ADAPTING ELIGIBILITY CRITERIA FOR PRESCRIBING FDA APPROVED ANTI-AMYLOID IMMUNOTHERAPEUTICS FOR ADULTS WITH DOWN SYNDROME WITH EARLY-STAGE ALZHEIMER'S DEMENTIA

An Advisory and Consensus Statement of the Working Group on Criteria for Access to Alzheimer's Therapeutics for Adults with Down Syndrome

Product of the LuMind IDSC Foundation, Burlington, Massachusetts, and National Task Group on Intellectual Disabilities and Dementia Practices (www.the-ntg.org)

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Executive Summary

Current prior authorization criteria for the use of anti-amyloid immunotherapeutics as promulgated by state drug formulary committees in the United States have been written as criteria for accessing sporadic, late onset Alzheimer's dementia (LOAD) treatments. This has led to language excluding adults with Down syndrome and other intellectual disabilities who may benefit from these disease-modifying therapeutics. Modification of current prior authorization prescriber criteria to include applicability to patients with Down syndrome is warranted for multiple reasons: (1) the elevated risk for AD at younger ages than sporadic AD; (2) equitable access to therapeutics that can slow symptom progression; (3) inappropriate exclusion for pre-existing lifelong cognitive impairment; (4) availability of alternative applicable measures of neurocognitive decline, and (5) absence of prescribing criteria equivalencies.

An international group of experts convened to determine prescribing criteria equivalences that would be inclusionary of adults with Down syndrome. This advisory and consensus statement is the result of the experts' deliberations and recommendations for addressing this inequity to treatment access and includes alternative inclusionary language and modified criteria, as well as providing a roadmap for prescribers when determining eligibility for adults with Down syndrome.

Key Recommendations

- Sharing these recommended criteria to all organizational stakeholders that influence the availability of FDA approved DMTs for Alzheimer's disease, including the FDA, CMS, and state pharmacological and insuring bodies, pharmaceutical firms, and prescriber networks.
- Creating a standing advisory group with a charter to refine and augment the recommended language and specifics of meeting the prescribing criteria when new knowledge becomes available, and when studies are published noting the validity and reliability of applicable instruments with the population of persons with intellectual disability, including those with Down syndrome.
- Developing a guide for use by primary care physicians and other eligible prescribers on how to best meet their state's criteria for determining appropriate use when prescribing newly approved Alzheimer's DMTs for patients with Down syndrome and adults with other etiologies for intellectual disability.
- Organizing continuing education and resources for the medical/health community on the issues related to assessing eligibility and prescribing Alzheimer's DMTs for persons with Down syndrome, and adults with other etiologies for intellectual disability.
- Consulting and partnering with the pharmaceutical industry to assure the inclusion of adults with Down syndrome and adults with other etiologies for intellectual disability in clinical trials, starting with the conduct of safety trials in adults with Down syndrome with FDA-approved anti-amyloid immunotherapies.

CONSENSUS STATEMENT

An expert working group, following review of issues faced by adults with Down syndrome with accessing the new class of anti-amyloid drug for mild cognitive impairment and early Alzheimer's dementia with respect to promoting equity in access, has proposed actions to improve access. Adults with Down syndrome have an estimated lifetime risk of up to 90% for Alzheimer's disease, which contributes to over 70% of their deaths. Adults with Down syndrome will face multiple years delayed access to these disease modifying treatments compared to other at-risk populations, because of state authorization prescribing criteria that excludes them. Without urgency in altering these criteria, potentially a generation of aging adults with Down syndrome will be deprived of access to new treatments. State drug formulary committees' prescribing criteria currently omit specific mention of adaptations or reasonable adjustments that would enable adults with Down syndrome to access these treatments, once they are approved for use. To shorten the time for access and avoid delay in treatment, the working group recommends access through two actions: (1) States and other payers adopt the proposed DS-focused equivalency criteria as soon as possible; and (2) Phase 4 clinical trials in adults with DS be undertaken with similar urgency so that clinicians gain information on the safety of this class of drugs for adults with DS. The working group recommends a series of wording changes to reflect equivalencies in the prescribing criteria, offers substantiation for such changes, and calls upon relevant organizations to provide education to prescribers, and for professional associations to issue protocols for guiding prescribers in the use of this class of AD drugs.

Introduction

Adults with Down syndrome are genetically predisposed toward early onset amyloid deposition in the brain and face a dramatically increased lifetime risk for Alzheimer's disease (AD), referred to as Down syndrome associated AD (DS-AD). Individuals with DS, with rare exceptions, show cerebral amyloid accumulation by age 40[1,2] with the cumulative risk for dementia reaching 50% by the mid-50s.[3] The estimated risk of developing DS-AD is as high as 90% by the late 60s[4,5] and DS-AD is the leading contributor to deaths of adults with Down syndrome.[6,7] Additionally, most adults with Down syndrome show behavioral expression of AD in their early 50s.[8] Therefore, it is vitally important for this high-risk population to have equitable and timely access to newly authorized and future anti-amyloid Alzheimer's therapeutics as these disease-modifying therapies (DMTs) become available. Given the high rate of dementia in adults with Down syndrome, access to DMTs for DS-AD will produce a large-scale impact for additional quality-of-life years.

This advisory:

- **Recognizes the need for access to DMTs for AD for the population of adults with DS.**
- **Proposes that state drug formulary committees consider equivalency adaptations to prescribing criteria that would enable clinicians to document AD and undertake assessments in adults with DS.**
- **Offers specific evidence-based and evidence-informed wording for use by state drug formulary committees.**
- **Recommends both guidelines and protocols be developed to aid in prescribing and administering anti-amyloid DMTs for DS-AD.**

The pressing need for improved treatments for DS-AD together with the recent development of a class of anti-amyloid medications raises a critically important health policy issue. Current prior authorization criteria for the use of anti-amyloid immunotherapeutics as promulgated by drug formulary committees[1,9] in the USA are developed for treating mild cognitive impairment (MCI) due to AD and mild AD dementia (either considered, early Alzheimer's Disease) in the general population.[10] This has led to language that risks excluding adults with Down syndrome who may benefit from these therapeutics. Adaptation of current inclusionary prior authorization criteria is necessary for several reasons, including age criteria that do not account for the elevated risk for DS-AD at an atypically younger age compared to sporadic AD population, inappropriate exclusion of adults simply due to pre-existing lifelong cognitive impairments, and the specified use of inapplicable neurocognitive measures.

