



December 19, 2022

Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
7500 Security Blvd
Baltimore, MD 21244

RE: Final and Formal Request for Reconsideration of National Coverage Determination (NCD) for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease (CAG-00460N)

Dear Administrator Brooks-LaSure:

The Alzheimer's Association formally requests a reconsideration of the Centers for Medicare & Medicaid Services' (CMS') coverage policy established in National Coverage Analysis (NCA) CAG-00460N.¹ Specifically, we respectfully request that CMS remove the requirements for Coverage with Evidence Development (CED) for Food and Drug Administration (FDA)-approved monoclonal antibodies (mAbs) directed against amyloid for the treatment of Alzheimer's disease (AD), in order to provide unrestricted coverage for FDA-approved mAbs directed against amyloid for the treatment of Alzheimer's disease consistent with their FDA-approved label.

Since the National Coverage Determination (NCD) was finalized in April 2022, new clinical data have been published that clearly demonstrate a meaningful clinical benefit from a new mAb product, lecanemab, currently under review by the FDA. CMS's original coverage policy, to apply CED under the NCD, was developed based on the evidence available to the agency as of April 2022. The agency has committed to rapidly reconsidering the NCD in light of new evidence, and, as the attached statement from over 200 Alzheimer's disease researchers and experts concludes, the lecanemab results represent precisely the significant new evidence that necessitates such a reconsideration. Lecanemab is expected to receive Accelerated Approval from FDA on or before January 6, 2023.

¹ National Coverage Determination (NCD) for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease (CAG-00460N), Centers for Medicare & Medicaid Services (Apr. 7, 2022), <https://www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=N&NCAId=305> (Apr. 2022 Alzheimer's Decision Memo).

As discussed below, the recently released data for lecanemab demonstrate that this mAb therapy slows cognitive and functional decline over 18 months and results in significant positive effects on classical biological markers of Alzheimer's disease. In light of the new data, the current CED policy for FDA-approved mAbs directed against amyloid for the treatment of Alzheimer's disease will result in significant limitations on beneficiary access to a product that has shown significant clinical benefit for patients who currently lack effective treatment options. The clear evidence of lecanemab's clinical benefit places it in line with products FDA has approved in the past to meet unmet needs, including through Accelerated Approval, none of which have been subject to restrictions on coverage by CMS.

Notably, CMS recently issued an NCD to cover all FDA-approved Chimeric Antigen Receptor (CAR) T-cell (CAR-T) therapies, setting a precedent for issuing an NCD to cover all FDA-approved therapies within a class that addresses a significant unmet need for a serious disease.² Treatments for those with mild cognitive impairment (MCI) due to Alzheimer's disease and early Alzheimer's dementia similarly address a significant unmet need. CMS should apply the CAR-T precedent here and cover all FDA-approved mAbs directed against amyloid for the treatment of Alzheimer's disease consistent with their label.

To avoid coverage gaps for Alzheimer's patients, we also encourage CMS to release a proposed decision memorandum concurrent with its notice of opening the NCD process, as it is permitted to do in its discretion.³ Given the progressive nature of Alzheimer's disease, early access to disease-modifying therapy is crucial. Processes that may delay coverage decisions by several months can impose significant access delays, resulting in irreversible disease progression for beneficiaries living with Alzheimer's, and added burdens for their caregivers and loved ones. Underscoring this urgency, based on our estimates, more than 2,000 individuals aged 65 or older may transition per day from mild dementia due to Alzheimer's disease to moderate dementia due to Alzheimer's disease, and therefore outside the anticipated indicated population for lecanemab, if approved.⁴ Given the progressive nature of this terminal disease and absence of treatment alternatives, delays would deny these Medicare beneficiaries the opportunity to benefit from this treatment.

² National Coverage Determination (NCD) for Chimeric Antigen Receptor (CAR) T-cell Therapy (CAG-00451N), Centers for Medicare & Medicaid Services (Aug. 7, 2019), <https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?ncdid=374&bc=CAAAAAAAAAAAAA>.

