AGS Geriatrics Healthcare Professionals
Leading Change. Improving Care for Older Adults.

THE AMERICAN GERIATRICS SOCIETY
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January 18, 2022

Steven D. Pearson
President
Institute for Clinical and Economic Review
14 Beacon Street, Suite 800,
Boston, MA 02108

Re: Draft Scoping Document for Beta-Amyloid Antibodies for Early Alzheimer's Disease

Dear Mr. Pearson:

The American Geriatrics Society (AGS) greatly appreciates the opportunity to comment on the draft scoping document outlining the assessment of beta-amyloid antibodies for the treatment of Alzheimer's disease (AD). The AGS is a nationwide, not-for-profit society of geriatrics healthcare professionals dedicated to improving the health, independence, and quality of life of older people. Our 6,000+ members include geriatricians, geriatrics nurse practitioners, social workers, family practitioners, physician assistants, pharmacists, and internists who are pioneers in advanced-illness care for older individuals, with a focus on championing interprofessional teams, eliciting personal care goals, and treating older people as whole persons. The AGS believes in a just society, one where we all are supported by and able to contribute to communities where ageism, ableism, classism, homophobia, racism, sexism, xenophobia, and other forms of bias and discrimination no longer impact healthcare access, quality, and outcomes for older adults and their caregivers. The AGS advocates for policies and programs that support the health, independence, and quality of life of all of us as we age.

We applaud the Institute for Clinical and Economic Review (ICER) for engaging stakeholders to refine the scope of the assessment of donanemab and lecanemab for the treatment of early AD. The AGS also supports a reassessment of aducanumab to update ICER's evidence review should new clinical evidence emerge. Given the heavy toll of AD on patients, caregivers, and their families, it is crucial to evaluate the clinical evidence of these treatments and their safety and effectiveness thoroughly.

The AGS appreciates the opportunity to review this draft scope and share our recommendations which we hope you will consider as you move through the process of developing the evidence report and presentation.

GENERAL COMMENT

The AGS recommends a revision of the fifth line on the second page, "…accumulate beta-amyloid in the brain, which can be detected in the cerebrospinal fluid (CSF)," which implies that individuals with AD have higher levels of beta-amyloid in the brain detected in the CSF. However, the levels of beta-amyloid are lower in the CSF for people with AD as the disease progresses.[1,2]

COMMENTS ON PICOTS

Populations

The AGS recommends greater granularity in the sociodemographic factors for subpopulations, particularly in age and race/ethnicity in order to assess the level of diversity, equity, and inclusion and determine whether the evidence can be generalized to underrepresented, disproportionately affected, or understudied populations. More detailed information (e.g., disaggregated data by age group such as <65, 65-74, 75-84, and >=85 years) will be important considering the racial and ethnic disparities in the prevalence of AD and other dementias among the subpopulations[3] and increasing diversity among older people.[4]

We believe that it would be helpful to acknowledge the relatively small percentage of people in the older subgroup of older adults with AD who are expected to be candidates for treatment. Older people with cognitive impairment, including early-stage dementia, often manage a number of concurrent chronic medical conditions[5] and beyond exclusion by age, older adults are often excluded in clinical trials due to their comorbid conditions.[6] it is essential to understand how the clinical trials for the beta-amyloid antibodies managed patients with comorbid conditions as it impacts the cost and outcome estimates.

Additionally, the populations section of the draft scope indicates that evidence of AD pathology can be determined by "amyloid positivity **OR** pathological tau." However, tau is abnormal in neurodegenerative disease other than AD.[7] The AGS strongly urges ensuring that amyloid accumulation is a required criterion, and not tau alone.[8]

Interventions

Further delineation of the non-pharmacologic and non-disease-modifying pharmacologic interventions that constitute supportive care would be helpful for a more in-depth understanding of the interventions' impact and effectiveness. The AGS also recommends clarification around the use of medications to treat symptoms (e.g., acetylcholinesterase inhibitors, memantine) – whether the prescription would change and the likelihood of medication suspension or nonuse.

