneficiaries. We believe that coverage of beta amyloid in a National Coverage Determination (NCD) is preferable to coverage at the discretion of Medicare Administrative Contractors (MACs) and Medicare Advantage (MA) plans. The transition from national to local coverage discretion would risk coverage gaps due to delays with local coverage decision-making and inconsistent coverage by region. This would result in limiting Medicare beneficiaries' access to beta amyloid PET imaging and anti-amyloid therapies.

MITA represents companies whose sales comprise more than 90 percent of the global market for medical imaging technology and we are the collective voice of PET and SPECT radiopharmaceutical developers, manufacturers, and distributors. Advances in nuclear medicine allow clinicians to more effectively identify and target disease, thereby providing more and potentially earlier options for treatment resulting in better patient outcomes.

I. MITA Supports Ending CED Data Collection Requirements and Removing the One Lifetime Scan Limit

MITA supports CMS' reconsideration of the NCD 220.6.20 for beta amyloid PET scans to end CED data collection requirements. Beta amyloid PET scans are a critical tool that enable clinicians to identify the presence of amyloid plaques and ensure appropriate treatment. We agree with CMS that "appropriate coverage of amyloid PET scans will greatly reduce provider and patient burden from the existing requirements and test limitation."

MITA and its members have a long history in the development of evidence on the clinical utility of beta amyloid PET imaging to aid diagnosis, help identify patients for treatment with monoclonal antibodies for Alzheimer's disease, and even inform ongoing treatment decisions in clinical trials. Beta amyloid PET supports the appropriate utilization of amyloid-targeting therapies by identifying patients for the therapies with early and accurate diagnoses. Since the NCD took effect in 2013, a considerable amount of published evidence has been developed that demonstrates that the use of beta amyloid imaging positively impacts patient management and leads to changes in diagnosis, even in the absence of a disease modifying therapy. For example, data from the Imaging Dementia—Evidence for Amyloid Scanning (IDEAS) Study support the importance of beta amyloid PET scans. The IDEAS investigators concluded that the use of Alzheimer's drugs was linked to amyloid status, finding that among patients with positive PET results, the overall use of Alzheimer's drugs in the population increased significantly.[1] Beyond the IDEAS study, at least 30 published studies involving thousands of patients have reviewed the utility of beta amyloid imaging for the diagnostic assessment of patients evaluated for cognitive impairment in memory clinics.[2]

CMS notes in the Proposed Decision Memorandum that "when the 2013 CED questions were created, advances in the application of amyloid PET scans and the importance of patient selection for promising treatments were not known." However, data has been developed over the past several years that demonstrates that the knowledge of amyloid status adds value to the management of patients, minimizes misdiagnosis, reduces the risk of adverse events due to inappropriate treatment, and informs clinical decision-making.[3] Data also demonstrates that the utilization of amyloid PET scans positively impact long-term health outcomes, including delays in institutionalization, improved utilization of healthcare resources, and delays in mortality.[4] CMS confirmed in the Proposed Decision Memorandum that "amyloid PET scans can be used to confirm presence of brain amyloid to select appropriate patients for proven anti-amyloid treatments." We appreciate CMS' recognition that it is appropriate for beta amyloid PET scans to be used to identify patients for treatment with monoclonal antibodies for Alzheimer's disease.

Similarly, MITA supports removing the coverage limitation of one-lifetime beta amyloid PET scan per patient to reflect clinical practice and patient management with new anti-amyloid

[1] Rabinovici, G. 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; 321(13):1286-1294.
[2] Barthel and Sabri, 2017, Fantoni et al., 2018, Shea et al., 2018, Kim et al., 2018.
[3] E.g., Hattori N, et al. J Alzheimer Dis Rep. 2020. Ceccaldi M, Jonveaux T, Verger A, et al. Alzheimers Dement. 2018;14(3):293-305. doi:10.1016/j.jalz.2017.09.009.
[4] Sims JR, Zimmer JA, Evans CD, et al. Donanemab in Early Symptomatic Alzheimer Disease: The TRAILBLAZER-ALZ 2 Randomized Clinical Trial. JAMA. Published online July 17, 2023. doi:10.1001/jama.2023.13239.

therapies. We appreciate that CMS noted in the Proposed Decision Memorandum that "stakeholders and patients have specifically noted that the once in a lifetime limit on amyloid PET is outdated and not clinically appropriate due to the development of anti-amyloid treatments." Deferring coverage decision-making to the MACs will not ensure that each MAC will agree to cover more than one scan, will likely result in variability across MACs and Medicare Advantage plans, so we, therefore, support CMS making a national coverage decision.

