

February 10, 2022

Joseph Hutter, M.D.  
Lead Medical Officer  
Centers for Medicare and Medicaid Services

Electronically Submitted: [CMS\\_caginquiries@cms.hhs.gov](mailto:CMS_caginquiries@cms.hhs.gov)

**Re: Public Comment on [NCA for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease](#) (CAG-00460N)**

Dear Dr. Hutter:

The American College of Radiology (ACR) representing more than 41,000 diagnostic radiologists, radiation oncologists, interventional radiologists, nuclear medicine physicians, and medical physicists, appreciates the opportunity to submit public comments in response to the Centers for Medicare and Medicaid Services' (CMS') National Coverage Analysis (NCA) for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease. Our organization fully supports CMS' process to review and analyze coverage mechanisms for this class of FDA approved therapeutics.

As CMS considers the extensive scientific evidence relevant to the Medicare population, we request that CMS reconsider the proposed coverage of beta-amyloid positron emission tomography (PET) under Coverage with Evidence Development (CED), as described in this NCA. The ACR strongly urges CMS to update its coverage of beta-amyloid PET not only for the purpose of therapeutic evaluation but as a diagnostic tool. The information presented below builds on this recommendation to further improve access to beta-amyloid PET imaging as a diagnostic tool for Alzheimer's Disease and to foster equitable care for those most at risk.

The ACR is a professional organization committed to advancing the science and quality of radiological care for patients. As part of that commitment, the ACR Center for Research and Innovation is a prominent leader in CED study sponsorship and operation. In May 2006, the ACR launched the CED-approved National Oncologic PET Registry (NOPR), with collaboration from the Academy for Molecular Imaging, The American Society of Clinical Oncology and the Society for Nuclear Medicine. Studies published in the *Journal of Clinical Oncology*, the *Journal of Nuclear Medicine* and *Cancer* analyzed data from more than 41,000 NOPR cases and found that results of PET scans led to an intended change in cancer management of nearly 40 percent of patients<sup>1</sup>. Approximately 10 percent of all Medicare covered PET scans in 2007 were performed under the auspices of the NOPR. In 2009, CMS duly expanded access and coverage of PET scans performed in both the initial and subsequent evaluation of patients with many types of cancer. This decision was based on significant clinical evidence regarding the effectiveness of PET for the management of patients with cancer gleaned from the NOPR.

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<sup>1</sup> Impact of Positron Emission Tomography/Computed Tomography and Positron Emission Tomography (PET) Alone on Expected Management of Patients With Cancer: Initial Results From the National Oncologic PET Registry  
Bruce E. Hillner, Barry A. Siegel, et.al. *Journal of Clinical Oncology* 2008 26:13, 2155-2161.

The hallmark molecular biomarker of Alzheimer’s Disease, beta-amyloid protein, can be non-invasively detected by PET. In 2013, CMS issued a National Coverage Determination (NCD) for Beta Amyloid Positron Emission Tomography in Dementia and Neurodegenerative Disease ([220.6.20](#)), stating “the evidence is insufficient to conclude that the use of positron emission tomography (PET) amyloid-beta (A $\beta$ ) imaging is reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member for Medicare beneficiaries with dementia or neurodegenerative disease, and thus PET A $\beta$  imaging is not covered under §1862(a)(1)(A) of the Social Security Act (“the Act”).” Under this NCD came CED requirements for beta-amyloid PET. Most recently, the ACR serves as the sponsor and operating center for the Imaging Dementia – Evidence for Amyloid Scanning (IDEAS) Study and subsequent New IDEAS Study. These studies are developed to address the CED requirements of CMS’s 2013 NCD 220.6.20. Thus far, these studies have provided access to diagnostic beta-amyloid PET imaging for a combined 20,000 Medicare beneficiaries as a covered procedure<sup>2</sup>.