Comparators

The AGS encourages the consideration of prescribed medications to treat symptoms of AD in the comparisons of anti-beta-amyloid therapies and supportive care to supportive care alone.

Outcomes

In addition to the outcomes of interest described in the draft scope, the AGS encourages the inclusion of other adverse events that occurred during treatment that are not necessarily related to amyloid-related imaging abnormalities (ARIA) or death. We believe that the data collected in the clinical trials on standardized adverse events—where the cause of the event is typically not hypothesized—should be included in the assessment.

The AGS supports the addition of a measure on the burden of prescribing, approving, and receiving the beta-amyloid antibody treatments for patients/caregivers, prescribers, and insurers. For patients/caregivers, it may be beneficial to know the number of visits and phone calls as well as time spent by patients and/or caregivers to qualify and arrange to receive each dose in addition to the supplementary appointments for monitoring, labs, and scans. The time spent to submit

information to meet prior authorization requirements for approval and appeals, referring patients to centers for the drug administration, monitoring efficacy, and arranging review and follow-up for labs and scans can be significant for prescribers and similarly for Medicare and other insurers (e.g., reviewing prioritization requests and appeals, payment processing). We hope to understand whether these tasks add to or reduce similar burden of caring for untreated patients.

Some additional measures that may be of interest include a caregiver assessment; the time spent outside of the medical care system; measures that patients and caregivers thought were missing from clinical trials; and additional geriatric patient-specific measures. The AGS believes that the outcomes should be aligned with what matters most to persons living with dementia and their caregivers and families. Geriatrics health professionals focus on the 5Ms of geriatrics: **M**ultimorbidity, What **M**atters, **M**edication, **M**entation (cognitive function), and **M**obility (physical function).[9] Multimorbidity describes the older person who has more complex needs often due to multiple chronic conditions, frailty, and/or complex psychosocial needs. What Matters, Medication, Mentation, and Mobility describe the four main areas where geriatrics health professionals focus their clinical attention and form the basis for the age-friendly health systems framework that is focused on ensuring that all older people have access to this type of coordinated care, while also making sure personal needs, values, and preferences are at the heart of that care.[10] Cognitive function and physical function are especially important to older adults as reflected in conceptual models for what matters most to older adults such as the 5Ms.[11]

Timing
We agree that studies of any duration should be considered when evaluating evidence on intervention effectiveness and evidence of harms. Additional considerations include whether studies were prematurely terminated and the factors that lead to that termination.

Settings
The AGS believes that the treatment setting should be inclusive of treatment team capacity. In addition to the site of care, we recommend exploring whether the treatment setting facilitates appropriate monitoring for any adverse events as well as cognitive function to assist in determining whether the patient is benefitting from treatment, and if not, to help decide whether to terminate treatment using shared decision-making. Ideally the patient's care team would be interprofessional, inclusive of cognitive specialists and clinicians with geriatrics expertise along with a social worker, registered nurse, and pharmacist.

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Thank you for taking the time to review our feedback and recommendations. For additional information or if you have any questions, please do not hesitate to contact, Anna Kim at akim@americangeriatrics.org.

Sincerely,

Peter Hollmann, MD
President

Nancy E. Lundebjerg, MPA
Chief Executive Officer

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[4] Ibid.
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[9] Adapted by the American Geriatrics Society (AGS) with permission from "The public launch of the Geriatric 5Ms" [on-line] by F. Molnar and available from the Canadian Geriatrics Society (CGS) at https://canadiangeriatrics.ca/2017/04/update-the-public-launch-of-the-geriatric-5ms/.
[10] Institute for Healthcare Improvement. Age-Friendly Health Systems: Guide to Using the 4Ms in the Care of Older Adults. Available at https://www.ihi.org/Engage/Initiatives/Age-Friendly-Health-Systems/Documents/IHIAgeFriendlyHealthSystems_GuidetoUsing4MsCare.pdf. Published July 2020. Accessed January 11, 2022.
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