As CMS also stated in the Proposed Decision Memo, "it is anticipated that clinical study protocols may involve more than one PET Aß scan per patient." For example, amyloid confirmation could be required as an inclusion criterion, or follow-up amyloid PET scans could also be used to monitor treatment response and determine when to end treatment in a study. Patients could also be removed from amyloid-targeting therapies upon reaching a target level of reduced amyloid. Recently announced Phase 3 study results for an amyloid-targeted therapy showed that over 50% of patients were able to stop therapy within 12 months.[5] The stopping criteria was primarily supported by amyloid PET.

Given that the one lifetime scan limit has been in place for over a decade, beneficiaries who had negative beta amyloid PET scans prior to approval of amyloid therapies—yet have legitimate reason to be retested—could face barriers to accessing treatment. More broadly, limitations on the number of beta amyloid PET scans covered should be considered in the context of the rapidly evolving evidence around amyloid-targeted therapies, with the goal of ensuring that beneficiaries will not be denied access to reasonable and necessary amyloid-targeted therapies because of outdated restrictions on the number of PET scans covered.

II. MITA Recommends CMS to Maintain National Coverage for Beta Amyloid PET Scans Based on Published Evidence

Based on the extensive effort to collect and publish evidence to meet the CED requirements over the past decade, MITA recommends that CMS maintain national coverage of beta amyloid PET based on the body of evidence that has accumulated from CMS-approved and other clinical studies. Numerous published studies involving thousands of patients clearly support that beta amyloid PET scans improve the clinical management of patients with cognitive impairment.

Within the IDEAS Study, the data has shown that beta amyloid PET scans led physicians to change their management in more than 60% of patients, whether they had mild cognitive impairment (MCI) or dementia. Moreover, 35.6% of patients with MCI and dementia received a change in diagnosis following the PET scan and 36.1% of patients that were considered to have Alzheimer's disease after the clinical assessment and before the PET scan turned out to be amyloid negative.[6] This underlines the important role that beta amyloid PET scans play in the

[5] Sims JR, Zimmer JA, Evans CD, et al. Donanemab in Early Symptomatic Alzheimer Disease: The TRAILBLAZER-ALZ 2 Randomized Clinical Trial. JAMA. Published online July 17, 2023. doi:10.1001/jama.2023.13239.

[6] Rabinovici, G. 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; 321(13):1286-1294.

diagnostic workup of patients with cognitive impairment, especially for ruling out an incorrect etiologic diagnosis.

Beyond the IDEAS study, as stated earlier, the more than thirty published studies[7] involving thousands of patients have reviewed the utility of beta amyloid imaging for the diagnostic assessment of patients evaluated. Several meta-analyses and systematic reviews[8] confirm the consistent impact of beta amyloid PET in the evaluation of patients with cognitive impairment, demonstrating that beta amyloid PET contributes to diagnostic revisions in approximately 30% of patients and increases diagnostic confidence in approximately 60% of subjects. Changes in management were observed in 32% to 87% of patients, with the most common type of change in management being either the initiation or discontinuation of planned Alzheimer's disease medication. Medication changes were observed in approximately 40% of patients. Other types of management changes included referral to clinical trials, Alzheimer's genetic testing, addition or removal of planned diagnostic tests, and counseling.

As described earlier, this published evidence shows that beta amyloid PET imaging changes diagnosis and treatment management plans. With this information, which can provide a more accurate and earlier diagnosis, beta amyloid PET imaging is able to improve patients' health outcomes by providing physicians with better diagnostic information resulting in appropriate treatment.