³ 78 Fed. Reg. 48,164, 48,169 (Aug. 7, 2013).

⁴ To determine this number, we started with prevalence estimates of individuals age 65 and older with Alzheimer's dementia (Rajan 2021) and mild cognitive impairment (Petersen 2018). We adjusted the Alzheimer's dementia estimate using Graham 1997 to estimate the number of those in the mild stage and used Petersen 2013 to estimate the number of those with MCI who are amyloid positive, resulting in the number of those who would be eligible for an Alzheimer's treatment. We then applied annual transition rates of amyloid positive individuals reported by Potashman 2021 and annual transition rates of people with all-cause MCI from Mitchell 2009 to determine the number of people with mild Alzheimer's dementia and the number of people with MCI due to Alzheimer's disease who progress to the more severe stages of dementia for which the treatments are not indicated.

I. Background on Coverage Framework for mAbs Directed Against Amyloid

A. CMS's Existing NCD Relied on Unclear Evidence of Benefit from mAbs Directed Against Amyloid

In July 2021, CMS opened an NCA for the class of mAbs directed against amyloid for the treatment of Alzheimer's disease. In April 2022, CMS published its final decision memo, restricting coverage of these products to two scenarios⁵:

1) Monoclonal antibodies directed against amyloid that are approved by FDA for the treatment of Alzheimer's disease based upon evidence of efficacy from a change in a surrogate endpoint (e.g., amyloid reduction) considered as reasonably likely to predict clinical benefit may be covered in a randomized controlled trial conducted under an investigational new drug (IND) application.

2) Monoclonal antibodies directed against amyloid that are approved by FDA for the treatment of Alzheimer's disease based upon evidence of efficacy from a direct measure of clinical benefit may be covered in CMS approved prospective comparative studies. Study data for CMS approved prospective comparative studies may be collected in a registry.

This coverage policy imposed two unprecedented restrictions on patient access. First, the agency had never limited coverage of a drug or biologic when used according to its FDA-approved label. Second, the decision prospectively applied the coverage restrictions to all future FDA-approved drugs within the class, rendering a decision on their coverage without considering any data on their potential clinical benefit.

In issuing the NCD, CMS relied heavily on its conclusion that there was significant uncertainty around the clinical benefit of the mAB class, and the agency's view that potential safety concerns had to be weighed against the uncertain clinical benefit. In its final decision memo, CMS noted that, "[t]o date, no large, pivotal RCT, or set of RCTs, of an anti-amyloid mAb has been completed, with a trial report published in the peer-reviewed medical literature demonstrating a clear (non-conflicting) improved health outcome (i.e., a meaningful clinical benefit in terms of slowing in the decline of cognition and function) for Medicare beneficiaries with Alzheimer's disease."⁶ As discussed below, in light of new data published on lecanemab, this statement no longer holds true.

Reconsidering the NCD in light of the new lecanemab data, which resolves CMS's uncertainty underlying the initial coverage determination, would demonstrate that the agency remains flexible and committed to evidence-based decision making. On the other hand, the failure to reconsider the NCD would severely limit Medicare coverage for all FDA-approved mAb products, in particular for historically disadvantaged populations.

⁵ Apr. 2022 Alzheimer's Decision Memo.

⁶ *Id.*

B. CMS Standards and Requirements for NCD Reconsideration

CMS has stated in guidance that a reconsideration request may be granted in one of two circumstances: 1) where the request includes “[a]dditional 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,” and 2) where the request raises “[p]lausible arguments that our conclusion materially misinterpreted the existing evidence at the time the NCD was decided.”⁷

As explained below, and as CMS recognized in releasing the April 2022 NCD, evidence of clinical benefit from a product within the class covered by the NCD represents “new evidence” that should lead to a change in the current coverage policy.