This advisory is intended to: (1) address this inequity by proposing alternative inclusionary wording and suggested accommodations; and (2) serve as a roadmap or guide for prescribers when determining eligibility for adults with Down syndrome by offering additive or alternative wording for the criteria and suggesting alternative measures. Defining equivalency is crucial to ensure timely access to these drugs once they are deemed appropriate for use in this population. Delaying the efforts to

[1] The term 'drug formulary committees' is used to encompass a variety of drug prescribing authorities within the states, as which body issues prescribing criteria is complicated. The process begins with the FDA which provides drug approval. Then, once the drug is available in the marketplace, most medication access issues are established and determined by 'Drug Formulary Committees' within the states across various sectors (i.e., insurers, pharmacy benefit managers [PBMs], governmental entities, hospitals, healthcare systems, etc.). Often the drug formulary decision process is outsourced to other entities. How this happens varies across the states, but these Drug Formulary Committees establish the criteria. At the federal level, CMS has a role as the national regulator and provider of guidance and put in place prescribing criteria based on the FDA Approved Drug Label (Michael Koronkowski, Personal communication, April 27, 2023).

implement adapted prior authorization criteria for this population could result in a significant delay to the access to treatments. To date, no adults with Down syndrome have been included amongst the 6,000 or more participants in clinical trials of Aduhelm™, Leqembi™ and donanemab, resulting in a possible delay of multiple years in access to these medications while safety for adults with Down syndrome remains unclear[11,12].

While this advisory concerns adults with Down syndrome, the recommendations may also be applicable to individuals with intellectual disabilities from other etiologies , who face similar barriers of exclusion under existing prior authorization prescribing criteria.

Background

Aduhelm™ and Leqembi™ are immunotherapies currently approved by the US Food and Drug Administration (FDA) for the treatment of mild cognitive impairment (MCI) and mild dementia due to Alzheimer's disease (in combination, referred to as “early Alzheimer’s disease"). The approval of another immunotherapeutic donanemab, which has also shown positive clinical trial results, is expected soon. As the proven efficacy of all these treatments is through targeting removal of brain amyloid beta deposits, and as individuals with Down syndrome typically develop this characteristic AD amyloid neuropathology by middle age, these anti-amyloid immunotherapies are likely to be beneficial for the prevention and treatment of DS-AD.

Current FDA label and state prior authorization prescribing criteria for Aduhelm™ and Leqembi™ vary with respect to applications and provisions that permit the inclusion and assessment of individuals with a history of an intellectual disability, including adults with Down syndrome.[2] Drug formulary committees in their varied iterations across the country have the purpose of overseeing and designating drugs of choice to guide rationale prescribing.[13] States, via drug formulary committees, have taken upon themselves to choose specific wording and criteria that receive particular focus.[14]

Criteria defining treatment eligibility for patients with sporadic AD focus varyingly on age, exclusion of non-Alzheimer’s causes , demonstrated cognitive decline or impairment due to mild cognitive impairment or mild AD, and biomarker indicators for the presence of amyloid plaques**.** A prominent issue for DS-AD is that the specific assessments recommended to identify cognitive impairment in the sporadic AD population are generally not effective for quantifying cognitive decline against a background of pre-existing intellectual impairments, pointing to a need for other methods specifically adapted for adults with Down syndrome.

[2] Complicating standardization is the peculiar way that in the United States medication and payment approval occurs. Pharmaceutical firms file applications for approval of a trialed drug to the Food and Drug Administration (FDA), which then evaluates the application and trial outcome data and either disapproves or approves the drug, in this case, an Alzheimer’s therapeutic. Another federal agency, the Centers for Medicaid and Medicare Services (CMS), serves as the approval agent for covering the cost of the medications for eligible persons (i.e., Medicaid recipients). This federal agency which normally covers payment for the Alzheimer’s treatments has not provided standardized guidance, as it has postponed payment authorizations for both FDA accelerated approval drugs, except for those adults enrolled in clinical trials, until the FDA provides full approval. In anticipation of eventual approval and to cover those patients with Medicare or Medicaid, private insurance or other sources of funds, the individual states have developed their own requirements for determining eligibility. While attending to the core criteria (exclusion of non-Alzheimer’s, cognitive impairment, and presence of amyloid) states have used a variety of objective measures.

Practitioners in clinical care have developed a battery of neuropsychological assessments and a process for monitoring cognitive decline in adults with Down syndrome .[15,16] This process generally involves both the adult and others involved in caregiving as informants providing information on physical health, mental health, and general function, together with the use of a range of directly administered tests to measure various functional capacities and signs of cognitive decline. In addition, the expectation is that physicians follow protocols for full clinical workups and medication reviews to identify and rule out any treatable causes for decline. Also, as many adults with Down syndrome have co-occurring conditions (often from childhood), the treatments for these conditions are monitored for any deleterious effects on behavior and/or function. Furthermore, there have been numerous studies of signs and symptoms of cognitive decline and more recently fluid biomarker profiles in the progression of DS-AD.[17, 18] Taken together, this knowledge is reflected in medical protocols and in assessment instruments developed specifically for assessing memory and function in adults with DS.

Some state prior authorization prescribing criteria for the current generation of DMTs are specifically exclusionary (e.g., "excluding Down syndrome due to other causes of cognitive impairment"[19]), and others are silent on inclusionary adaptations for populations with a long-standing history of developmental or neuropsychiatric conditions.[20] In addition, obtaining MRI and PET scans or lumbar punctures for CSF collection to meet brain imaging and fluid biomarker criteria, respectively, in adults with Down syndrome can be challenging due to limited access to specialized clinics or clinicians familiar with neuroatypical populations. As this access barrier may be the unavoidable circumstance for many adults with Down syndrome at-risk for AD, consideration should be given to empirically supported alternatives that can be more easily obtained, such as empirically validated blood biomarkers, given the extremely high likelihood of early-age amyloid neuropathology.[21]

Thus, given the high risk for early onset dementia in adults with Down syndrome there is an urgent need to adapt and make reasonable accommodations to the currently used prescribing criteria, while at the same time ensuring that safety risks are managed, consistent with best clinical practice guidelines for the general population. The purpose of this report is to provide evidence-based and evidence-informed recommendations for modifying wording in state prior authorization prescribing criteria. The outcome would be maximizing equitable access for adults with Down syndrome to anti-amyloid immunotherapeutics, and recognition of the diversity of the population that may benefit from these therapeutics.

This advisory and Consensus Statement is consistent with the Appropriate Use Recommendations of the Alzheimer's Disease and Related Disorders Therapeutics Work Group[22, 23, 24] Rather that endorsing the use of anti-amyloid immunotherapy class of drugs for adults with Down syndrome, it is a call for equitable access to treatments for adults with Down syndrome and creating the preparatory language environment with state drug formulary committees. Further, it calls for the careful monitoring of safety for DS-AD as these newly approved agents are used in clinical practice.

