

July 15, 2022

Tamara Syrek Jensen, JD
Director, Coverage and Analysis Group
Center for Clinical Standards and Quality
Centers for Medicare & Medicaid Services

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

Dear Ms. Syrek Jensen:

The 20 undersigned organizations appreciate the opportunity to offer comments to the Centers for Medicare & Medicaid Services (“CMS” or the “Agency”) regarding its reconsideration of scan limits in the National Coverage Determination (NCD) for Beta Amyloid Positron Emission Tomography (PET) in dementia and neurodegenerative disease. Collectively, our organizations represent people living with Alzheimer’s disease and related dementias (“ADRD”); family caregivers; healthcare providers; researchers; coalitions and advocacy organizations focused on chronic disease, aging, and minority and women’s health; private-sector leaders; and clinical trial sites. **Together, we strongly urge CMS to not only end the coverage limit of one lifetime beta amyloid PET scan but also to end CED for amyloid PET and provide national coverage for 1) diagnostic evaluation and 2) assessment to start or continue an Alzheimer’s therapeutic. Medicare beneficiaries should have coverage for these scans when recommended by their healthcare providers.**

Patients are currently assessed for Alzheimer’s disease in the clinical setting based on their symptoms. It is typically a diagnosis of exclusion, where other potential causes for memory problems are ruled out first. Before PET imaging, a definitive diagnosis of the disease could only be made by examining brain tissue post-mortem for the presence and distribution of both amyloid-beta plaques and tau neurofibrillary tangles. With the availability of FDA-approved radiopharmaceuticals targeting amyloid plaques and tau tangles, evaluation through PET imaging has become central to patient diagnosis and is commonly used in clinical trials to assess the staging of the disease and to identify patients that may benefit from treatment. Just as importantly, PET imaging allows providers to rule out Alzheimer’s disease for beneficiaries that have symptoms consistent with the disease, but for whom amyloid-beta plaques are not present. For these individuals, a amyloid beta PET scan can prevent inappropriate treatment.

Despite these steps forward in innovation, patients of color are far less likely to have Alzheimer’s disease diagnosed¹ and less likely to be referred to dementia specialists.² CMS’ current NCD under CED for PET³ turns a blind eye to the known disparity being caused by negative social determinants of health for older Black and Hispanic populations compared with older white populations. Chronic health conditions associated with higher dementia risk, such as cardiovascular disease and diabetes, disproportionately

¹ https://www.alz.org/aaic/downloads2020/2020_Race_and_Ethnicity_Fact_Sheet.pdf

² Landon BE, Onnela JP, Meneades L, et al, “Assessment of Racial Disparities in Primary Care Physician Specialty Referrals,” JAMA 2021;4(1):e2029238.

³ [NCD - Beta Amyloid Positron Tomography in Dementia and Neurodegenerative Disease \(220.6.20\) \(cms.gov\)](#)

affect Black and Hispanic populations.⁴ Social and environmental disparities, including lower levels and quality of education, higher rates of poverty, and greater exposure to adversity and discrimination, increase the risk for these chronic conditions and risk for dementia in Black and Hispanic populations.⁵ Yet, in setting up its PET CED trials, CMS ignored this reality and perpetuated guidelines that created an unharmonized set of diversity requirements and constraints that make access overly challenging.

Our organizations caution CMS not to inadvertently contribute to, and exacerbate, the massive racial and ethnic inequalities in access to Alzheimer’s disease detection and treatment. As CMS evaluates the amyloid beta PET NCD, we strongly urge CMS not to use “lack of evidence on minority populations” as part of the rationale to continue a coverage policy that restricts access to those very same populations who have the highest need.

Statement of Interest

Many of the organizations listed here will present their own responses to CMS and will actively advocate for those positions. These comments are not intended to impact adversely the ability of individual organizations, alone or in combination, to pursue separate comments with respect to the proposed NCD for beta amyloid PET in dementia and neurodegenerative disease.