CMS requires that a request for NCD reconsideration be labeled as a final and formal request, identify the scientific evidence supporting the request for reconsideration, and include as attachments the supporting documentation.⁸ Consistent with this standard, we are attaching additional scientific evidence, described below, showing a clinical benefit from a new mAb directed against amyloid for the treatment of Alzheimer's disease.

II. New Clinical Data Demonstrates Clinical Effectiveness of a New mAb Directed at Amyloid for the Treatment of Alzheimer's disease

A. New Data Regarding Lecanemab

On November 29, 2022, researchers published the results of a confirmatory Phase III placebo-controlled, double-blind, parallel-group, randomized study showing a clinical benefit from the use of lecanemab, known as Clarity-AD.⁹ In a patient population living with MCI due to Alzheimer's disease and mild dementia due to Alzheimer's disease, treatment with lecanemab met the primary endpoint (CDR-SB: Clinical Dementia Rating-Sum of Boxes), as well as all key secondary endpoints, with highly statistically significant results.¹⁰ Specifically, lecanemab reduced decline on the CDR-SB scale by 27 percent compared with placebo at 18 months, representing a difference in the score of -0.45 ($p=0.00005$). This difference in decline translated into a 5.3-month slowing of progression over the course of the 18-month trial even with allowing time within this trial for the titration of dosage in the treatment arm. These differences appeared as early as six months into treatment, and the effects on the primary and secondary endpoints widened over the course of 18 months of treatment. All key secondary endpoints also saw statistically significant change at 18 months from baseline when compared with placebo, with differences appearing earlier than the primary endpoint, including amyloid levels in the brain measured by amyloid positron emission tomography (PET), the Alzheimer's disease Assessment Scale-cognitive subscale14 (ADAS-cog14), AD Composite Score (ADCOMS) and the AD

⁷ 78 Fed. Reg. 48,164, 48,167.

⁸ *Id.*

⁹ Christopher H. van Dyck et al., *Lecanemab in Early Alzheimer's Disease*, *NEW ENGLAND J. MED.* (Nov. 29, 2022) (“Van Dyck et al.”).

¹⁰ CDR-SB is a numerical scale based on interviews of patients with Alzheimer's disease, their caregivers, and healthcare providers to assess the clinical progression of Alzheimer's disease.

Cooperative Study-Activities of Daily Living Scale for Mild Cognitive Impairment (ADCS MCI-ADL).

As discussed in greater depth in the attached researchers' statement, this trial represents a "foundational advance" in the treatment of Alzheimer's disease, and the new evidence fundamentally alters the evidence landscape that CMS considered in developing the April 2022 NCD.

Notably, the trial included individuals aged 50 to 90 years of age with substantial proportions of traditionally underrepresented ethnic and racial populations in the United States, with Hispanic/Latinos and African American/Black American patients living with early Alzheimer's disease composing approximately 25% of U.S. enrollment. Given this representation among the patient population and the fact that the study's exclusion criteria allowed patients with a relatively broad range of comorbidities, the study population is stated to be "generally comparable" to the Medicare population.¹¹ The comparability of the Clarity AD trial population to the Medicare population exceeds that of the Phase III trial populations of many other treatments covered by Medicare today.

B. New Data Regarding Gantenerumab

In addition to the lecanemab trial results, one other significant piece of evidence has emerged since April 2022: the November 14, 2022, announcement that gantenerumab, another anti-amyloid mAb for the treatment of Alzheimer's disease, did not meet its primary endpoint in a Phase III trial.¹² While the product did show a small reduction in cognitive decline in comparison to the placebo, the reduction did not reach statistical significance ($p=0.0954$ in one trial, $p=0.2998$) in another. However, the study also demonstrated that gantenerumab had lower than expected effectiveness in reducing levels of beta-amyloid, the intended mechanism of action. Therefore, the results from gantenerumab illustrate, rather than undermine, the relationship between the removal of beta-amyloid and the reduction of clinical decline. Moreover, because gantenerumab failed to meet its primary endpoint in sporadic Alzheimer's, it will not be submitted to FDA for approval. Accordingly, the results of its trials to date do not have any direct effect on coverage decisions for FDA-approved anti-amyloid mAbs.