The derivation of the recommendations

To provide evidence-based and evidence-informed guidance for the adaptation of existing state criteria for prescribing newly authorized immunotherapeutics, a Working Group was constituted of a multinational group of experts in the clinical, biomarker, and cognitive and behavioral assessment aspects for determining the presence of AD in adults with Down syndrome. The group, drawn from noted Down syndrome and Alzheimer's researchers who study biomarkers and dementia assessments, as well as clinicians treating adults with Down syndrome, represented various perspectives and

proffered their expertise to adapt prescribing criteria that is appropriate for assessing DS-AD. The group was charged with examining existing prescribing criteria used in various states for the sporadic AD population to determine which criteria applied equally to adults with DS-AD and which criteria necessitated an alternative wording. The primary prescribing use criteria examined included: (1) age, (2) prescriber, (3) validated early AD diagnosis assessment scales, (4) biomarkers for amyloid positivity, (5) test evidence of progressive cognitive impairment, (6) MRI baseline, and (7) exclusion of non-Alzheimer's causes for cognitive decline. The Working Group also proffered recommendations on additional criteria used by the US Department of Veterans Affairs and specific Leqembi™ appropriate use criteria (See Table B).

The work process occurred in four stages. The first stage was a discussion that parsed the salient issues related to creating the equivalencies and narrowed the focus on key elements from known science and clinical practice. Working Group members were provided with a matrix that listed existing criteria and wording from a cross-sectional sample of 12 states (drawn from formularies available on the Internet – Appendix C).[25] A review by the project principals showed that these 12 states represent a broad segment of prescriber guidance, and there are sufficient consistencies and variations among those state guidelines to permit focusing on key elements for creating the equivalencies. In the second stage, Working Group members proffered their informed comments on a summative document, which permitted the production of targeted discussions around nuances for each set of criteria. In the third stage, these comments were first machine analyzed using the AI ChatGPT program (www.openAI.com/blog/ChatGPT, personal communication, April 4, 2023), then reviewed by the project principals (HH, RF, MPJ) for logic and validity, and finally reduced to key prescribing limitations, which in turn were converted by the Working Group into recommendations for adoption by state drug formulary committees.

In the fourth stage, the recommendations were included in a Consensus Statement that was reviewed by all Working Group members for accuracy, utility, and soundness. The overriding principle was that this Statement needed to consider scientific validity as well as the practicality and availability of resources that would aid prescribers when treating a patient with Down syndrome. Commentary was added by the Working Group to reflect concerns and varying clinical applications and practices. The Consensus Statement is included in this document.

Working Group members also cited several resources that prescribers might use for consultation on particular aspects of assessment and diagnosis of dementia and the presence of Alzheimer's disease in adults with Down syndrome and those with intellectual disability resulting from other etiologies. These resources were seen as offering a 'roadmap' that would direct any prescriber unfamiliar with assessing adults with Down syndrome and formulating justifications for the presence of dementia and cognitive decline, as discerned from pre-existing intellectual impairment in adults with Down syndrome. These resources are cited in Appendix B.

Criteria and equivalency recommendations

What follows are the key state authorization criteria and the recommendations for modifications to accommodate adults with Down syndrome (see Table A and Table B).

Table A: State core criteria and harmonization recommendations for prescribers treating adults with Down syndrome	
Criteria	**Recommendations and Commentary**
STATE AUTHORIZATION CRITERIA	

Age	**RECOMMENDATION:** Patient with Down syndrome may be 50 to 85 years old – or if younger and meets other criteria for early DS-AD. Wording derivation: State of California
	Expert Working Group Commentary Working Group agreed that while an age statement may be necessary, there should be flexibility due to the early age of significant amyloid presence in Down syndrome. The California criterion was seen as sufficient as it allows for inclusion of younger adults with AD, but noting earlier onset in Down syndrome would provide clarity. Further, as eventually biomarker criteria would be adopted that will help with diagnosis irrespective of age, the Working Group suggested that a minimum age of 40 would be appropriate (although it cautioned to ensure that non-AD causes of decline are considered in individuals younger than 40).
Prescriber	**RECOMMENDATION:** For patients with Down syndrome, prescriber should consult with specialist health provider/ clinician knowledgeable in DS-AD or in dementia in intellectual disability, if feasible.
	Expert Working Group Commentary Working Group agreed that various prescribers would be appropriate when a patient with Down syndrome is being treated but recommended that prescribers not familiar with Down syndrome or others with intellectual disability seek guidance from a consultant expert with this population. Working Group noted the availability of existing articles and guides that define processes for dementia assessment and diagnosis that could serve as consultation (Appendix B).
Validated MCI/ mild AD diagnosis assessment scales	**RECOMMENDATION:** For patients with Down syndrome (DS), provider attestation for diagnosis of early DS-AD via evidence of cognitive, functional, and behavioral decline from DS-appropriate assessments and/or caregiver/informant/clinician interview reports.
	Expert Working Group Commentary Working Group noted that although there has been progress in identifying measures that are sensitive and valid to MCI and early dementia in Down syndrome (DS) in research applications, there is no consensus on the use of specific scales or cut-off scores in clinical settings. As the severity of premorbid ID will impact the outcomes of cognitive assessments means there is a wide range of scores among adults with Down syndrome on these measures prior to MCI or early dementia making it difficult to establish a single cut off score. Working Group recommended using at least two validated measures (one of which must be an informant-report and one must be a directly administered measure) and that scores should be interpreted while considering the adult's premorbid level of intellectual functioning, medical conditions, and any recent life events. Working Group noted that there may be a conflating diagnosis of MCI and early-stage dementia in DS-AD, as disease progression may accelerate in people with Down syndrome due to compressed aging. Working Group noted the availability of existing articles and guides that define processes for dementia assessment and diagnosis that can be consulted prior to undertaking assessment (Appendix B).
Biomarkers for amyloid positivity	**RECOMMENDATION:** For patients with Down syndrome, Positron Emission Tomography (PET) scan is positive for amyloid beta plaque indicative of AD.
	Expert Working Group Commentary

