

**Comment on**

**CMS NCD Analysis for Beta Amyloid Positron Emission Tomography in Dementia and Neurodegenerative Disease**

July 15, 2022

The Honorable Xavier Becerra  
Secretary of Health and Human Services  
200 Independence Ave., SW  
Washington, DC 20201

The Honorable Chiquita Brooks-LaSure  
Administrator  
Centers for Medicare & Medicaid Services  
Department of Health and Human Services  
7500 Security Blvd.  
Baltimore, MD 21244

Dear Secretary Becerra and Administrator Brooks-LaSure:

Thank you for the opportunity to comment on the Centers for Medicare and Medicaid Services' (CMS's) National Coverage Determination (NCD) analysis for Beta Amyloid Positron Emission Tomography in Dementia and Neurodegenerative Disease. UsAgainstAlzheimer's (UsA2) is an organization founded by people whose families have been savaged by Alzheimer's disease (AD) and who have created a national, patient-centric movement to end this disease. We speak to you with the voice of our own families as well as the millions of Alzheimer's patients whose care and health outcomes will be directly affected by CMS's decision.

People with dementia deserve a definitive diagnosis and monitoring just like people with other diseases. CMS must change its coverage determination to make that possible.

As you know, NCD 220.6.20 (finalized in 2013) covers one PET amyloid-beta (A $\beta$ ) scan per patient, and only for the small numbers enrolled in CMS-approved studies under coverage with evidence development (CED). UsA2 remains strongly opposed to this policy, and we applaud CMS for finally opening this new NCD analysis.

The restrictions on the use of this tool impedes the timely and accurate diagnosis of Alzheimer's and giving patients, caregivers, and clinicians the information necessary to develop an appropriate course of treatment. In addition, these restrictions cause predictable, evidence-based harm to patients who suffer from different causes of psycho-neurological disturbances, requiring a wholly different clinical regimen and presenting a very different challenge for the patient, the clinician, the family, and all involved. At their base, the restrictions eliminate the most important tool patients, caregivers, and physicians could have to understand the underlying disease process in a particular patient.

As discussed below, we request that CMS **reconsider this NCD and provide coverage without CED for the FDA-approved use of an A $\beta$  PET scan.** To support this request, we offer the following comments:

**1. The available scientific evidence and consensus is more than adequate to warrant coverage without evidence development for the use of PET amyloid imaging and, in so doing, to avoid the risk of adverse outcomes through misdiagnosis, late diagnosis, and mistreatment.**

In its 2013 comments on CMS's proposed NCD, UsA2 pointed out that the results of PET A $\beta$  imaging would assist in making a differential diagnosis that meaningfully informs the management of a patient presenting with clinical signs of dementia, avoiding the use of medications that are either futile or potentially harmful.

For example, one study found that among patients misdiagnosed with Alzheimer's, more than 18 percent were treated with potentially inappropriate medication. When using a broader definition of potentially inappropriate medication, this rate increased to more than 67percent.<sup>1</sup>

In the last nine years, further evidence confirms this argument. The Imaging Dementia—Evidence for Amyloid Scanning (IDEAS) study, published in 2019, showed that among 11,409 participants with mild cognitive impairment (MCI) or dementia of uncertain cause, patient management 90 days after amyloid PET changed (compared with the pre-PET plan) in more than 60 percent of patients with MCI and 63.5 percent of patients with dementia. Over a dozen other studies published between 2012 and 2015 have documented changes in the management of patients with AD following PET A $\beta$  imaging; showing that changes in patient management occurred in 37-87 percent of cases and changes in AD medications (i.e., initiation or discontinuation of planned AD medication) occurred in 20-60 percent of cases.<sup>2</sup>

Since the original NCD went into effect, it has become clear that A $\beta$  PET is an essential tool in ensuring that patients receive the treatments—and that CMS only pays for the treatments—they need. Given this extensive body of evidence, failure to cover would be unconscionable.