III. The Existing NCD Must Be Modified in Light of New Data Showing Clinical Benefit

A. Lecanemab's Data Demonstrates a Meaningful Clinical Benefit for an Anti-Amyloid mAb in the Medicare Population

As discussed above, in the Clarity AD trial, lecanemab demonstrated a clear and statistically significant benefit versus placebo in a large, diverse, randomized clinical trial representative of the Medicare population, on both its primary endpoint and all secondary endpoints. And, as discussed in the attached researchers' letter, patients treated with lecanemab

¹¹ Lecanemab Confirmatory Phase 3 Clarity AD Study Met Primary Endpoint, Eisai (Sept. 28, 2022), <https://www.eisai.com/news/2022/news202271.html>

¹² Roche Provides Update on Phase III GRADUATE Programme Evaluating Gantenerumab in Early Alzheimer's Disease, Roche (Nov. 14, 2022), <https://www.roche.com/media/releases/med-cor-2022-11-14>.

progressed in cognitive decline almost 6 months slower than those who received a placebo, while also seeing a slower reduction in quality-of-life measures. Although such results do not represent a cure for Alzheimer's disease, they offer a benefit to patients and their caregivers of months of comparatively higher cognitive functioning and better quality of life. As the researchers' letter concludes, "[t]he Clarity AD trial represents an unprecedented and foundational leap in the search for a disease-modifying treatment for AD. It is the first to show an unequivocal effect in changing the rate of decline on diverse clinical, cognitive, and functional endpoints, converging with validated, AD-associated brain, cerebrospinal fluid and blood biomarker endpoints."

In the context of a progressive disorder like Alzheimer's disease, it is appropriate to consider statistically significant slower progression as a meaningful clinical benefit. Because MCI and mild dementia due to Alzheimer's disease are the phases of symptomatic illness when patients most value a delay in progression, this delay should be viewed as equivalent to a delay in mortality for other terminal diseases. FDA recognized this in agreeing with lecanemab's sponsors that the Phase III Clarity AD trial, designed to detect slower progression of cognitive decline, would be able to serve as a confirmatory trial for traditional FDA approval that requires a clinical benefit to be demonstrated. Further, while few disease areas are comparable to Alzheimer's disease, FDA has granted approval to products for the treatment of multiple sclerosis on the basis that they demonstrated a longer period of time before significant increase in disability versus the placebo.¹³

CMS also emphasized in the April 2022 NCD that the agency believed "[i]t is important that there is evidence that demonstrates that the positive RCT results for FDA approval are generalizable both to broader community care settings, and to the broader Medicare population that includes patients with co-morbidities such as hypertension, heart disease, diabetes, and the like."¹⁴ As discussed above, the lecanemab Phase III trial used exclusion criteria that were intended to include more patients with co-morbidities than typically would be the case, addressing this concern and producing data that is applicable to and representative of the Medicare population. The median age of participants was around 71 years of age. While the desire for data that is closely matched to the Medicare population is understandable, requiring further studies within the Medicare population specifically, after a clinical benefit has been demonstrated, would represent another unprecedented step by CMS to limit coverage for the on-label use of an FDA-approved drug given the demographics of many other Phase III trials for treatments that have been covered by CMS.

B. CMS Recognized That Evidence of Clinical Benefit Requires an Expedient Reassessment of Medicare Coverage of Anti-Amyloid mAbs

CMS's April 2022 NCD relied on both lack of evidence and uncertainty surrounding clinical benefit from aducanumab—the one mAb product directed at amyloid for the treatment of

¹³ Prescribing Information – TYSABRI, Food and Drug Administration (“The primary endpoint at 2 years was time to onset of sustained increase in disability ... Time to onset of sustained increase in disability was longer in TYSABRI-treated patients than in placebo-treated patients.”), available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/1215104s9591bl.pdf.

¹⁴ Apr. 2022 Alzheimer's Decision Memo.