	Working Group expressed a range of opinions on the use of biomarkers for amyloid positivity, specifically PET imaging and blood-based biomarkers. Working Group members agreed that PET imaging remains the most direct and reliable measure of amyloid deposition, but emerging blood-based biomarkers as potential screening methods may have more utility. Working Group recommended flexibility in regulatory policies to accommodate advances in the field and to improve diagnostic certainty. While PET procedures are generally well-tolerated in the population with Down syndrome and mild to moderate intellectual disability, PET amyloid beta cut points for "positivity" in Down syndrome are largely the same as for Alzheimer's disease in neurotypical populations, CSF and/or blood biomarker confirmation should be required. CSF Abeta42/40 ratio and amyloid-PET appear to be interchangeable for amyloid positivity, but PET imaging is needed for tracking the removal of amyloid from the brain. The Working Group noted the equivalence of plasma P-tau217 with CSF in the diagnosis of sporadic AD. It is expected that eventually abnormal blood biomarker results (such as P-tau) may be approved to diagnose amyloid positivity. When and if blood biomarkers are available, these will be highly preferred for the population with Down syndrome. MRIs are required to detect ARIA (amyloid-related imaging abnormalities) which may occur with lowering amyloid therapeutics, both at baseline and during treatment. The Working Group noted that all available imaging and biofluid-based biomarkers for detection of AD neuropathology work as well in adults with Down syndrome as in adults without DS. This will facilitate the diagnosis of DS-AD considerably.
Test evidence of cognitive impairment	**RECOMMENDATION:** For patients with Down syndrome, evidence of cognitive decline relative to premorbid cognitive functioning level, as evidenced by informant-reported and directly administered assessment measures showing poorer than expected performance. Wording derivation: State of Florida
	Expert Working Group Commentary Working Group position was that the evidence of cognitive decline relative to prior premorbid intellectual functioning level, as evidenced by both informant-reported and directly administered measures validated in the population with DS, is an appropriate way to diagnose cognitive decline in adults with DS. Working Group recommended that the premorbid level of functioning needs to be considered, and that sequential testing with a baseline in early adulthood would be ideal but may not be practical for all cases. Working Group suggested focusing on "changes judged to be of clinical significance".
MRI at baseline	**RECOMMENDATION:** For patients with Down syndrome, a baseline brain magnetic resonance imaging (MRI) to assess ARIA prior to initiating treatment (within 1 year prior).
	Expert Working Group Commentary Working Group noted that MRI is an important component of monitoring for safety, as it can detect potential risks associated with the use of certain treatments. Working Group raised concerns regarding the potential risk of ARIA in adults with Down syndrome, which may require more frequent monitoring and that patients and carers should be informed of the potential risks of amyloid-lowering treatments to support informed decisions. Working Group agreed that MRI protocols can be developed that are quicker and easier, including shorter sequences that can be completed in approximately 15 minutes. Working Group noted that baseline and during-treatment MRIs are necessary to monitor for safety in patients with Down syndrome, as they are for other patients.
Exclusion of other causes of cognitive impairment	RECOMMENDATION: Patients with Down syndrome are not to be excluded based on lifelong DS-associated pre-existing cognitive impairment.
	Expert Working Group Commentary

	Working Group agreed upon the importance of excluding other causes of cognitive decline before administering anti-amyloid therapy to adults with Down syndrome. Working Group suggested that the requirement to exclude other neuropathologies as the primary cause of cognitive decline should be dropped for adults with Down syndrome due to the rarity of non-AD aging-related neuropathology without co-occurring evidence of amyloid deposition. Working Group recommended looking for presence of mixed vascular or psychiatric conditions that might affect monitoring responses and side effects and that a thorough work-up prior to treatment be undertaken with patients to identify and treat other medical conditions that may mimic MCI or mild AD in Down syndrome. Working Group noted the importance of consultation with experts in the intellectual disability medical/health field who are more familiar with discerning dementias of other causes than AD.

Table B: Other Criteria Related Department of Veteran Affairs Authorization or to Leqembi™ Appropriate Use Criteria	
The following is taken from additional criteria issued by the US Department of Veteran Affairs (DVA)	
Most of the DVA criteria categories mirror those generally cited by the states	
Thyroid levels	**RECOMMENDATION:** For patients with Down syndrome, hypothyroidism diagnosed and treated according to standard of care with TSH levels monitored.
	Wording from DVA authorization criteria: Thyroid stimulating hormone above normal range (TSH > 5 mU/L if < 65 years old; TSH > 7.5 mU/L if >65 years old
The following are taken from additional lecanemab appropriate use criteria	
BMI	**RECOMMENDATION:** No significant difference in Down syndrome
	Wording from Appropriate Use criteria: Physician judgment used for patients at the extremes of BMI
Care Partner	**RECOMMENDATION:** No significant difference in Down syndrome
	Wording from Appropriate Use criteria: Have a care partner or family member(s) who can ensure that the patient has the support needed for treatment protocols with lecanemab.
Understand requirements for therapy	**RECOMMENDATION:** No significant difference in Down syndrome
	Wording from Appropriate Use criteria: Patients, care partners, and appropriate family members should understand the requirements for lecanemab therapy and the potential benefit and potential harm of treatment.
Recent history of stroke, transient	**RECOMMENDATION:** For patients with Down syndrome (DS), no significant difference of criteria for stroke or transient ischemic attacks, however, as a history of seizures is more likely for individuals

ischemic attacks and seizures	with Down syndrome and adult onset seizures can occur with AD progression, their presence should not be a contra-indication for treatment with immunotherapies.
	Wording from Appropriate Use criteria: Recent history (within 12 months) of stroke or transient ischemic attacks or any history of seizures.
Mental issues	**RECOMMENDATION:** For patients with Down syndrome, mental health criteria are not appropriate as contra-indication for immunotherapy treatment, as severe mental illness comorbidities are uncommon.
	Expert Working Group Commentary Working Group noted that in all cases of treatment of adults with Down syndrome will involve supervision and support by a caregiver who will oversee management requirements and adults with Down syndrome will not be living in a situation without oversight. Also, mental illness symptoms are often part of how DS-AD manifests in adults with DS, so should therefore not be a contraindication for anti-amyloid immunotherapy treatment.
	Wording from Appropriate Use criteria: Mental illness (e.g., psychosis) that interferes with comprehension of the requirements, potential benefit, and potential harms of treatment and are considered by the physician to render the patient unable to comply with management requirements.
Depression	**RECOMMENDATION:** No significant difference in Down syndrome
	Wording from Appropriate Use criteria: Major depression that will interfere with comprehension of the requirements, potential benefit, and potential harms of treatment; patients for whom disclosure of a positive biomarker may trigger suicidal ideation. Patients with less severe depression or whose depression resolves may be treatment candidates.
Bleeding disorder	**RECOMMENDATION**: No significant difference in Down syndrome
	Wording from Appropriate Use criteria: Patients with a bleeding disorder that is not under adequate control (including a platelet count <50,000 or international normalized ratio [INR] >1.5 for participants who are not on anticoagulants).
Anti-coagulants	**RECOMMENDATION:** No significant difference in Down syndrome
	Wording from Appropriate Use criteria: Patients on anticoagulants (coumadin, dabigatran, edoxaban, rivaroxaban, apixaban, betrixaban, or heparin) should not receive lecanemab; tPA should not be administered to individuals on lecanemab.
Immunological disease	**RECOMMENDATION:** For patients with Down syndrome (DS), rheumatoid arthritis, celiac disease, and alopecia areata or totalis , should not be exclusionary in DS-AD when these conditions are stable. No significant difference in Down syndrome for the other immunological diseases referred to in the Appropriate Use criteria.
	Expert Working Group Commentary Rheumatoid arthritis, celiac disease, and alopecia areata or totalis are often common co-morbidities for adults with DS and should therefore not be exclusionary.
	Wording from Appropriate Use criteria: Any history of immunologic disease (e.g., lupus erythematosus, rheumatoid

