CENTER FOR
Science IN THE
Public Interest
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Nutrition Action Healthletter

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Tamara Syrek Jensen, JD
Director, Coverage and Analysis Group
Office of Clinical Standards and Quality
Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244

Re: National Coverage Analysis (NCA) Proposed Decision Memo: Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease (CAG-00460N)

Dear Ms. Syrek Jensen:

The Center for Science in the Public Interest (CSPI), an organization that promotes independence, scientific rigor, and transparency, submits the following comments regarding the Centers for Medicare and Medicaid Services' (CMS) National Coverage Determination (NCD) memorandum on Aduhelm (aducanumab), released on January 11, 2022.

CSPI shares the belief of many scientists and researchers that FDA approval of aducanumab was not based on adequate scientific evidence of the drug's effectiveness. The clinical trial data submitted to the FDA were based on one favorable study of the two conducted, and that study only showed a 0.4 point improvement on an 18-point scale. This is less than half of what surveyed patients and caregivers stated was the minimum improvement to be clinically meaningful. This implicit benefit was only seen for the high dose. As a result, FDA's Peripheral and Central Nervous Systems Drugs Advisory Committee unanimously voted, with one member uncertain, that it was not reasonable to consider the one study as primary evidence of the drug's effectiveness for the treatment of Alzheimer's Disease. Further, the approval of aducanumab was widely criticized for the uncommon involvement of the drug's sponsor in the preparation of briefing materials for the advisory committee, questionable use of amyloid plaques as a surrogate biomarker, and harmful side effects of the drug that include minor brain swelling and bleeding, which occurred in 40% of patients.

Although aducanumab received FDA approval, it's important to note that CMS has a more restrictive standard for coverage under Medicare. Under the Food, Drug, and Cosmetic Act, a drug must demonstrate "reasonable assurance of...safety and effectiveness" for FDA approval. In contrast, the Social Security Act allows for reimbursement by Medicare only if the drug is deemed "reasonable and necessary." Thus, FDA approval alone does not guarantee coverage of the drug under Medicare's more rigorous standard.

For these reasons, if aducanumab is to be covered at all under the Medicare program, we strongly support CMS' proposal that Medicare will not pay for aducanumab or similar FDA-approved

monoclonal antibodies that target amyloid for the treatment of Alzheimer's Disease unless patients are participating in qualifying clinical trials (i.e., follows a "Coverage with Evidence Development" provision). As stated by CMS, qualifying trials must include a nationally representative sample of participants diagnosed with Alzheimer's Disease and demonstrate a clinically meaningful difference in cognition and function. Only such trials can provide the information that is currently lacking and that is critical before aducanumab can be prescribed to other Medicare patients.

In addition to supporting CMS' NCD, we recommend the following:

1. Qualifying clinical trials include a nationally representative sample of patients diagnosed with Alzheimer's Disease with respect to age, comorbidities, race, and ethnicity.
2. Qualifying clinical trials should place equal focus on safety and efficacy and include free brain scans for monitoring adverse effects.

The "Coverage with Evidence Development" provision is a valuable tool that can be leveraged by CMS to apply a more rigorous scientific standard beyond FDA's standard for approval. Given the limitations of FDA's approval process in this instance, this seems like the ideal opportunity to use this unique authority and place CMS squarely on the side of scientific rigor – while sparing many patients the dangers of ineffective and potentially harmful drug use.

Stephanie Rogus
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Peter Lurie
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