Alzheimer's disease the agency was considering at the time. According to CMS, further data would be necessary to reconsider the NCD if future data were to emerge from the class of drugs. But, notably, the agency regarded the evidence from mAbs directed against amyloid in general, and lecanemab in particular, as “promising.”¹⁵

The NCD process is by its very nature heavily dependent on data and evidence. Decisions reached through the process maintain their appropriateness only as long as the evidence used to reach the decision remains fundamentally unchanged. This is made clear by the agency’s own criteria for potential NCD reconsideration, which include “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.”¹⁶

CMS acknowledged that an anti-amyloid mAb demonstrating clinical benefit and gaining FDA approval would represent a reason to reconsider the NCD decision. The April 2022 decision memorandum explained that CMS planned to revise its coverage criteria as soon as a clinical benefit was demonstrated for an anti-amyloid mAb, explaining, “[w]hen an anti-amyloid mAb demonstrates evidence of efficacy from a direct measure of clinical benefit for a selective population in one or more large, pivotal RCTs (Phase 3 or 4), and obtains FDA approval, CMS wants Medicare beneficiaries who are similar to those trial patients to have expeditious access to that biologic.”¹⁷

In issuing its final decision memorandum, CMS stated that it had structured the NCD “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.”¹⁸ CMS officials committed to a rapid reconsideration of the agency’s coverage policy—including of the entire class of products—in the event of new evidence emerging. Following the release of the NCD, CMS Coverage and Analysis Group Director Tamara Syrek Jensen explained that, “[i]f there is any new evidence, we can reopen this NCD at any time to reconsider our coverage determination as a class, or on a specific drug,” stating that the agency “intends to be nimble and flexible” regarding NCD reconsideration.¹⁹ As recently as December 8, 2022, CMS Administrator Brooks-LaSure commented that the agency will “look at [lecanemab’s] new data as it comes” and the previous decision “was based on information that was available at the time.” She noted that the decision is open to being reevaluated “as new products come to market.”

C. Broader Access to Anti-Amyloid mAbs is Necessary Now That Clinical Benefit Has Been Demonstrated

¹⁵ *Id.*

¹⁶ 78 Fed. Reg. at 48,167.

¹⁷ Apr. 2022 Alzheimer’s Decision Memo.

¹⁸ Dr. Lee Fleisher, CMS Chief Medical Officer, CMS Finalizes Medicare Coverage Policy for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer’s Disease (Apr. 7, 2022), <https://www.cms.gov/newsroom/press-releases/cms-finalizes-medicare-coverage-policy-mono-clonal-antibodies-directed-against-amyloid-treatment>.

¹⁹ Tamara Syrek Jensen, Stakeholder Call on the Medicare Coverage Policy for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer’s Disease (May 11, 2022).

Unless CMS reconsiders the April 2022 NCD, access to disease-modifying therapy for Alzheimer's disease will be extremely limited by the agency's CED requirements. In particular, although lecanemab has shown clinical benefit, because lecanemab is being considered by the FDA under the FDA's Accelerated Approval pathway, the current NCD could potentially further restrict coverage only through randomized controlled trials (RCTs). Coverage only through RCTs is highly limited and imposes significant cost and other burdens on patients, caregivers, and providers, limiting access for underserved and disproportionately affected patient populations, in particular (e.g., Black/African Americans, Hispanic/Latinos). In fact, it is our understanding that there may be no RCTs for lecanemab admitting new patients next year, meaning that this will effectively deny coverage to all beneficiaries except those wealthy enough to pay for the treatment out of pocket. While the sponsor has indicated it plans to file for traditional FDA approval as soon as possible, estimates suggest that process may take a half year or more.