	arthritis, Crohn's disease) or systemic treatment with immunosuppressants, immunoglobulins, or monoclonal antibodies or their derivatives.
Medications	**RECOMMENDATION:** No significant difference in Down syndrome
	Wording from Appropriate Use criteria: Patients may be on cognitive enhancing agents (donepezil, rivastigmine, galantamine, or memantine) for AD, and patients may be on standard of care for other medical illnesses.

Discussion

Overall, there was consensus by Working Group members that equivalency prior authorization prescribing criteria issued by states are crucial for providing treatment access to adults with DS-AD and avoiding the exclusion of people with Down syndrome and other intellectual disabilities from this important class of emerging AD therapies. The rationale for special attention to inclusion and equity for adults with Down syndrome is based on three factors: (1) the recognized high risk and early onset of Alzheimer's disease among adults with DS; (2) the compressed aging factor which shortens lifespan by about 15 years from others in the general population;[26,27] and (3) the probability of the efficacy of new immunotherapeutics in reducing beta amyloid in middle age and potential for improving life span and maintaining brain health into older age.

As precedent for adapting criteria, the Working Group noted that when acetylcholinesterase inhibitors (AChEI) were introduced for treatment of Alzheimer's disease, some criteria for use also initially excluded individuals with Down syndrome and other etiologies of intellectual disability. These exclusions included the requirement for thresholds on specific cognitive assessments that were not appropriate for this population (as noted in the initial guidance by NICE in the UK).[28] After input from clinicians and other stakeholders, the guidance was changed to acknowledge that dementia assessments used to determine thresholds for treatment should consider any physical, sensory or intellectual disability, or communication difficulties that could affect the results and that clinicians should make any adjustments they consider appropriate, such as to use another appropriate method of assessment as necessary. Additionally, it was shown that treatment with most AChEI drugs was well-tolerated and effective in individuals with Down syndrome demonstrating the potential benefit of including people with Down syndrome in guidance for dementia treatments.[29]

The Working Group recognized that there are a limited number of experts in DS-AD in the United States, Europe, and internationally, so that finding and enlisting clinical consultants may be problematic. The Working Group suggested that governmental entities and academic health sciences/medical institutions should institute programs of education or provision of continuing education for prescribers on assessing adults with neuroatypical conditions, particularly those adults at high risk of amyloid build-up, such as Down syndrome.[30] While the recommendations point to accessing and using consultants familiar with discerning dementia in adults with Down syndrome, this may be impractical, if they are not geographically available. However, the Working Group would prefer to see such consultations take place if feasible.

Given the dearth of such experts, the Working Group also recommends that nonprofits and professional organizations create technical resources to be alternatives to conferring with an expert on

Down syndrome on the proper use of assessment scale instruments or a clinical work-up. Additionally, training in cognitive testing for adults with Down syndrome should be organized by American medical and dementia-related professional organizations, such as the AADMD, AAIDD, AGS and DSMIG-USA, or by others, via in-person continuing education, webinars, or other teaching media (e.g., Project ECHO[31]) to increase the number of clinicians and prescribers who are capable and comfortable seeing patients with Down syndrome.

The Working Group believes that it is important that prescribers have an appreciation of the nuances of Down syndrome and its cognitive phenotype. While some small number of adults with Down syndrome have developmental histories that make them appropriate for assessment using standard practices for sporadic AD, the vast majority will need to be assessed using techniques generally ascribed for use with adults with lifelong cognitive impairments, including the use of commonly used informant-reported brief screening measures, such as the DSQIIID,[32] DLD,[33] or the NTG-EDSD.[34] These measures can be implemented by caregivers to note cognition, daily functioning, and behavior; and when considered together with validated directly administered measures of cognitive functioning such as the DSMSE, TSI, modified Cued Recall Test, and CAMCOG-DS may lead to validated diagnoses.[35] These assessments, among others, have been reported to have good sensitivity and specificity for MCI and/or AD dementia in DS. However, these directly administered measures require specialized training, which may not make them feasible for use in all office or clinic settings.[36] Notwithstanding these limitations, assessment of cognitive decline can be made and prescribers with awareness can usually discern decline from lifelong cognitive limitations.

The Working Group also noted that discerning MCI from mild dementia in adults with Down syndrome may be challenging. This has been explored in research studies and the DSM-5 criteria for dementia in people with intellectual disability has been adapted to account for some of the identified difficulties.[37] Attempting to make this distinction in a clinical setting may be more difficult and the differences in cognition or function discerned may not be that useful. The Working Group noted that prescribers should initiate an investigation prior to prescribing, noting the significant difference in function from pre-morbid to morbid. Resources exist that can aid prescribers with understanding the specific means of ascertaining dementia in adults with Down syndrome and other intellectual disabilities.[38,39,40]

An issue related to the current prescribing criteria is the recommendation of the use of specific brief assessments (e.g., MMSE or CDR-SB) that indicate the presence of MCI or mild dementia in sporadic AD. The instruments noted most in the state prescribing criteria are those that were selected for use in the clinical trials associated with the approved DMTs.[41] Unfortunately, these procedures will be less likely to discern innate cognitive impairment from cognitive decline in most adults with intellectual disability, including Down syndrome. Thus, listings of specific brief cognitive assessments (BCAs) as part of the prescribing criteria will most likely be inadequate and inappropriate for use.[42] Regrettably, most listings of BCAs fail to consider the diversity of the American population and do not consider atypical ethnic and primary language backgrounds, nor the needs for specialized BCAs applicable to persons with innate cognitive impairments or diagnosed with severe mental illness or sensory and other conditions that may impair acquiescence in an assessment situation.

Clinicians experienced with intellectual disability, including Down syndrome, have become familiar with assessing these adults and with using select BCAs specially designed for this group. While the field has not centered on one or two specific BCAs, the ones available have proven to be applicable in such assessment situations. The Working Group noted this aspect within the field and recommended

further investment in research on assessment measures that would be equivalent in ease of use and timing as those measures that are common to the prescribing criteria. Also, although many of the cognitive measures shown to be promising for detecting MCI or early AD in Down syndrome may be applicable to non-verbal adults with Down syndrome and/or those adults with severe or profound premorbid ID levels, there is still a gap in recommending assessments for them.