The Alzheimer's Association, the ACR, the American Society of Neuroradiology, and the Department of Biostatistics at Brown University School of Public Health, along with other clinical research experts, are partnering to launch The National Treatment and Diagnostic Alzheimer's Registry. This new national registry will be an FDA-approved-agent agnostic approach to gathering routine clinical practice data and outcomes for sharing quickly and transparently with all stakeholders<sup>3</sup>. The registry will be designed to continuously collect routine clinical practice data over time from healthcare providers caring for patients diagnosed with Alzheimer's who are taking an FDA-approved disease-modifying treatment. The registry will be designed to grow with scientific and medical advancements. As new drugs are approved and implemented in care, these will also be captured by the registry. CMS should reconsider its proposed determination of limiting CED approval under this NCA to only randomized controlled trials and instead consider real-world examples, including clinical data registries and other longitudinal cohort studies.

We encourage CMS to review the latest ACR and our collaborating medical specialty societies (ACNM, ASNR, and SNMMI) Practice Parameter for Brain PET-CT Imaging in Dementia, which was revised and approved by the ACR Council in 2020 (Resolution 41) and includes indications for beta-amyloid PET.<sup>4</sup> Amyloid PET studies should be performed at the request of physicians knowledgeable in the clinical diagnosis and management of dementia and under circumstances in which the results of the examination are likely to impact patient care.

A recently published primary analysis of the IDEAS study included 11,409 participants initially characterized as having mild cognitive impairment (MCI) or dementia of uncertain cause. 90 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 characterizes as having dementia of unknown cause. Hence, beta-amyloid PET was associated with substantial subsequent changes in the management of diagnostically challenging patient cognitive disorders<sup>5</sup>.

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<sup>2</sup><https://www.ideas-study.org>

<sup>3</sup> <https://www.alz.org/news/2021/alzheimers-association-announces-national-effort>

<sup>4</sup> <https://www.acr.org/-/media/ACR/Files/Practice-Parameters/Brain-PET-CT-Dementia.pdf>

<sup>5</sup> 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;321:1286-94

Coverage of beta-amyloid PET will increase patient access to this diagnostic tool. Currently, there are three FDA-approved radiopharmaceuticals for the identification of amyloid plaque in the brain: 18F florbetapir, 18F flutemetamol, and 18F florbetaben. These are currently covered (under CED) in the New IDEAS Study, a successor to the IDEAS Study that is focused on minority populations. Outside of this trial, however, these tracers are not covered by CMS. It is essential that CMS find a mechanism to immediately cover beta-amyloid PET scans so that all Medicare beneficiaries have access. Without coverage for beta-amyloid PET, only those who can afford to pay full charges out of pocket or the means to enroll in a CED study will have access, which will result in inequitable access.

The ACR agrees directionally with CMS's proposed decision to cover beta-amyloid PET for beneficiaries seeking access to an FDA approved therapy targeting Alzheimer's Disease. However, we are disappointed that proposed coverage requirements limit broad access by aligning with CMS' almost decade old NCD 220.6.20 and limiting coverage to only one beta-amyloid PET scan per beneficiary, who must also be enrolled in an approved CED clinical research study. Rather than retiring or revising NCD 220.6.20, CMS has proposed to perpetuate the current barriers to access of gold-standard diagnostic imaging for populations most at risk for MCI and Alzheimer's dementia. **Beta-amyloid PET imaging should be covered for Medicare beneficiaries diagnosed with MCI or dementia, without a CED requirement.**

The ACR commends CMS's proposed requirement for study approval to promote inclusion of traditionally underrepresented populations by stating, "The diversity of patients included in each trial must be representative of the national population diagnosed with AD." The proposed ruling also states, "The study protocol must explicitly discuss beneficiary subpopulations affected by the item or service under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion criteria affect enrollment of these populations, and a plan for the retention and reporting of said populations in the trial." However, we believe CMS would be imprudent to confidently believe that accurate representation of the Alzheimer's population will occur under the proposed requirements of this NCA, as it stands. Within this NCA, CMS includes discussion on health disparities while specifically citing data from surveys conducted as part of the Alzheimer's Association's 2021 Special Report: Race, Ethnicity, and Alzheimer's in America. Research has shown that AD is more prevalent in Blacks and Hispanics when compared to Whites, with Blacks being up to two times more likely to have AD and other dementias when compared to Whites, and Hispanics being about one and a half times more likely than Whites to have AD and other dementias (AA 2020, Mayeda 2016). Despite the higher prevalence of AD and other dementias among non-white populations, non-white Americans are less likely to be enrolled in clinical research trials that prevent or slow the progression of Alzheimer's Disease (AA 2021). **We believe the proposed determination is an incomplete solution to ensuring appropriate representation of traditionally underrepresented populations that also bear the greatest burden of Alzheimer's and related dementia, and fails to eliminate known access barriers to comprehensive healthcare, specifically, innovative diagnostic imaging.** CED coverage is traditionally a highly respected methodology for coverage of evidence-based medicine, however, it is still subject to many of the same systemic barriers to health equity.