Any delays in reconsidering the NCD to extend unrestricted Medicare coverage to mAbs directed against amyloid for the treatment of Alzheimer's disease will harm beneficiaries. Alzheimer's disease is a devastating progressive condition. The need for patient access to mAbs directed against amyloid, once approved by the FDA, has grown dramatically now that a product in the class has demonstrated a significant clinical benefit. For patients who do not receive access to lecanemab, as the attached researchers' statement explains, "every day of delay" in access "may result in treatable patients progressing beyond the window of therapeutic opportunity." Given the transition rates out of lecanemab's indicated population discussed above, delays could mean hundreds of thousands of Medicare beneficiaries would become ineligible to receive coverage for the treatment. There is no scientific or medical justification for CMS to restrict access to a product that has demonstrated a clinical benefit in a peer-reviewed RCT solely because it received approval from FDA under a different pathway.

Moreover, while we appreciate that lecanemab was associated with certain adverse events, those findings do not justify imposing restrictions on coverage. Virtually all FDA-approved drugs come with some risks, and the FDA's tolerance for adverse events tends to be higher for therapies that treat diseases for which therapeutic alternatives are currently limited. Indeed, there is extensive precedent for FDA approval of products with significant safety issues through Accelerated Approval in areas with significant unmet need where the product may be a patient's last or only option.²⁰ Rather, in disease areas with significant unmet need, such as Alzheimer's disease, our health care system has traditionally deferred to patients and their providers to assess the relative benefits and risks of FDA-approved treatments.

The fact that mAbs directed against amyloid currently target patients earlier in the disease is also not an adequate justification to limit coverage. In deciding to limit access to anti-amyloid mAbs based on the April 2022 data landscape, CMS expressed particular concern about safety indicators for the class of products for those with "early or mild disease (MCI or mild AD)" and who "are relatively high functioning." However, these patients have historically lacked

²⁰ See, e.g., FDA Label for Betaserson, (2003), noting the elevated risk of suicide for patients using the product, which was consistently demonstrated in both the study used to file for Accelerated Approval in 1993 as well as the confirmatory studies used for traditional approval.

treatment options and, now that a product has demonstrated clinical benefit in slowing disease progression in this population, these patients should be given the option to weigh both the benefits and risks of receiving this new therapy with their treating clinician. In fact, as a clinical matter, this is precisely the most valuable phase of symptomatic disease to extend.

Finally, it is also worth noting that, although CMS makes its coverage decisions with reference to the Medicare population, these decisions also have significant influence on commercial payors' decisions regarding coverage for non-Medicare populations (e.g., patients under 65). By recognizing that the new data justifies coverage for FDA-approved mAb products directed against amyloid for the treatment of Alzheimer's disease, CMS may help expand coverage outside of the Medicare program, providing a broader patient population in which to gather post-approval data regarding FDA-approved products in this class.

IV. Broader Access Is Even More Urgent In Light of Health Equity Considerations.

CMS has rightly made health equity a priority for the agency as a whole and for Alzheimer's disease, in particular.²¹ Broader and more equitable access to mAbs directed at amyloid for the treatment of Alzheimer's disease is even more urgent now that a clinical benefit has been demonstrated.

However, the limitations on access imposed by the current CED requirements represent particular barriers for historically underserved and disproportionately affected populations (e.g. Black/African Americans, Hispanic/Latinos, rural populations). Any new burdens on access, such as those that inevitably come with CED provisions, first exclude those with the greatest difficulty accessing the health care system. These difficulties may prevent these beneficiaries from seeking treatment that could benefit not only their quality of life but the lives of their caregivers and families. This burden is likely to fall the heaviest on rural and disproportionately underserved racial and ethnic populations and is essentially, denial of coverage and threat to health equity for those populations in greatest need. It is also worth noting that, while all forms of CED requirements can impose these kinds of barriers, the limitation of coverage for some products under the NCD to RCTs imposes an even greater burden. In fact, it is our understanding that there may be no RCTs available at all for enrolling new patients in 2023, reflecting the impractical and inequitable nature of extending coverage with these restrictions.