Remove the One Scan Limit

In its final NCD for mAB therapies targeting amyloid for the treatment of AD, CMS appropriately requires patients to be screened through amyloid PET scan (or other screening technology), but allows coverage for only one PET scan (or other amyloid screen) per patient enrolled in a clinical trial.⁶ This means that CMS will preclude coverage for any follow-up scans or screens needed to compare to the enrollment screen, even if the second scan is necessary to measure changes in the clinical trial subjects’ conditions (i.e., to measure changes in the accumulation and distribution of amyloid and tau tangles in the brain). Consequently, CMS puts the financial burden on patients to pay for follow-up PET scans. Unlike the IDEAS study, which was an open-label longitudinal study measuring whether the results of an amyloid PET scan would influence provider diagnosis and treatment,⁷ the mAB CED trial is a RCT that would study treatment outcomes, which require a comparison of amyloid measurements.

For CMS to propose paying for one scan, but not the second, eviscerates sponsors’ or the NIH’s ability to confirm one of the endpoints the community wants to measure—the reduction of BA loads in patients. Further, it will limit clinicians’ ability to determine whether a particular patient should be taken out of the clinical trial. Ultimately, the limit compromises the ability of the trial sponsor(s) to complete the RCTs and

⁴ Lisa Lines and Joshua Wiener, *Racial and Ethnic Disparities in Alzheimer’s Disease: A Literature Review*, U.S. Dep’t of Health & Human Servs. Off. of the Assistant Sec’y for Planning & Evaluation (Feb. 2014), <https://aspe.hhs.gov/reports/racial-ethnic-disparities-alzheimers-disease-literature-review-0>.

⁵ Jennifer Weuve, et al., *Cognitive Aging in Black and White Americans: Cognition, Cognitive Decline, and Incidence of Alzheimer Disease Dementia*, 29(1) EPIDEMIOLOGY 151, 154 (Jan. 2018).

⁶ [NCA - Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer’s Disease \(CAG-00460N\) - Decision Memo \(cms.gov\)](#).

⁷ New IDEAS Study, Original IDEAS Study Protocol, available at https://www.ideas-study.org/-/media/Ideas/Files/Original-IDEAS/Original-IDEAS-Study_Protocol.pdf.

add significant cost to beneficiaries who require additional scans and implicate the diagnosis and treatment of AD. CMS must end the coverage limit of one lifetime beta amyloid PET scan, which will facilitate the collection of mAB clinical trial data in the future.

End NCD Under CED and Provide National Coverage

In 2013, Medicare decided to limit coverage of amyloid PET imaging under the restricted CED protocol, citing insufficient evidence that the imaging would make a difference for patients with a disease due to the lack of a disease-modifying treatment for the disease and limited symptomatic treatment.⁸ Published appropriate use criteria, which CMS adopted in its two designated CED studies required that 1) knowledge of amyloid PET results was expected to change diagnosis and management and 2) whether amyloid PET is associated with improved clinical outcomes.

The ability to test the accumulation and distribution of amyloid and tau tangles in the brain through PET imaging will aid diagnosis and ultimately help physicians make more informed decisions about patient care, including whether to treat with mABs. PET imaging has significantly helped in the diagnosis and staging of AD as well as in identifying which patients may benefit from treatment. A negative PET result rules the disease out. The IDEAS data analysis, published in *JAMA* in April 2019, found approximately 36% of patients clinically diagnosed with AD and 61% of patients with mild cognitive impairment (“MCI”) were negative for amyloid plaque by amyloid PET scan.⁹ These PET results profoundly impacted the primary study endpoint, which was the post-PET care management plan. More than 60% of study participants in both the MCI and dementia patient groups had changes in care plans post-PET, most notably in the starting, stopping, or modification of AD drug therapy, but also in the use of other drug therapy and/or counseling about safety and future planning. Additionally, physicians reported that PET results contributed substantially to the post-PET management plan in 85.2% of instances in which a change was made, further validating the usefulness of the diagnostic.¹⁰ Therefore, PET scans had a direct impact on changing patient diagnosis and management.