**2. PET A $\beta$  is reasonable and necessary for beneficiaries.**

UsA2 has previously noted that the Alzheimer's Imaging Taskforce (AIT) has issued comprehensive Appropriate Use Criteria (AUC) for PET A $\beta$  imaging [3].<sup>3</sup> As a result of AIT's work, CMS has before it compelling, evidenced-based expert consensus recommendations on the specific characteristics of the subpopulation of patients who present with dementia, where AD is a possible diagnosis but where this diagnosis remains uncertain after a comprehensive evaluation by a dementia expert, and where the knowledge of the presence or absence of A $\beta$  pathology is expected to increase diagnostic certainty and alter management. This set of patients is entitled to access to PET A $\beta$  imaging tests today to guide immediate treatment decisions, to avoid the potential, continued misuse of harmful medications and, in partnership with their doctor, to make life altering decisions armed with the best diagnosis the clinical field can offer using available technology.

It is important to note that in limiting coverage of PET A $\beta$  imaging to clinical trial participants, the CED limits treatment access for people of color, and perpetuates the lack of inclusion that CMS, and the Biden administration more broadly, has sought to address. African Americans and Latinos are disproportionately affected by AD as they are more likely than Whites to have AD.

Despite this, there is evidence that they are more likely to be misdiagnosed or receive a delayed diagnosis of AD or dementia.<sup>4,5,6,7</sup> Moreover, as CMS has recognized, these groups make up a miniscule percentage of participants in clinical trials, including those funded by the NIH.<sup>8,9</sup>

Although new studies, including the ongoing New IDEAS Study, are working to improve representation of Black or African American and Hispanic or Latino participants in Alzheimer's and dementia clinical studies, doing so is insufficient to ensure equal access to PET A $\beta$  imaging. Removing the CED

requirement for this technology is an important step in addressing these inequities and increasing access to appropriate medical care for minorities living with Alzheimer's disease. Failure to do so would exacerbate existing inequities and perpetuate a system already working against these patients.

**3. Today's Medicare beneficiaries face needless fear and confusion due to the restrictions on access, particularly in difficult-to-diagnose cases. Science has done its job in making tools available to reduce that fear and confusion; policy needs to make them available.**

For the Alzheimer's patient whose life is held in limbo by not knowing the underlying cause of their dementia, access to PET A $\beta$  imaging offers an otherwise unavailable tool to guide their doctor in making an accurate diagnosis and to prevent the risk of adverse health outcomes through the avoidable misuse of medications.

These benefits also fall squarely in the camp of improved health outcomes whether viewed through the lens of published studies, expert analysis, or clinical and practical logic. Indeed, when considered in reverse, lack of coverage for PET A $\beta$  scans is, in fact, neither reasonable nor necessary for the patient who today is suffering from dementia with an unknown and confounding cause and whose treatment and life choices could be immediately altered and improved by the power of knowing their disease state.

## **Conclusion**

For patients suffering from Alzheimer's (and other neurodegenerative diseases) and their families, and for patients incorrectly diagnosed with Alzheimer's, the results of PET A $\beta$  imaging tests can mean access to and appropriate management of the most appropriate treatment possible. As CMS is aware, for the first time ever, one disease-modifying therapy has been approved by the FDA for the treatment of Alzheimer's, and other therapies are currently in late-stage development. While CMS's April 2022 NCD for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease severely limits access to therapies in this class, a small number of patients may still be able to access these treatments. Even without disease-modifying therapies, patients and families benefit from a positive diagnosis of Alzheimer's disease.

Lifting restrictions permits appropriate application of presently available symptomatic and non-pharmacologic treatments. It also permits families to anticipate continued cognitive decline and ascertain their loved one's preferences before the disease progresses to an advanced stage. Importantly, a negative result would help direct clinicians to pursue other reasons for a patient's cognitive decline and inform treatment decisions.

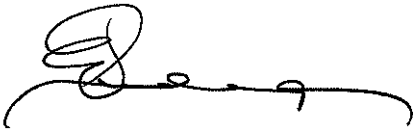
Coverage decisions by CMS are among the most important decisions made by the agency for American citizens. Decisions must be grounded on the best science, data, and evidence available. In 2013, when CMS issued its NCD for PET A $\beta$  imaging, carefully reviewed and validated evidence was already available; even more such evidence is available now.