Further, CED requirements may undermine CMS's important objective of generating evidence that is representative of the Medicare population. CED requirements make it difficult to achieve the goal we share with CMS of generating evidence about anti-amyloid mAbs' efficacy in the Medicare population at large, including in historically underrepresented populations. CMS has recognized the difficulties in achieving greater representation from low-income and racial and ethnic minority populations in clinical studies due to factors related to language, logistical barriers such as time and travel, and/or a long-standing mistrust of the medical establishment. We agree that this underrepresentation restricts researchers' knowledge of how an approved therapy or diagnostic may affect populations that are most likely to need the

²¹ "CMS remains committed to the advancement of health equity by addressing the health disparities that underlie our health system." Apr. 2022 Alzheimer's Decision Memo.

treatment. We are concerned, however, that given the access issues outlined above, the CED requirements of the NCD may hamper the collection of such representative information.

V. Recommendation for Sequence of NCD Reconsideration

We recommend that the agency use the discretion afforded to it within the NCD reconsideration process to concurrently publish a new proposed decision memo with its announcement of reconsideration of the NCD.

In the past, CMS has used the discretion provided to it within the statutory NCD process²² to post a proposed decision memo simultaneously with the announcement of the agency's decision to reconsider an NCD.²³ Releasing the proposed decision memo concurrent with reopening the NCD process allows a coverage determination to proceed more rapidly—in as little as two months as opposed to more than a year in others—providing faster patient access to products deemed reasonable and necessary.

A rapid reconsideration process is even more important where, as here, each day matters when it comes to slowing the progression of this disease. Every day beneficiaries lack access to Alzheimer's disease treatment is one more day the disease progresses unhindered and that they potentially progress beyond the point that they are able to receive the treatment.

Moving expeditiously to begin a reconsideration, including through the concurrent release of a proposed decision memo, would also be consistent with the agency's commitment to quickly reconsidering the existing NCD in light of new data, especially data demonstrating clinical benefit.

VI. Recommended Revisions to the NCD Language

CMS's long standing precedent has been to provide coverage for Medicare beneficiaries of FDA-approved drugs. The agency's decision to depart from that precedent was based on the agency's uncertainty around whether there was reliable evidence that anti-amyloid mAbs can have a significant effect on the progression of Alzheimer's disease. With the release of the lecanemab data, the evidence landscape has fundamentally changed and the agency has an opportunity to return to its traditional posture of providing broad patient access to disease-modifying therapies.

We therefore recommend the revision of the current NCD in order to provide coverage of all FDA-approved anti-amyloid mAbs for Alzheimer's disease, consistent with the decision CMS made regarding CAR-T products and Medicare's general policy of covering FDA-approved drugs to the FDA-approved label. Our recommended language is as follows:

²² 78 Fed. Reg. 48,164, 48,169.

²³ See, e.g., National Coverage Analysis for Next Generation Sequencing (NGS) for Medicare Beneficiaries with Advanced Cancer (CAG-00450N), available at <https://www.cms.gov/medicare-coverage-database/details/nca-details.aspx?NCAId=290&type=Open&bc=ACAAAAAAAAAAAA&>.

“The Centers for Medicare & Medicaid Services (CMS) covers Food and Drug Administration (FDA) approved monoclonal antibodies directed against amyloid for the treatment of Alzheimer’s disease (AD) when used for a medically accepted indication as defined at Social Security Act section 1861(t)(2).”

These revisions will ensure beneficiary access to FDA-approved treatments in a class that has recently shown demonstrated clinical benefit and real promise for patients in a disease area where treatment options are lacking, while fulfilling the agency’s commitment to rapid reconsideration of its existing coverage policy in the event of new data demonstrating clinical benefit.

Thank you for your consideration of this request. Please contact Robert Egge, chief public policy officer, at regge@alz.org if you have any questions or would like additional information.



Joanne Pike, DrPH
President

Appendix / List of Attachments

1. Christopher H. van Dyck et al., Lecanemab in Early Alzheimer’s Disease, NEW ENGLAND J. MED. (Nov. 29, 2022).
2. [Alzheimer’s Researchers Letter](#).