CMS’ authority to tie together both the CED trial for PET scans and the CED trial for mABs targeting amyloids also is unclear. CMS has not clarified the statutory and regulatory basis for integrating these two CED trials. To resolve the issue, we call on CMS to reconsider its NCD for amyloid PET scans and issue a final coverage decision without limitation on the number of scans. The original justification for the CED—the lack of available treatment—is no longer valid given the FDA’s approval of aducanumab in June 2021 and the upcoming FDA reviews of Phase III trial data for additional mABs targeting amyloid for the treatment of Alzheimer’s disease.

Nine years ago, when CMS finalized its amyloid PET NCD for dementia, there were no FDA-approved disease-modifying therapies (“DMTs”) for AD. In the absence of effective dementia therapies, it was postulated that amyloid PET would need to show significant changes in dementia diagnosis and

⁸ [Centers for Medicare & Medicaid Services. Decision memo for beta amyloid positron emission tomography in dementia and neurodegenerative disease \(CAG-00431N\).](#)

⁹ Gil Rabinovici et al., *Association of Amyloid Positron Emission Tomography With Subsequent Change in Clinical Management Among Medicare Beneficiaries With Mild Cognitive Impairment or Dementia*, 321(13) *JAMA* 1286, 1286–94 (Apr. 2019).

¹⁰ *Ibid.*

management and demonstrate improved clinical outcomes compared to those beneficiaries with dementia who had not undergone amyloid PET. **Now that a disease modifying mAB therapy has received the FDA’s approval, CMS should end CED for amyloid PET and provide national coverage.**

We caution, however, that CMS must take further action beyond coverage, and address payment, to allow any future clinical trials (or treatment) to proceed by “unpackaging” the diagnostic radiopharmaceuticals used in amyloid PET imaging from the respective procedure payment. As CMS is aware and has been referenced by the Office of Inspector General (“OIG”), the inability of the NEW IDEAS trial (the improvident extension of the amyloid PET CED) to enroll clinical trial sites has been directly related to hospital outpatient departments’ unwillingness to conduct amyloid PET scans and face financial shortfalls due to a lack of reimbursement for the PET scan agents. More specifically, while the original IDEAS trial enrolled over 125 sites, at the time of this comment the NEW IDEAS trial has enrolled only 15 sites.

As reported by the Government Accountability Office “[t]he study organizers said that those hospitals, which had all participated in the original IDEAS Study, declined to participate because the packaged payment would cause them to incur a financial loss for each procedure performed.”¹¹ The reimbursement issue is significant, and could itself derail the entirety of the proposed CED clinical trials. We call upon CMS to address this issue and “unpackage” diagnostic radiopharmaceuticals from hospital outpatient procedure payments so that hospitals and other viable non-hospital sites of care will be able to participate in the proposed clinical trials should CMS continue with the CED pathway.

Conclusion

Thank you for considering our views and for CMS’ commitment to improved detection of and quality care for people with Alzheimer’s disease. If you have questions, please contact Sue Peschin, President and CEO of Alliance for Aging Research, at speschin@agingresearch.org or the Alliance's Vice President of Public Policy and Government Relations, Michael Ward, at mward@agingresearch.org.

Sincerely,

Alliance for Aging Research
Alliance for Patient Access
Alzheimer's Drug Discovery Foundation
Alzheimer's Orange County
BrightFocus Foundation
Caregiver Action Network
HealthyWomen
HFC
Infusion Providers Alliance
Livpact
Men's Health Network

National Minority Quality Forum
Ohio Council for Cognitive Health
Partnership to Fight Chronic Disease
Patients Rising Now
RetireSafe
The Association for Frontotemporal
Degeneration (AFTD)
The Global CEO Initiative on Alzheimer's Disease
UsAgainstAlzheimer's
Voices of Alzheimer's

¹¹ U.S. GOV’T ACCOUNTABILITY OFF., GAO-21-252, MEDICARE PART B: Payments and Use for Selected New, High-Cost Drugs (Mar. 2021), available at <https://www.gao.gov/assets/gao-21-252.pdf>.