Working Group members recognized that a delay in planning of state prior authorization prescribing criteria by state drug formulary committees for the adaptations for the population with Down syndrome would significantly delay access to treatment once the initial prior authorization prescribing criteria are released. This would essentially deprive the current 'at-need' generation of potentially beneficial therapeutics that could increase their quality-of-life years. The Working Group noted the significant interval of time until drug formulary committees modify their prior authorization criteria and when adults with Down syndrome would be able to receive one of the prescribed anti-amyloid immunotherapeutics. Therefore, there is urgency for the relevant stakeholders to act now. Also, as most adults with Down syndrome demonstrate precocious aging,[43] the remaining quality of life years from recognition of 'onset' to treatment will be problematic if prescribing criteria are not in place in anticipation of the availability of safety data for these immunotherapeutics in adults with DS. To wait until such data are available and only then make the formulary changes will deprive adults with Down syndrome who may in their limited remaining years of life access to anti-amyloid DMTs. *To enable access, the Working Group strongly advises that state drug formulary committees review these recommendations and incorporate them into existing prior authorization prescribing criteria as soon as possible.*

The Working Group acknowledged the urgent need for safety data of anti-amyloid immunotherapies in adults with Down syndrome. Issues of safety, efficacy, and access arose when the pharmaceutical firm Biogen first received FDA approval for Aduhelm™. While the second approved drug Leqembi™ may be more effective both in reducing amyloid and potentially mitigating memory decline, questions remain over its safety in adults with Down syndrome. Concerns for this class of drugs include the increased presence of cerebral amyloid angiopathy (CAA) in adults with Down syndrome and its potential for exacerbating ARIA side effects. As apparently no one with Down syndrome was included in the clinical trials of Aduhelm™, Leqembi™, and donanemab to date, this means safety studies specifically for people with Down syndrome are required prior to use.

The Working Group's recommendation is in line with the Appropriate Use Criteria for Aduhelm™[44] and Leqembi™[45] which recommend not treating people with Down syndrome until more data are obtained. Importantly, this report and consensus statement does not carry a recommendation for the current use of this class of anti-amyloid drugs with the Down syndrome population. If appropriate, registries for sporadic AD should be adapted to include adults with DS. Before prescribing this class of DMTs in adults with Down syndrome, clinicians should have access to, at a minimum, appropriate published safety data.

KEY RECOMMENDATIONS

We have noted the importance of addressing these recommended equivalencies by state drug formulary committees and by other payers as soon as possible for all anti-amyloid immunotherapies approved for early-stage Alzheimer's disease. Therefore, we recommend the following:

1. Sharing these recommended criteria to all organizational stakeholders that influence the availability of FDA approved DMTs for Alzheimer's disease, including the FDA, CMS, and state pharmacological and insuring bodies, pharmaceutical firms, and prescriber networks.

2. Creating a standing advisory group with a charter to refine and augment the recommended language and specifics of meeting the prescribing criteria when new knowledge becomes available, and when studies are published noting the validity and reliability of applicable instruments with the population of persons with intellectual disability, including those with Down syndrome.
3. Developing a guide for use by primary care physicians and other eligible prescribers on how to best meet their state's criteria for determining appropriate use when prescribing newly approved Alzheimer's DMTs for patients with Down syndrome and adults with other etiologies for intellectual disability.
4. Organizing continuing education and resources for the medical/health community on the issues related to assessing eligibility and prescribing Alzheimer's DMTs for persons with Down syndrome, and adults with other etiologies for intellectual disability.
5. Consulting and partnering with the pharmaceutical industry to assure the inclusion of adults with Down syndrome and adults with other etiologies for intellectual disability in clinical trials, starting with the conduct of safety trials in adults with Down syndrome with FDA-approved anti-amyloid immunotherapies.

Appendix A: States and sources of prior authorization criteria for anti-amyloid Alzheimer's therapeutics	
State	**Web address**
Alaska	https://health.alaska.gov/dhcs/Documents/pharmacy/Criteria/202109.%20Aduhelm_criteria_2021.pdf
California	https://files.medi-cal.ca.gov/pubsdoco/publications/masters-mtp/part2/injectdruga-d.pdf
Florida	http://mcgs.bcbsfl.com/MCG?mcgId=09-J4000-01&pv=false
Kentucky	https://www.chfs.ky.gov/agencies/dms/dpo/ppb/Documents/AduhelmCriteriaFINAL4422.pdf
Louisiana	https://ldh.la.gov/assets/medicaid/PharmPC/9.13.21/Aduhelm.09092021.pdf
Maryland	https://health.maryland.gov/mmcp/pap/pages/Clinical-Criteria.aspx
Minnesota	https://mn.gov/dhs/partners-and-providers/policies-procedures/minnesota-health-care-programs/provider/types/rx/pa-criteria/aduhelm.jsp
Montana	https://medicaidprovider.mt.gov/docs/priorauth/physicianadministereddrugs/Aduhelm01072022.pdf
North Carolina	https://www.nctracks.nc.gov › content › dam
New York	https://www.health.ny.gov/health_care/medicaid/program/dur/meetings/2022/07/attachment.pdf
Pennsylvania	https://www.dhs.pa.gov/providers/Pharmacy-Services/Documents/Clinical%20Guidelines%20Non-PDL/Aduhelm%20HB%2002.01.2022.pdf
Texas	https://www.tmhp.com/news/2022-01-21-prior-authorization-criteria-aducanumab-avwa-aduhelm-effective-february-1-2022

Appendix B: Resources for prescribers on assessing adults with intellectual disability for dementia			
ID	Citation	Format	Content
1	British Psychological Society. (2015). Dementia and People with Intellectual Disabilities: Guidance on the Assessment, Diagnosis, Interventions and Support of People with Intellectual Disabilities Who Develop Dementia. https://www.rcpsych.ac.uk/docs/default-source/members/faculties/intellectual-disability/id-assessment-guidance.pdf?sfvrsn=fd3c2aea_2	Report	Comprehensive guide to various facets related to dementia in adults with intellectual disability, including assessment and diagnostics, care management, and other topics.
2	Evans, E., & Trolllor, J. (2015). Dementia in People with Intellectual Disability: Guidelines for Australian GPs. Department of Developmental Disability Neuropsychiatry University of New South Wales. https://www.3dn.unsw.edu.au/sites/default/files/Guidelines%20for%20Australian%20GPs%20Dementia%20in%20Intellectual%20Disability.pdf	Report	Overview guide to assessing adults with intellectual disability suspected of having symptoms of a later life cognitive impairment; designed as an information overview for general practitioners.
3	Moran JA, Rafii MS, Keller SM, Singh BK, Janicki MP. The National Task Group on Intellectual Disabilities and Dementia Practices consensus recommendations for the evaluation and management of dementia in adults with intellectual disabilities. *Mayo Clin Proc*. 2013 Aug;88(8):831-40. doi: 10.1016/j.mayocp.2013. 04.024. Epub 2013 Jul 10.	Journal article	Consensus recommendations for the evaluation and management of dementia in adults with intellectual disabilities to guide primary care practitioners examining adults with dementia.
4	Tsou AY, Bulova P, Capone G, et al. Medical care of Adults with Down Syndrome: A Clinical Guideline. *JAMA*. 2020;324(15):1543–1556. doi:10.1001/jama.2020.17024	Journal article	Evidence-based clinical guidelines providing recommendations to support primary care of adults with Down syndrome, includes a section on assessing dementia.

