

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

Re: CMS Proposed National Coverage Determination for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease

Dear Ms. Jensen:

On behalf of the Society for Women's Health Research (SWHR), I appreciate the opportunity to provide comments in response to the Centers for Medicare & Medicaid Services (CMS) January 2022 proposed National Coverage Determination (NCD) for monoclonal antibodies directed against amyloid treatment of Alzheimer's disease (AD).

SWHR is a 30-year-old education and advocacy nonprofit organization dedicated to promoting research on biological differences in disease and improving women's health through science, policy, and education. Given AD's disproportionate impact on women, SWHR has engaged with its AD network to raise awareness about biological sex differences in AD and has created recommendations for future research and policies in this field.¹

As CMS continues in this National Coverage Analysis (NCA) process, SWHR would like to share its concerns—spanning patient access and outcomes, equity, and future innovation—on the NCD proposal for consideration.

Patient Access and Outcomes

Alzheimer's disease affects an estimated 6 million Americans,² with well-documented sex and racial and ethnic disparities among those affected. While SWHR believes CMS' work through this NCA process has the potential to improve the evidence and care for those touched by AD, we are concerned that the agency's current proposal to cover monoclonal antibodies directed against amyloid for the treatment of AD under Coverage with Evidence Development (CED) in CMS approved randomized controlled trials (RCTs) could not only present challenges to patient access and outcomes, but also exacerbate inequalities in care.

¹ Waters, A, Society for Women's Health Research Alzheimer's Disease Network, Laitner, MH. Biological sex differences in Alzheimer's preclinical research: A call to action. *Alzheimer's Dement.* 2021; 7:e12111. <https://doi.org/10.1002/trc2.12111>

² Alzheimer's disease and related dementias, Centers for Disease Control and Prevention. <https://www.cdc.gov/aging/aginginfo/alzheimers.htm>. Accessed 2 Feb 2022.

While SWHR recognizes RCTs as the gold standard of scientific evidence and is aware of their value for assessing new interventions and treatments, there are important factors in the current landscape—including the dearth of other AD treatments currently available and how prolonged delays resulting from instituting RCTs could affect individuals wishing to receive treatment—that must also be considered.

It is SWHR’s understanding that, once a draft of the NCD is finalized, there will be no coverage in place until the study protocol is established and approved by CMS and patients are enrolled. That process will take months at a minimum, but could (and is more likely to) take years, especially considering the need to enroll a population that “is representative of the national population diagnosed with AD.” Even the slightest delay of treatment for a progressive neurodegenerative disease such as AD means there is a chance that, for a portion of this population, they may qualify for a study at present but would no longer qualify in the months to years it would take for the trial to be established. This would have very real implications and be a missed opportunity for patients with mild cognitive impairments and early-stage AD wishing to explore this class of treatment.

Beyond the considerations for how establishing the trial itself could affect patient access, there are also provisions within the proposal that could hinder access once a trial is launched, including factors that could have a disproportionate impact on women and underrepresented populations:

Ensuring Equitable Representation of Women. CMS notes within its “Covered Indications and Coverage Criteria for CMS Approved Trials” that patients “must not have medical conditions, other than AD, likely to increase significant adverse events.” While CMS does not specify what may qualify as a medical condition for its coverage criteria, SWHR is concerned that a broad interpretation of the NCD will impact women’s ability to be covered. There are a wide range of diseases and conditions that exclusively or disproportionately occur in women. This includes not only mental disorders like major depressive disorder (MDD), which is nearly twice as likely to occur in women,³ but also for conditions like osteoporosis, of which more than 80% of individuals affected are women,⁴ and autoimmune diseases, which occur in women at a rate of 2 to 1.⁵ Further, studies have shown that among the most common comorbidities in AD are osteoarthritis (38.2%) and depression (32.3%), both of which disproportionately affect women and could point to a higher exclusion of women from these clinical trials.⁶

³ Albert, PR (2015). Why is depression more prevalent in women? *Journal of Psychiatry & Neuroscience*, 40(4), 219-221. doi: 10.1503/jpn.150205

⁴ Osteoporosis, Office of the Assistant Secretary for Health’s Office on Women’s Health. <https://www.womenshealth.gov/a-z-topics/osteoporosis>. Accessed 2 Feb 2022.

⁵ About Autoimmunity, Autoimmune Association. <https://autoimmune.org/resource-center/about-autoimmunity/>. Accessed 2 Feb 2022.

⁶ Wang JH, Wu YJ, Tee BL, Lo RY. Medical Comorbidity in Alzheimer's Disease: A Nested Case-Control Study. *J Alzheimers Dis*. 2018;63(2):773-781. doi: 10.3233/JAD-170786. PMID: 29660933.

CMS has stated in its study requirements that “the diversity of patients included in each trial must be representative of the national population diagnosed with AD.” This undoubtedly includes gender representation, yet the CED’s exclusion of patients with medical conditions could unduly impact the number of women able to enroll, and therefore, conflicts with the agency’s representative trial requirement. The same argument can be made for minority groups, who may also be affected by certain medical conditions disproportionately, exacerbating already prevalent health inequities.

