

February 10, 2022

Comments Regarding the Centers for Medicare and Medicaid Services' Proposed National Coverage Decision Memo for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease (CAG-00460N)

Public Citizen, a consumer advocacy organization with more than 500,000 members and supporters nationwide, strongly supports the Centers for Medicare and Medicaid Services' (CMS') proposed national coverage decision for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease (CAG-00460N), under which the Medicare program would cover the drug aducanumab (and any future FDA-approved monoclonal antibodies directed against amyloid for the treatment of Alzheimer's disease) only for beneficiaries who enroll in CMS-approved randomized, controlled clinical trials meeting certain criteria or in trials supported by the National Institutes of Health (NIH).

As we explained in detail in our August 11, 2021, written comments regarding CMS' National Coverage Determination Analysis for CAG-00460N, the Food and Drug Administration's (FDA's) decision to approve aducanumab for treatment of Alzheimer's disease showed a stunning disregard for science and eviscerated the agency's standards for approving new drugs. Because of this reckless action, the agency's credibility has been irreparably damaged.

The approval of aducanumab was based on seriously flawed post hoc analyses of two identical phase 3 trials that were stopped early because a preliminary review of the data found that the trials, if continued to completion, were unlikely to show the drug benefitted Alzheimer's disease patients. Moreover, the integrity of the FDA's review of the marketing application for aducanumab was dangerously corrupted by the unprecedented and inappropriately close collaboration between Biogen and the FDA during the analyses of data from the key clinical trials of the drug after the termination of the phase 3 clinical trials because of futility.

Unlike the FDA, the European Medicines Agency and a Japanese Health Ministry expert panel have opposed marketing authorization for aducanumab based on the available data.

Implementation of CMS' proposed national coverage decision would significantly mitigate the damage done by the FDA's egregious error in approving aducanumab under the Accelerated Approval pathway on June 7, 2021. Given the lack of scientific evidence that aducanumab provides any clinically meaningful benefit in terms of cognitive function outcomes in Alzheimer's disease patients and unmistakable evidence that it can cause serious brain injury, the drug cannot be deemed reasonable and necessary for treatment of any patients outside the context of a clinical trial at this time. Unlike the FDA, CMS wisely chose to follow the available scientific evidence in developing its proposed national coverage decision for aducanumab for treatment of Alzheimer's disease.

Below we provide comments regarding specific provisions of the proposed national coverage decision and responses to some comments submitted by others.

Comments regarding specific provisions of the proposed national coverage decision

(1) We agree that any CMS-approved trials under the proposed national coverage decision must address, at a minimum, the following research questions:

- Does use of monoclonal antibodies directed against amyloid for the treatment of Alzheimer's disease result in a statistically significant and clinically meaningful difference in decline in cognition and function?
- What are the adverse events associated with the use of monoclonal antibodies directed against amyloid for the treatment of Alzheimer's disease?

The inclusion of "clinically meaningful difference in decline in cognition and function" in the first question is critically important. We further commend CMS for requiring that "any proposed threshold for what constitutes a 'clinically meaningful' improvement for a given trial's primary outcome (which may be over and above statistical significance) be supported by peer-reviewed, published literature."

(2) We agree that patients to be enrolled any CMS-approved trials under the proposed national coverage decision must have a clinical diagnosis of mild cognitive impairment due to Alzheimer's disease or mild Alzheimer's disease dementia.

(3) We commend CMS for requiring that the diversity of patients included in any CMS-approved trials under the proposed national coverage decision "must be representative of the national population diagnosed with [Alzheimer's disease]," unlike the randomized, controlled clinical trials of aducanumab conducted by Biogen.

(4) Under the proposed national coverage decision, CMS proposes that the CMS-approved randomized clinical trials must include "an appropriate control representing the standard of care." We recommend that CMS further require that any CMS-approved trials under the proposed national coverage decision be placebo-controlled and double-blinded, which are essential design features for minimizing potential bias in efficacy outcomes measuring cognition and function.

Responses to other comments submitted to CMS regarding the proposed national coverage decision

(1) None of the comments opposing CMS' proposed national coverage decision offer any new valid scientific evidence demonstrating that aducanumab provides clinically meaningful benefit in terms of cognition and function in Alzheimer's disease patients. In the absence of such evidence, the drug does not meet criteria for a reasonable and necessary treatment of Alzheimer's disease outside the context of a clinical trial at this time.

(2) Many comments opposing CMS' proposed national coverage decision were submitted by Alzheimer's disease patients or family members of such patients who out of desperation — desperation on which Biogen is preying — are willing to try any treatment that might

alter the course of this devastating disease. Such comments are indicative of the false hope that resulted from the FDA's reckless decision to approve aducanumab.

- (3) More than a dozen commenters opposing CMS' proposed national coverage decision asserted that the decision would impede innovation in the development of treatments for Alzheimer's disease and other diseases. However, drugs like aducanumab, for which there is a lack of scientific evidence that they provide any clinically meaningful benefit in terms of cognitive function outcomes in Alzheimer's disease patients, do not represent innovation but anti-innovation. CMS' proposed national coverage decision — unlike the FDA's decision to approve aducanumab — will promote innovation by signaling to pharmaceutical companies that they must, as a condition of approval, provide robust scientific evidence from well-designed, randomized clinical trials demonstrating that new drugs for Alzheimer's disease actually provide clinically meaningful benefit to patients.
- (4) Some commenters have suggested that CMS expand the proposed national coverage decision to include coverage of aducanumab for Alzheimer's disease patients who enroll in a registry. We oppose such an expansion because such an uncontrolled registry study will not be able to establish whether aducanumab provides any clinically meaningful benefit in terms of cognitive function outcomes in Alzheimer's disease patients but will open the flood gates to use of this unproven drug, without the safety protections of a clinical trial.

In closing, Public Citizen urges CMS to issue a final national coverage decision under which the Medicare program would cover the drug aducanumab only for beneficiaries who enroll in CMS-approved randomized, controlled clinical trials meeting certain criteria or in trials supported by the NIH. The lack of evidence that aducanumab provides meaningful clinical benefit and the fact that the reduction in amyloid-beta plaques following administration of the drug is not an established, validated surrogate endpoint for such clinical benefit, combined with the known risks of the drug, clearly justify such limitation on Medicare coverage for aducanumab.

Thank you for the opportunity to comment on this important public health issue.



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