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VIA ELECTRONIC DELIVERY

Re: National Coverage Analysis (NCA) for Beta Amyloid Positron Emission Tomography in Dementia and Neurodegenerative Disease

Dear Dr. Conway,

Leaders Engaged on Alzheimer's Disease (LEAD) is a diverse and growing coalition of 57 member organizations including patient advocacy and voluntary health non-profits, philanthropies and foundations, trade and professional associations, academic research and clinical institutions, and biotechnology and pharmaceutical companies. LEAD works collaboratively to focus the nation's strategic attention on Alzheimer's disease (AD) and related disorders and to accelerate transformational progress in care and support, detection and diagnosis, and research leading to prevention, effective treatment and eventual cure. One or more participants may have a financial interest in the subjects addressed.

We recommend that the Centers for Medicare & Medicaid Services (CMS) issue a National Coverage Decision with immediate effect for PET amyloid imaging in the evaluation of progressive cognitive decline when its use follows the appropriate use criteria (AUC)[1] developed by the Alzheimer's Association and Society of Nuclear Medicine and Molecular Imaging (SNMMI). We do not support Coverage with Evidence Development (CED).

Nearly everything medical professionals do depends on an accurate diagnosis. Patients and families want, deserve and need to know the cause of cognitive impairment. Currently, far too few people experiencing symptoms of cognitive impairment receive a timely, accurate and clear diagnosis. Amyloid PET is a major advance in Alzheimer's disease (AD) diagnosis and has the capacity both to facilitate appropriate treatment and avert inappropriate treatment. Thanks to amyloid PET, dementia experts (typically neurologists, geriatric psychiatrists or geriatric

[1] http://www.alzheimersanddementia.com/article/S1552-5260(13)00034-4/abstract

medicine specialists with formal training and/or extensive clinical experience in dementia treatment and devoting a substantial percentage of the clinical practice to the diagnosis and treatment of dementia) have the means to safely and reliably detect fibrillar forms of amyloid, one of the hallmarks of AD. No longer is a post-mortem exam the only definitive way to differentiate among causes of AD and other cognitive decline. Amyloid PET allows more timely and precise advice on available courses of treatment, and gives patients and families greater clarity about what they face and the planning decisions to be weighed.

The U.S. Food and Drug Administration (FDA) has set rigorous standards for the approval of amyloid PET imaging requiring that the abnormalities seen on PET closely correlate with neuritic amyloid pathology seen post-mortem. The results of imaging vs. post-mortem studies with Amyvid met those rigorous standards and led to FDA's 2012 approval of Amyvid for imaging of amyloid pathology.

The SNMMI and Alzheimer's Association convened the Amyloid Imaging Taskforce (AIT) to provide guidance for dementia care practitioners, patients and caregivers. The AIT developed a consensus of evidence-based expert opinion to establish a specific and judicious AUC defining the types of patients and clinical circumstances in which amyloid PET beneficially could be used. The AUC recommend amyloid imaging in patients experiencing cognitive impairment. The utility of amyloid imaging is greatest in patients with objectively confirmed cognitive impairment and an uncertain diagnosis despite thorough examination by a dementia expert. The amyloid scan should increase diagnostic certainty and productively alter clinical management.

Under the AUC, appropriate candidates for amyloid PET imaging include:

- Those complaining of persistent or progressive unexplained memory problems or confusion and demonstrating impairments using standard tests of cognition and memory -- patients with persistent or progressive unexplained mild cognitive impairment (MCI).

- Individuals with dementia meeting criteria for possible AD, but with unusual clinical presentation (either an atypical clinical course or an etiologically mixed presentation).

- Individuals with progressive dementia and atypically early age of onset (before age 65).

We support the AUC recommendations that limit amyloid PET to the three listed patient groups and that amyloid imaging be considered as part of a comprehensive evaluation by a dementia expert in patients with objectively determined cognitive impairment. Adherence to these criteria will restrict use to patients who are most likely to benefit. Amyloid imaging, governed by the AUC, is of particular importance for evaluating MCI, but limited to cases where the dementia expert has concluded the patient "would benefit from greater certainty of the underlying pathology and whose clinical management would change as a result of this greater certainty."