Considering Underrepresented Minority Populations. According to the Alzheimer’s Association, African Americans and Hispanics are roughly 2 to 1.5 times more likely, respectively, to have AD and other dementias than white Americans but are less likely to have a diagnosis of the condition.⁷ Further, the Alzheimer’s Association’s 2021 special report, *Race, Ethnicity, and Alzheimer’s in America* revealed that nearly two-thirds of Black Americans (62%), Asian Americans (45%), Native Americans (40%), and Hispanic Americans (36%) believe that medical research is biased against people of color.⁸ SWHR is concerned that CMS’ decision to utilize CED, which would involve additional clinical studies, coverage requirements, and mandated health outcomes collection, could inadvertently exacerbate the racial and ethnic inequalities already present in the access to AD detection and treatment. Related to this point and due to similar reasons as outlined above, SWHR would advise CMS not to use “lack of evidence on minority populations” as part of its rationale to establish a coverage policy that could restrict access to these populations.

Achieving Access via Trial Settings. CMS’ decision summary states that “All trials must be conducted in a hospital-based outpatient setting,” eliminating the potential to utilize other credible sites, such as independent infusion centers, for monoclonal antibody administration. This criterion would result in additional access restrictions through geography, limiting treatment options to only certain geographic areas. This further builds on inequities for patients who either lack resources or support to travel for treatment or for those living in rural areas who already face challenges related to accessing health care, including a shortage of health care providers, and whose significant travel time to these trials may deter their enrollment altogether.

The Effect on Caregivers

According to the Institute on Aging, upwards of 75 percent of all caregivers are women, and female caregivers may spend as much as 50% or more time providing care than men.⁹ When it

⁷ Fact Sheet: Race, Ethnicity, and Alzheimer’s. (March 2020).

https://www.alz.org/aaic/downloads2020/2020_Race_and_Ethnicity_Fact_Sheet.pdf. Accessed 2 Feb 2022.

⁸ New Alzheimer’s Association Report Examines Racial and Ethnic Attitudes on Alzheimer’s and Dementia Care, Alzheimer’s Association. (March 2021). <https://www.alz.org/news/2021/new-alzheimers-association-report-examines-racial>

⁹ Read how IOA Views Aging in America, Institute on Aging. <https://www.ioaging.org/aging-in-america>. Accessed 2 Feb 2022.

comes to AD and dementias, approximately two-thirds of dementia caregivers are women.¹⁰ The implications of the current CMS proposal, as written, would extend to these caregivers.

The responsibility of taking patients to the clinical trial sites, which would fall disproportionately on women, would be compounded not only by the geographic considerations outlined above, but also by the fact that most medications within this class of monoclonal antibodies have to be administered every 4 weeks.¹¹ Family caregivers already spend an average of 24.4 hours per week providing care;¹² the extra time and resources required to transport patients to clinical trial sites every month presents important quality of life considerations for not only the patients, but also for their caregivers.

Any therapy that could slow the progression of AD—extending the period of time when those with the disease may remain in a stage where they have some level of independence and ability to contribute to their own care—provides a huge value not just to themselves, but also to their caregivers.

Research and Development Implications

Finally, SWHR urges CMS to weigh how this class-based decision for monoclonal antibodies could affect future research and development in this space. This drug class, in which there are currently several drugs in development, could open doors to additional, new therapies that might alter the progression of this disease. By lumping all future monoclonal antibodies that target amyloid together in this decision, CMS may prematurely deter future, potentially groundbreaking research into this class of drugs, which could have different target populations and efficacy profiles.

Future projections for Alzheimer’s disease have important implications for the American health care system and the American people, particularly women and underrepresented minorities. While SWHR recognizes the complicated nature of CMS’ coverage decision for this drug class, SWHR is concerned that the NCD proposal could unintentionally create a ripple effect for some of the populations most in need of treatment.

We appreciate the opportunity to provide comment on this consequential Proposed National Coverage Determination for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer’s Disease and stand ready to work with CMS to ensure that the agency’s final policy enables, and does not unnecessarily restrict, patients’ access to safe, effective, and potential quality-of-life improving treatments for AD and more.

¹⁰ Caregiving for a Person with Alzheimer’s Disease or a Related Dementia, Centers for Disease Control and Prevention. <https://www.cdc.gov/aging/caregiving/alzheimer.htm>. Accessed 2 Feb 2022.

¹¹ van Dyck, Christopher H. “Anti-Amyloid- β Monoclonal Antibodies for Alzheimer’s Disease: Pitfalls and Promise.” *Biological psychiatry* vol. 83,4 (2018): 311-319. doi:10.1016/j.biopsych.2017.08.010

¹² Caregiver Statistics: Demographics, Family Caregiver Alliance. <https://www.caregiver.org/resource/caregiver-statistics-demographics/>. Accessed 2 Feb 2022.

If you have questions about these comments or require additional information, please do not hesitate to contact me at kathryn@swhr.org or 202.297.5122.

Sincerely,

A handwritten signature in black ink that reads "Kathryn G. Schubert". The signature is written in a cursive, flowing style.

Kathryn G. Schubert, MPP
President and Chief Executive Officer
Society for Women's Health Research

cc: Chiquita Brooks-LaSure, Administrator, Centers for Medicare & Medicaid Services