Again, we ask CMS to fully reconsider NCD 220.6.20, and provide **immediate coverage without CED of PET A $\beta$  according to FDA labels.**

USAgainstAlzheimer's looks forward to working with the agency to refine the policy in a manner that will not delay access to PET A $\beta$  imaging tests for Alzheimer's patients who deserve to have an accurate diagnosis and receive appropriate treatments to help manage this devastating disease.

Thank you for your consideration.

Sincerely,



George Vradenburg  
Chairman and Co-Founder  
UsAgainstAlzheimer's

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**About UsAgainstAlzheimer's<sup>10</sup>**

UsAgainstAlzheimer's was founded in 2010 to disrupt and diversify the movement to cure Alzheimer's. Through urgent, inclusive and catalytic mobilization and venture philanthropy, UsA2 has attacked the most pressing issues slowing progress against AD by working to dramatically increase funding for Alzheimer's and dementia research, advancing public health steps to reduce risk of dementia, incubating an inclusive clinical trials network, and advancing equity. Our advocacy focuses on a wide array of issues including prevention, treatment, research, access to care, and equity and inclusion. Everything we do is grounded in the needs of Alzheimer's patients and caregivers around the country. Our goal is to ensure that brain-span equals lifespan – for everyone.

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<sup>1</sup> Gaugler JE, Ascher-Svanum H, Roth DL, Fafowora T, Siderowf A, Beach TG. Characteristics of patients misdiagnosed with Alzheimer's disease and their medication use: an analysis of the NACC-UDS database. *BMC Geriatr.* 2013 Dec 19;13:137.

<sup>2</sup> Kim Y, Rosenberg P, Oh E: A Review of Diagnostic Impact of Amyloid Positron Emission Tomography Imaging in Clinical Practice. *Dement Geriatr Cogn Disord* 2018;46:154-167.

<sup>3</sup> Johnson KA, Minoshima S, Bohnen NI, Donohoe KJ, Foster NL, Herscovitch P, Karlawish JH, Rowe CC, Carrillo MC, Hartley DM, Hedrick S, Pappas V, Thies WH. Appropriate use criteria for amyloid PET: A report of the Amyloid Imaging Task Force, the Society of Nuclear Medicine and Molecular Imaging, and the Alzheimer's Association. *Alzheimer's Dement.* 2013 Jan;9(1):e-1-16.

<sup>4</sup> Clark PC, Kutner NG, Goldstein FC, Peterson-Hazen S, Gamer V, Zhang R, et al. Impediments to timely diagnosis of Alzheimer's disease in African Americans. *J Am Geriatr Soc* 2005;53(11):2012-7.

<sup>5</sup> Fitten LJ, Ortiz F, Ponton M. Frequency of Alzheimer's disease and other dementias in a community outreach sample of Hispanics. *J Am Geriatr Soc* 2001;49(10):1301-8.

<sup>6</sup> Lang L, Clifford A, Wei L, Zhang D, Leung D, Augustine G, et al. Prevalence and determinants of undetected dementia in the community: A systematic literature review and a meta-analysis. *BMJ Open* 7(2):e011146.

<sup>7</sup> Lin PJ, Daly AT, Olchanski N, Cohen JT, Neumann PJ, Faul JD, Fillit HM, Freund KM. Dementia diagnosis disparities by race and ethnicity. *Med Care* 2021;59(8):679-86.

<sup>8</sup> [UsAgainstAlzheimer's. Key Findings and Policy Recommendations: The Costs of Alzheimer's and Other Dementia for African Americans. 2018.](#)

<sup>9</sup> [UsAgainstAlzheimer's. Latinos and Alzheimer's Disease: New Numbers Behind the Crisis. 2018.](#)

<sup>10</sup> Disclosure: UsAgainstAlzheimer's is governed by a Board of Directors with no representation from pharmaceutical companies. UsA2 is supported by thousands of individuals, companies, and foundations, including pharmaceutical companies developing mAbs.