III. The Transition to Local Contractor Discretion Could Result in Delay and Variability in Coverage for Medicare Beneficiaries

While MITA appreciates CMS' proposal to expand coverage of beta amyloid PET scans, we are concerned that leaving coverage to the discretion of local contractors could result in variability of coverage and beneficiary access delays to anti-amyloid therapies. Patients that are candidates for treatment with anti-amyloid therapies are required to have a diagnostic test for amyloid identification under the National Patient Registry Portal. If CMS finalizes the Decision Memorandum to leave coverage to contractor discretion, there would be significant uncertainty with whether those scans are covered at the local level.

An NCD would provide consistent and clear coverage immediately once such a policy was finalized, instead of months of uncertainty as MACs each determine their local coverage policy. Based on past experience with MAC coverage of diagnostics, many contractors opt to provide coverage on a claim-by-claim basis without a posted policy providing coverage. Other MACs have used Local Coverage Articles (LCAs) for imaging agents and advanced imaging for oncologic and nononcologic PET scans.

A concern with either claim-by-claim coverage or an LCA is that Medicare Advantage (MA) plans frequently assert they are not required to cover PET in the absence of an NCD or LCD, nor are they required to cover items and services only included on LCAs. MA plans often point to

[7] Amyloid Beta PET Scans: By the Numbers (see citations on page 1). Available at https://www.fightchronicdisease.org/sites/default/files/PFCD%20PET%20By%20The%20Numbers%20%281%29.pdf.

[8] Barthel and Sabri, 2017, Fantoni et al., 2018, Shea et al., 2018, Kim et al., 2018.

section 90.3 of the Medicare Managed Care Manual, which allows MA plans to follow coverage for NCDs and LCDs but not articles or claim-by-claim coverage.[9] If MA plans attempt to assert that coverage is not required for beta amyloid PET, there could be access issues for anti-amyloid therapies. This is particularly problematic in states like California, Florida, and Texas which have the highest MA enrollments in the country and a sizable portion of the Medicare population. CMS would need to issue guidance and transmittals to the MA plans to instruct them to follow the coverage established by the MACs.

Even for MACs that decide to issue LCDs, this process could also take several months to establish final policies. Additionally, once a final LCD is issued, it is not effective for 45 days. During this time, there would be a lack of clarity for ordering physicians and coverage gaps for beneficiaries in need of beta amyloid PET imaging to receive anti-amyloid therapy.

In the event that CMS finalizes a policy to give MACs the discretion to cover beta amyloid PET at the local level, we would urge CMS to coordinate with the MACs to ensure that there is transparency and clarity to ensure seamless coverage for all Medicare beneficiaries. In particular, for patients who are already under consideration for treatment with anti-amyloid therapy, these patients would need to obtain access to amyloid imaging once the NCD is no longer in place but before MACs finalize their policies. We would welcome the opportunity to assist CMS and the MACs to support appropriate coverage of beta amyloid PET imaging in this context.

Thank you for your consideration of our comments. If you have any questions or request any additional information, please contact Sue Bunning at 703-340-4100 or by email at sbunning@medicalimaging.org.

Sincerely,

Patrick Hope
Executive Director, MITA

MITA is the collective voice of manufacturers of medical imaging equipment, radiopharmaceuticals, contrast media, and focused ultrasound therapeutic devices. It represents companies whose sales comprise more than 90 percent of the global market for medical imaging innovations. These products include magnetic resonance imaging (MRI), medical X-Ray equipment, computed tomography (CT) scanners, ultrasound, nuclear imaging, radiopharmaceuticals, and imaging information systems. MITA Member company technologies are an important part of our nation's healthcare infrastructure and are essential for the screening, diagnosis, staging, managing and effectively treating patients with cancer, heart disease, neurological degeneration, and numerous other medical conditions.

[9] CMS, Medicare Managed Care Manual Chapter 4 - Benefits and Beneficiary Protections, §§ 10.2; 90.3. *Available at* https://www.cms.gov/regulations-and-guidance/guidance/manuals/downloads/mc86c04.pdf.