Based on available evidence, we concur with the AUC's identification of circumstances in which amyloid imaging would be inappropriate: 1) patients with core clinical criteria for probable AD with typical age of onset; 2) to determine dementia severity; 3) based solely on a positive family history of dementia or APOE-ε4 presence; 4) patients with a cognitive complaint that is unconfirmed on clinical examination; 5) in lieu of genotyping for suspected autosomal mutation

carriers; 6) in asymptomatic individuals; and 7) nonmedical use (e.g. legal, insurance coverage or employment screening). The Medicare Coverage Advisory Committee (MEDCAC) and AUC correctly emphasize that amyloid imaging would be inappropriate in asymptomatic individuals. Amyloid imaging does not substitute for a careful history and examination, both of which are required to understand the clinical context necessary to incorporate imaging results into clinical decision-making. Imaging is one tool among many that clinicians should employ carefully to manage patient care.

Early and accurate diagnosis of AD and other causes of cognitive decline leads to better outcomes and higher quality of life for patients and their families by:

- reducing disease-related stigma;
- allowing the family to build a care team and seek out education and support services;
- providing access to approved medications and behavioral interventions;
- offering an opportunity for timely development of advance directives, financial planning and declaration of end-of-life wishes; and
- facilitating clinical trial enrollment.

These choices represent health outcomes and demonstrate that the beneficial effect of early and accurate diagnosis enhanced by amyloid imaging is a substantial improvement in outcome for which Medicare beneficiaries deserve covered access.

Amyloid PET imaging is an unprecedented medical advance that provides an early milestone in meeting the National Plan to Address Alzheimer's Disease *Goal 1: Prevent and Effectively Treat Alzheimer's Disease by 2025.*[2] Restricting its use to dementia experts and specific patient populations, in accordance with the AUC recommendations, will avoid misuse and excessive cost. CMS requires similar limitations for FDG PET.

Accurate diagnosis to improve health outcomes for people with dementia and their families is reasonable and necessary for Medicare beneficiaries who qualify under the AUC. We recommend that CMS approve PET amyloid imaging via a National Coverage Decision with immediate effect. This opportunity is vital to patients, their families and caregivers, dementia experts, and all physicians and health care professionals for people experiencing cognitive impairment. We appeal to CMS to consider the information provided in this letter and the abundance of data, expert opinion, case examples, and perspectives supplied by other groups in support of providing access to this class of imaging procedures for Medicare beneficiaries who qualify under the AUC.

Thank you for considering our views and for your commitment to advancing diagnosis, treatment and care for all people. Please contact Ian Kremer, LEAD's executive director, at ikremer@leadcoalition.org or (571) 383- 9916, with questions or for additional information.

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[2] http://aspe.hhs.gov/daltcp/napa/NatlPlan.shtml#goal1

Sincerely,

Abe's Garden

Academy of Radiology Research

Alliance for Aging Research

Alzheimers North Carolina

Alzheimer's & Dementia Alliance of Wisconsin

Alzheimer's Drug Discovery Foundation

American Association for Geriatric Psychiatry

American Association for Long Term Care Nursing

Assisted Living Federation of America

Banner Alzheimer's Institute

Beating Alzheimer's by Embracing Science

BrightFocus Alzheimer's Disease Research

Caregiver Action Network

Coalition for Imaging and Bioengineering Research

Cortica Neurosciences, Inc.

Cure Alzheimer's Fund

Rachelle S. Doody, MD, PhD (Baylor College of Medicine*)

Geoffrey Beene Foundation Alzheimer's Initiative

Gerontological Society of America

Global Coalition on Aging

Janssen Alzheimer's Immunotherapy

Janssen Research & Development, LLC

Linked Senior, Inc.

National Alliance for Caregiving

National Association of States United for Aging and Disabilities

National Down Syndrome Society

Neurotechnology Industry Organization

New York Academy of Sciences

Prevent Alzheimer's Disease 2020

Project Lifesaver International

RemeGenix, Inc.

Smith & Harroff, Inc.

R. Scott Turner, MD, PhD (Georgetown University Memory Disorders Program*)

USAgainstAlzheimer's

USF Health Byrd Alzheimer's Institute

Volunteers of America

Vradenburg Foundation

* *Affiliations of individual researchers are for identification purposes only and do not necessarily represent the endorsement of the affiliated institution.*