The proposed ruling's requirement that "all trials must be conducted in a hospital-based outpatient setting" **immediately disqualifies numerous settings that are credentialed and qualified to provide care, such as Independent Diagnostic Testing Facilities (IDTFs).** These IDTFs serve as accessible and reliable imaging providers to communities across the country. **Disqualifying these sites from providing needed care under the proposed NCA ruling immediately creates an additional access barrier to**

**already underserved communities.** Additionally, Medicare’s current reimbursement structure in the Hospital Outpatient Prospective Payment System (OPPS) setting limits patient access to innovative diagnostic imaging tools, such as beta-amyloid PET. The diagnostic radiopharmaceuticals used in beta-amyloid PET imaging are statutorily considered drugs, but they are treated differently by CMS, which has packaged them into procedural bundles known as Ambulatory Payment Classifications (APCs). Unfortunately, this has proven to be a serious problem as the costs associated with these diagnostic radiopharmaceuticals at times are greater than the entire APC procedure payment. The packaging of these diagnostic radiopharmaceuticals into procedural bundles has created a strong disincentive for hospitals to utilize these innovative diagnostic imaging agents, even when covered under CED, and significantly undermines patient access. To mitigate this issue, the ACR continues to strongly urge Congress to pass the Facilitating Innovative Nuclear Diagnostics (FIND) Act of 2021 (S. 2609/H.R. 4479)<sup>6</sup>.

The ACR’s experience in conducting CMS-approved CED studies allows for insight into real-world barriers that a hospital outpatient-only study imposes. In the aforementioned IDEAS Study, over 125 hospital imaging facilities participated, accounting for only one-third of the overall activated imaging locations. Since then, CMS categorized the diagnostic radiopharmaceuticals into APCs and now, the minority-focused New IDEAS Study has seen a significant decline of participation in hospital imaging facilities, with only sixteen having been fully activated to date. Most of the hospital imaging facilities that have declined participation have cited the lack of appropriate reimbursement for beta amyloid PET scans from CMS, compared to the original IDEAS study. Failure to provide equitable payment, agnostic to the setting where the patient receives a beta-amyloid PET scan, will limit the use of this valuable diagnostic procedure to certain facilities, thus creating additional access barriers for already underserved populations.

The ACR requests that CMS reconsider the current NCA and develop national coverage for the use of beta-amyloid PET scans as a diagnostic test as well as for the purpose of estimating beta-amyloid neuritic plaque density in adult patients who are being evaluated for Alzheimer’s disease and other causes of cognitive decline.

The ACR appreciates the opportunity to submit recommendations to CMS on diagnostic imaging for MCI and Alzheimer’s Dementia. If you have any questions or comments on our letter, please do not hesitate to contact Charlie Apgar, Executive Vice President for Research, at [capgar@acr.org](mailto:capgar@acr.org).

Respectfully Submitted,



William T. Thorwarth, Jr. MD, FACR  
Chief Executive Officer

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<sup>6</sup> Congress.gov. H.R.4479 Facilitating Innovative Nuclear Diagnostics Act of 2021. Retrieved January 31, 2022 at <https://www.congress.gov/bill/117th-congress/house-bill/4479?q=%7B%22search%22%3A%5B%22hr%22%2C%224479%22%2C%224479%22%5D%7D&s=1&r=1>