Appendix C: Matrix of 12 state drug formularies' prescribing criteria

State Criteria - Age of Patient											
ALASKA	**CALIFORNIA**	**FLORIDA**	**KENTUCKY**	**LOUISIANA**	**MARYLAND**	**MINNESOTA**	**MONTANA**	**NEW YORK**	**NORTH CAROLINA**	**PENNSYLVANIA**	**TEXAS**
Patient is 50 years of age or older	Patient must be 50 to 85 years old. Or patient is 50 years old or younger and has early onset Alzheimer's disease (AD) and meets eligibility criteria.	Patient must be ≥ 18 years of age	[Not mentioned]	The recipient is 50 years of age or older on the date of the request	Adults ≥ 50 years	Patient is at least 50 years of age	Member must be 50 years of age or older	[Not mentioned]	Beneficiary is age 50 or older	[Not mentioned]	[Not mentioned]

State Criteria - Prescriber											
ALASKA	**CALIFORNIA**	**FLORIDA**	**KENTUCKY**	**LOUISIANA**	**MARYLAND**	**MINNESOTA**	**MONTANA**	**NEW YORK**	**NORTH CAROLINA**	**PENNSYLVANIA**	**TEXAS**
Prescribed by or in consultation with a neurologist	Must be prescribed by or in consultation with a neurologist, geriatrician, or psychiatrist.	Drug must be prescribed by, or in consultation with, a specialist in neurology or gerontology; AND	Prescribed by or in consultation with a Neurologist, Geriatrician, Geropsychiatric	The medication is prescribed by a neurologist	Neurologist, geriatric provider	Aduhelm must be prescribed by a neurologist	Must be prescribed by a neurology specialist	Not defined	Not defined	Is prescribed Aduhelm (aducanumab) by a dementia specialist (e.g., neurologist, psychiatrist, or geriatrician) who will monitor and assess the beneficiary at least once every 3 months	Not defined

State Criteria - Validated MCI/ mild AD diagnosis assessment scales											
ALASKA	**CALIFORNIA**	**FLORIDA**	**KENTUCKY**	**LOUISIANA**	**MARYLAND**	**MINNESOTA**	**MONTANA**	**NEW YORK**	**NORTH CAROLINA**	**PENNSYLVANIA**	**TEXAS**
Patient has the diagnosis of Alzheimer's disease	Patient must have a diagnosis of mild cognitive impairment (MCI) due to AD or mild AD and must have: • A global Clinical Dementia Rating (CDR) score of 0.5 • A Mini-Mental State Examination (MMSE) score of 24 to 30	Patient has mild cognitive impairment (MCI) due to Alzheimer's disease or mild Alzheimer's dementia (there is insufficient evidence in moderate or severe AD) as evidenced by all the following: • Clinical Dementia Rating (CDR)-Global Score of 0.5; AND • Mini-Mental Status Exam (MMSE) score between 24 and 30 (inclusive)	Provider attestation that the member has a diagnosis of mild cognitive impairment (MCI) due to AD or mild dementia associated with AD disease dementia.	The prescriber has documented objective evidence of mild cognitive impairment or mild dementia due to Alzheimer's disease using BOTH of the following tests: • The recipient has a Clinical Dementia Rating-Global Score (CDR-GS) of 0.5 (score must be stated on the request); AND • The recipient has a Mini-Mental State Exam (MMSE) score of ≥ 24 (score must be stated on the request)	Submit baseline evaluation and monitoring (all objective data must be submitted with PA request). Include documentation of: • Recent (within one year) brain MRI prior to initiating treatment • Baseline cognitive testing (establishing mild cognitive impairment or mild dementia): CDR-SB, MMSE, ADAS-Cog 13 and ADCS-ADL-MCI • Assessment of CNS bleed risk including no history of stroke/TIA within the past year	Patient has a diagnosis of Alzheimer's disease with mild cognitive impairment or mild dementia as demonstrated by 3 validated scales, one of which must be the MMSE (Mini Mental State Exam)	Member has mild cognitive impairment due to Alzheimer's disease or has mild Alzheimer's dementia stage of disease as evidenced by all of the following: • Clinical Dementia Rating (CDR)-Global Score of 0.5 • Repeatable Battery for Assessment of Neuropsychological Status (RBANS) delayed memory index score ≤ 85 • Mini-Mental Status Exam (MMSE) score between 24 and 30	Prescribers must attest that the patient has been diagnosed with mild cognitive impairment due to Alzheimer's Disease or mild Alzheimer's dementia by meeting one of the following: • Clinical Dementia Rating (CDR)-Global score of 0.5 to 1 • Mini-Mental Status Exam (MMSE) score between 24 and 30 • Montreal Cognitive Assessment (MoCA) score of at least 18	Beneficiary has mild cognitive impairment (MCI) due to Alzheimer's disease or has mild Alzheimer's dementia as evidenced by all of the following: a. Clinical Dementia Rating (CDR)-Global Score of 0.5; AND b. Objective evidence of cognitive impairment at screening; AND c. Mini-Mental Status Exam (MMSE) score between 24 and 30 (inclusive) OR equivalent tool indicating MCI or mild dementia (NOTE: range of scores may be adjusted based on educational status of patient	Has at least two of the following: a. Mini-Mental State Examination (MMSE) score of at least 24, b. Montreal Cognitive Assessment (MoCA) score of at least 18, c. Global Clinical Dementia Rating Scale (CDR) score of 0.5;	The client has a confirmed diagnosis of Alzheimer's disease (diagnosis code G300, G301, G308, or G309).

