Council for Informed
Drug Spending Analysis

February 1, 2022

Chiquita Brooks La-Sure
Administrator
Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244

RE: Proposed National Coverage Determination "Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease" (CAG-00460N)

Dear Administrator Brooks-LaSure:

On behalf of the Council for Informed Drug Spending Analysis (CIDSA), we are writing in support of the Centers for Medicare & Medicaid Services' (CMS') proposed National Coverage Determination (NCD), "Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease" (CAG-00460N). CIDSA is a group of prescription drug policy experts without ties to the pharmaceutical industry that offers a central, objective source of information on drug spending and regulatory policy for policymakers and the media. Specifically, as members of CIDSA, we write in support of the use of a Coverage with Evidence Development (CED) requirement, the requirement for use of randomized controlled trials, the patient criteria requirements, and the inclusion of a clinically meaningful standard for the required trials. We applaud CMS for its appropriate use of an NCD with CED as a condition for reimbursement of these monoclonal antibodies for Alzheimer's treatment ("antiamyloid mAbs"), as the current evidence base is insufficient to determine whether this treatment modality is reasonable and necessary for any given patient. While we recognize that neither the cost of antiamyloid mAbs themselves nor their overall spending implications for the Medicare program are a component of CMS' reasonable and necessary determination, we believe that an appropriate use of the reasonable and necessary criteria will have an important effect on Medicare spending, patient out-of-pocket costs, and the pricing trends for new antiamyloid mAbs. Therefore, the rigorous standards proposed are an essential component in not only developing the future evidence necessary to determine whether antiamyloid mAbs are indeed clinically-efficacious, but also to manage drug spending and address ever-rising launch prices of clinician-administered therapies.

Coverage with Evidence Development

We support the proposal to require CED. We agree with CMS' assessment that "[t]o date, no trial of an antiamyloid mAb has confidently demonstrated a clinically meaningful improvement in health outcomes (i.e., cognition and function) for AD patients. Thus, there is insufficient evidence to conclude that the use of monoclonal antibodies directed against amyloid is reasonable and necessary for the treatment of Alzheimer's disease." However, absent CED as a condition of antiamyloid mAb coverage, development of the clinical evidence necessary to show meaningful improvements in health outcomes may proceed slowly and without the appropriate rigor to demonstrate true clinical efficacy, driving increasing costs to the Medicare program as well as individual patients and their families. Therefore, CMS' coverage of

antiamyloid mAbs under a CED requirement is critical to properly assess whether antiamyloid mAbs are reasonable and necessary for the treatment of Alzheimer's Disease, ensuring that Medicare is only paying for truly effective services.

Randomized Controlled Trials

We support the proposal that only randomized controlled trials (RCTs) be considered approved trials under the CED. This standard is necessary to determine true clinical efficacy of antiamyloid mAbs on cognition and function, given the limited and contradictory evidence presented to date. Moreover, this standard will ensure that Medicare coverage of a particular approved antiamyloid mAb does not hamper research into additional antiamyloid mAbs, which may eventually drive both therapeutic and price competition that can lower Medicare and patient spending. Antiamyloid mAbs that are not yet approved by the Food and Drug Administration (FDA) will generally only be available to patients who enroll in RCTs developed under the FDA approval process. If Medicare were to make approved antiamyloid mAbs available outside of an RCT despite the lack of demonstrated clinical efficacy, patients may be discouraged from participating in RCTs for antiamyloid mAbs still in clinical development, as they would have a significant chance of receiving a placebo in the pre-approval RCT but not under Medicare coverage of the approved antiamyloid mAb. Therefore, the proposed RCT standard not only will help generate evidence on the clinical efficacy of approved antiamyloid mAbs, it will also support the development of future antiamyloid mAbs by not discouraging clinical trial participation. By encouraging a robust antiamyloid mAb marketplace, the RCT requirement may promote future competition that will result in lower Medicare spending.

Patient Criteria

We support the proposed comprehensive patient criteria. The proposed patient criteria appropriately balance access to treatment against the risk of known side effects in the interest of rapidly generating clear evidence of any clinical efficacy of antiamyloid mAbs, ensuring that Medicare only pays for services for patients who are likely to benefit. We support the two proposed criteria of 1) a clinical diagnosis of mild cognitive impairment (MCI) due to Alzheimer's disease or mild Alzheimer's disease dementia and 2) evidence of amyloid pathology consistent with Alzheimer's disease. Given the demonstrated adverse events associated with approved antiamyloid mAbs, we support the proposal to limit participation to individuals without conflicting comorbidities or who would be expected to die during the study duration.

Clinically Meaningful Standard

We support the proposed requirement that all approved trials be designed to test for statistically significant and clinically meaningful differences in cognition and function due to antiamyloid mAbs. Given the use of surrogate endpoints in prior clinical trials for approved antiamyloid mAbs, we believe that these clinical trial requirements are essential to determining whether Medicare coverage of antiamyloid mAbs for the treatment of Alzheimer's Disease is reasonable and necessary, a determination with substantial cost implications.

We further support the proposal that approved clinical trials will be considered to meet the CED requirements in the Beta Amyloid Positron Emission Tomography in Dementia and Neurodegenerative

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Disease NCD (220.6.20). We also support CMS' proposal not to change the frequency of the single lifetime scan per Medicare beneficiary. While these scans may provide evidence of changes in beta amyloid plaques, they do not demonstrate evidence of clinically meaningful changes in cognition and function. Therefore, additional scans are not reasonable and necessary services. Should additional scans be a component of an RCT, their cost should be borne by the trial sponsor. Absent this requirement, Medicare spending on both antiamyloid mAbs and associated PET scans will continue to grow beyond what is justified by clinical evidence.

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CIDSA supports CMS' proposed NCD with CED for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease. We commend CMS for its rapid and thorough approach to this proposed NCD, which will ensure appropriate access to antiamyloid mAb treatment while limiting Medicare spending growth and fostering a competitive marketplace for antiamyloid mAb treatments. Should you have any questions regarding our comments, please contact the Chair of CIDSA, Sean Dickson, at sdickson@westhealth.org.

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