DEPARTMENT OF HEALTH & HUMAN SERVICES
Centers for Medicare & Medicaid Services
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Baltimore, Maryland 21244-1850

Center for Clinical Standards and Quality
Coverage and Analysis Group

February 22, 2023

Dr. Joanne Pike
225 N. Michigan Ave., Fl. 17
Chicago, IL 60601

Dear Dr. Pike:

I am writing to respond to your December 19, 2022 request on behalf of the Alzheimer's Association for reconsideration of the National Coverage Determination (NCD) for Monoclonal Antibodies (mAbs) Directed Against Amyloid for the Treatment of Alzheimer's Disease (AD) (see https://www.cms.gov/medicare-coverage-database/view/nca.aspx?ncaid=305). Alzheimer's disease is a highly destructive illness that affects millions of Americans and their families. The Centers for Medicare & Medicaid Services (CMS) is committed to timely access to treatments, including drugs, that demonstrate clinically meaningful improvement in health outcomes. We greatly appreciate the Association's leadership in research to find effective treatments, and we look forward to continuing our dialogue with the Association on improving care for people with AD.

At this time, because the FDA has not yet assessed the clinical benefit of lecanemab and we have not received new evidence that meets the required criteria, we must deny the request for reconsideration. We regret that the decision could not be more favorable. We will continue to monitor and review the evidence on this drug and similar products as they become available. If the FDA determines a clinical benefit for a drug within this class through its traditional approval program, CMS will provide enhanced access and coverage for people with Medicare participating in CMS-approved studies, such as a registry-based study where the drug is tested in real-world settings.

CMS will reconsider an NCD if the requester presents documentation that meets one of the following criteria[1]:

- Additional scientific evidence that was not considered during the most recent review along with a sound premise by the requester that new evidence may change the NCD decision.
- Plausible arguments that our conclusion materially misinterpreted the existing evidence at the time the NCD was decided.

[1] August 7, 2013 *Federal Register Notice* https://www.federalregister.gov/articles/2013/08/07/2013-19060/medicare-program-revised-process-for-making-national-coverage-determinations

Unfortunately, we have not received the required evidence. As of the date of this letter, there has not been an antiamyloid mAb that has been approved by the FDA for the treatment of AD based upon evidence of efficacy from a direct measure of clinical benefit. We are aware that Eisai has submitted a supplemental Biologics License Application (BLA) to FDA for traditional approval of lecanemab. As part of its assessment, FDA is independently evaluating the lecanemab Phase 3 Clarity AD trial data for safety, as well as efficacy in terms of clinical benefit. This FDA assessment is both different from, and valuable to, CMS assessment under its reasonable and necessary statutory authority.

At the same time that FDA is reviewing the application, we are also aware that publications may be forthcoming that include more detail about characteristics of the trial patients (e.g., number and type of comorbid diseases), and trial sites (e.g., inclusion of sites beyond selective, advanced centers), which did not appear in the report or supplementary appendix of the Clarity AD trial recently published in the *New England Journal of Medicine*. This information is relevant to the Coverage with Evidence Development (CED) questions included in the current NCD.

These CED questions are designed to assess the drug's longer-term harm/benefit profile, and generalizability of use in the Medicare population in broader community practice. The CED questions are:

a. Does the antiamyloid mAb meaningfully improve health outcomes (i.e., slow the decline of cognition and function) for patients in broad community practice?
b. Do benefits, and harms such as brain hemorrhage and edema, associated with use of the antiamyloid mAb, depend on characteristics of patients, treating clinicians, and settings?
c. How do the benefits and harms change over time?

CMS believes these important questions still need to be answered to support people with Medicare, caregivers, and their referring and treating physicians to make informed, appropriate decisions about use of any drug in this particular class. The NCD was structured to provide flexibility and assurance that CMS can respond quickly to providing coverage for any new drugs in this class when a clinical benefit is determined. Accordingly, CMS is continuing conversations with interested parties, including trial investigators, about the CED questions, and how peer-reviewed, published studies may address them. We welcome feedback on these questions from the Association as well.

As noted in the NCD, if supported by evidence, registry-based studies to answer the CED questions may be considered. As appropriate, registry-based studies may include patients excluded from the initial randomized controlled trials designed for FDA traditional approval, and being treated at more treatment locations, with the aim of reflecting real-world care for people with AD. This could potentially provide much greater access nationwide, and more rapidly, than any other coverage pathway. CED could also help fill evidence gaps for patients who were vastly underrepresented in the randomized controlled trials – as was the case in the Clarity AD trial for lecanemab.

CMS is committed to continuing to explore ways to improve care for people with Alzheimer's disease. We will continue to monitor the evidence and engage in discussions with all interested

parties, including the Association. As part of this, we would welcome the opportunity to discuss how a registry may serve as a standardized, nationwide platform which investigators (for potentially multiple drugs) could use for their studies addressing CED questions.

Thank you for your advocacy on behalf of people with Alzheimer's disease. Please feel free to contact David Dolan at david.dolan@cms.hhs.gov or 410-786-3365 for further discussion.

Sincerely,

Tamara S. Jensen -S

Digitally signed by Tamara S. Jensen -S
Date: 2023.02.22 15:57:33 -05'00'

Tamara Syrek Jensen
Director, Coverage and Analysis Group