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Tamara Syrek-Jensen, JD
Director, Coverage & Analysis Group
Center for Clinical Standards and Quality
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Attention: CMS–1751–P
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 Director Syrek Jensen:

The Medical Imaging Technology Alliance (MITA) is writing to comment on the reconsideration of the National Coverage Determination (NCD) for Beta Amyloid Positron Emission Tomography (PET) in dementia and neurodegenerative disease. While MITA strongly supports CMS' initial step to withdraw the coverage limit of one lifetime beta amyloid PET scan, it is critical that CMS reassess all provisions of the NCD, including CED. Revising the scan limit while continuing to limit access to beta amyloid imaging to CED studies would have little impact on expanding beneficiary access and moving towards optimal care for patients with Alzheimer's.

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.

Since 2013, section 220.6.20 of the Medicare NCD Manual does not cover beta amyloid PET imaging for Alzheimer's and other neurodegenerative diseases outside of Coverage with Evidence Development (CED) studies. As outlined below, there is now a decade of utilization and clinical data on beta amyloid PET sufficient to justify Medicare coverage for beta amyloid PET imaging outside of CED to support or exclude a diagnosis of Alzheimer's Disease. MITA believes it is appropriate for CMS to

reconsider the NCD non-coverage language more broadly and allow national coverage of beta amyloid PET, or at a minimum, coverage at the discretion of Medicare Administrative Contractors (MACs).

Evidence Supports Broader Reconsideration of Beta Amyloid PET NCD

MITA believes that CMS' reconsideration must go beyond the one test per lifetime limitation in order for patients to appropriately access this critical service. Moreover, independent of the availability of amyloid targeting therapies, the data developed over the past several years have consistently demonstrated that the knowledge of amyloid status adds value to the management of patients, minimizes misdiagnosis, increases physician confidence in diagnosis, and reduces the risk of adverse events due to potentially inappropriate treatment.

A formal request for reconsideration was submitted to CMS in Fall 2020 to revise the NCD established in 2013 based on a decade of research on the role of beta amyloid PET in the pathogenesis of Alzheimer's disease. Stakeholders requested revision of the NCD to provide national coverage for adult patients suffering from cognitive impairment who are being evaluated for Alzheimer's disease and other causes of cognitive decline. Beta amyloid PET imaging is reasonable and necessary for patients with cognitive impairment who are being evaluated for Alzheimer's disease, including patients suffering from mild cognitive impairment due to Alzheimer's disease.

In the years since the existing NCD took effect in 2013, beta amyloid PET has become a key tool in the diagnostic workup of dementia patients, and there is a considerable amount of published evidence that the use of beta amyloid imaging positively impacts patient management and leads to changes in diagnosis. For example, data from the Imaging Dementia—Evidence for Amyloid Scanning (IDEAS) Study, which scanned over 18,000 patients, supports the importance of beta amyloid PET.

The data showed that beta amyloid PET scans led physicians to change their management in more than 60% of patients, whether they had mild cognitive impairment 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. This underlines the important role that beta amyloid PET scans play in the diagnostic workup of patients with cognitive impairment, especially for ruling out an incorrect etiologic diagnosis.[1]

Beyond the IDEAS study, at least thirty published studies involving more than 4,000 patients have reviewed the utility of beta amyloid imaging for the diagnostic assessment of patients evaluated for cognitive impairment in memory clinics. Several meta-analyses and systematic reviews[2] confirm the

[1] *See* 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*Id.*

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

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.[3] 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.

Altogether, the data developed over the past several years have consistently demonstrated that the knowledge of amyloid status adds value to the management of patients, minimizes misdiagnosis, reduces the risk of adverse events due to potentially inappropriate treatment, and informs decisions that may offer clinical benefit. We include a more detailed white paper with clinical data as an Appendix. Based on the evidence that beta amyloid PET imaging can positively impact the management of patients with Alzheimer's Disease, it is appropriate for Medicare to provide coverage, or, at minimum, allow the local MACs to do so.

MITA Supports Removing the One Scan Limit on Beta Amyloid PET Coverage

MITA believes that ensuring beneficiary access to beta amyloid PET technology necessitates a full reconsideration of the NCD. MITA supports the removal of the coverage limitation of one lifetime beta amyloid PET scan per patient. MITA previously commented during the finalization of the NCD for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease that drug development clinical study protocols may involve more than one PET Aß scan per patient.

The one scan per lifetime limitation is problematic because it interferes with evolving clinical practice. Some developers of amyloid-targeting therapeutics utilize amyloid PET as part of their protocols, e.g., with amyloid confirmation as inclusion criterion, follow-up amyloid PET scans to monitor treatment response and determine when to end treatment. Within these studies, patients are removed from amyloid-targeting therapy upon receiving a negative amyloid PET scan. This promotes both clinically appropriate and cost-effective care by reducing the number of unnecessary therapeutic doses.

The one scan per lifetime limit interferes with the use of amyloid PET in clinical practice and patient management, as described above. For example, it is expected that study protocols and drug labels (package inserts) for anti-amyloid mABs will include multiple beta amyloid scans to assess therapeutic response. The current NCD would thwart treatment by limiting coverage to a single scan. Additionally, a beneficiary who had a negative beta amyloid PET scan in the past, but whose disease has progressed, would be unable to be considered for treatment years later if they are limited to one scan per lifetime. The amyloid status observed in earlier scans may no longer reflect a patient's present beta amyloid status.

At minimum, coverage should include follow-up scans to determine the extent of plaque removal as a result of mAB therapy necessary to make informed decisions about continuing or terminating

[3] *Id.*

therapy. However, more broadly, limitations on the number of beta amyloid PET scans covered should be considered in the context of the rapidly evolving evidence around anti-amyloid mABs, with the goal of ensuring that beneficiaries will not be denied access to a reasonable and necessary anti-amyloid mAB because of outdated restrictions on the number of PET scans covered. For this reason, we respectfully believe that there should not be a set limit on the number of beta amyloid PET scans which are covered in a lifetime.

Conclusion

For the reasons set forth above, MITA urges CMS to allow Medicare beneficiaries to benefit from this important diagnostic tool by fully reconsidering all provisions of the beta amyloid PET NCD (NCD Manual § 220.6.20) as part of this reconsideration. CMS should nationally cover beta amyloid PET and allow additional scans informed by clinical practices.

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.