State Criteria - Biomarkers for amyloid positivity											
ALASKA	**CALIFORNIA**	**FLORIDA**	**KENTUCKY**	**LOUISIANA**	**MARYLAND**	**MINNESOTA**	**MONTANA**	**NEW YORK**	**NORTH CAROLINA**	**PENNSYLVANIA**	**TEXAS**
Patient has the presence of beta-amyloid plaques verified by either a positron emission tomography (PET) scan or cerebrospinal fluid (CSF) testing	A positive amyloid Positron Emission Tomography (PET) scan or cerebrospinal fluid (CSF) testing for tau proteins.	Positron Emission Tomography (PET) scan is positive for amyloid beta plaque;	Confirmation of beta-amyloid plaques verified by one of the following: • Positron emission tomography (PET) scan OR • Lumbar puncture for cerebrospinal fluid (CSF) testing	Presence of beta-amyloid plaques is verified by one of the following (must be stated on the request): • Positron emission tomography (PET) scan; OR • Cerebrospinal fluid (CSF) testing;	[Not mentioned]	Patient's Alzheimer's disease is of confirmed beta amyloid pathology as evidenced by ONE of the following: • A positive amyloid PET scan interpreted by a radiologist or nuclear medicine specialist OR • Amyloid is detected in CSF from a lumbar puncture	Member must have had a positive amyloid Positron Emission Tomography (PET) scan	Prescribers must attest that the patient has undergone the following pre-treatment testing: • Genetic testing to assess apolipoprotein Eε4 carrier status AND • Positron emission tomography (PET) scan or cerebrospinal fluid (CSF) analysis to confirm the presence of amyloid beta deposits	[Not mentioned}	Has baseline magnetic resonance imaging (MRI) results as recommended in the FDA-approved package labeling; AND Has a positron emission tomography (PET) scan positive for beta-amyloid plaques	The prescriber confirms that amyloid-beta plaques are present.

State criteria - Test evidence of cognitive impairment											
ALASKA	**CALIFORNIA**	**FLORIDA**	**KENTUCKY**	**LOUISIANA**	**MARYLAND**	**MINNESOTA**	**MONTANA**	**NEW YORK**	**NORTH CAROLINA**	**PENNSYLVANIA**	**TEXAS**
Must have objective evidence of cognitive impairment at screening AND; • Patient has a Clinical Dementia Rating (CDR) global score of 0.5 AND; • Patient has a Mini-Mental State Exam (MMSE) of greater than or equal to 24	An objective evidence of cognitive impairment at screening	Objective evidence of cognitive impairment at screening	Prescriber has assessed and documented baseline disease severity utilizing one of the following scores (within the past 6 months): • Mini-Mental Status Exam (MMSE) score ≥ 24 • Montreal Cognitive Assessment (MoCA) ≥ 15	The prescriber has assessed and documented baseline disease severity utilizing a validated tool including, but not limited to, the following: • Alzheimer's Disease Assessment Scale – Cognitive Subscale (ADAS-Cog-13); OR • Repeatable Battery for the Assessment of Neuropsychological Status (RBANS); OR • Clinical Dementia Rating – Sum of Boxes (CDR-SB); OR • Montreal Cognitive Assessment (MoCA). [name of tool and date of test must be stated on the request]	Baseline cognitive testing (establishing mild cognitive impairment or mild dementia): CDR-SB, MMSE, ADAS-Cog 13 and ADCS-ADL-MCI	[Not mentioned]	Objective evidence of cognitive impairment at screening	[Not included]	Prescriber has assessed and documented baseline disease severity utilizing an objective measure/tool (e.g., MMSE, Alzheimer's Disease Assessment Scale-Cognitive Subscale [ADAS-Cog-13], Alzheimer's Disease Cooperative Study-Activities of Daily Living Inventory-Mild Cognitive Impairment version [ADCS-ADL-MCI], Clinical Dementia Rating-Sum of Boxes [CDR-SB]).	Has repeat testing and documented results of at least two of the following: a. MMSE b. MoCA c. CDR	Clinical testing must confirm that the client has mild cognitive impairment caused by Alzheimer's disease or a mild stage of Alzheimer's disease.

State criteria - MRI at baseline											
ALASKA	**CALIFORNIA**	**FLORIDA**	**KENTUCKY**	**LOUISIANA**	**MARYLAND**	**MINNESOTA**	**MONTANA**	**NEW YORK**	**NORTH CAROLINA**	**PENNSYLVANIA**	**TEXAS**
Patient must have a documented brain magnetic resonance imaging (MRI) within the last year showing no localized superficial siderosis, has less than 10 brain microhemorrhages , and no brain hemorrhages that are greater than 1 cm in the past year	Patient must have an MRI at baseline and at 7 and 12 months to monitor for amyloid-related imaging abnormalities (ARIA).	Patient has received a baseline brain magnetic resonance imaging (MRI) prior to initiating treatment (within 1 year prior);	[Not included]	The recipient has no contra indications to magnetic resonance imaging (MRI) and has had a brain MRI within the past 12 months (date must be specified) demonstrating all of the following (must be stated on the request): • No localized superficial siderosis; AND • Less than 10 brain microhemorrhages; AND • No brain hemorrhage > 1 cm within the past year. The recipient does not have a history of unstable angina, myocardial infarction, advanced chronic heart failure, clinically significant conduction abnormalities or unexplained loss of consciousness within 1 year of treatment initiation; AND • The recipient has not had a seizure in the past 3 years	Recent (within one year) brain MRI prior to initiating treatment	Patient has had a brain MRI within the past 12 months that does NOT show ANY of the following: • Pre-treatment localized superficial siderosis OR • 10 or more brain microhemorrhages- OR • A brain hemorrhage greater than 1 cm	• Adult must have recent brain MRI (within one year) prior to initiating treatment. • Adult must not have had a stroke or TIA within past year. • Member must not be currently taking any medication with platelet anti-aggregate or anti-coagulant properties (unless aspirin ≤ 325mg daily).	[Not included]	Beneficiary has had a recent (within one year) brain magnetic resonance imaging (MRI) prior to initiating treatment.	Patient does not have a brain MRI showing evidence of acute or sub-acute micro- or macro-hemorrhage, greater than 4 microhemorrhages , coretical infarct or greater than 1 lacunar infarct.	Documentation shows that the client has received a baseline magnetic resonance imaging (MRI) scan of the brain within the year prior to initiating treatment. The client must not be currently taking any anti-coagulant (except for aspirin at a prophylactic dose or less) or have a history of a clotting disorder.

State criteria - Exclusion of other causes of cognitive impairment											
ALASKA	**CALIFORNIA**	**FLORIDA**	**KENTUCKY**	**LOUISIANA**	**MARYLAND**	**MINNESOTA**	**MONTANA**	**NEW YORK**	**NORTH CAROLINA**	**PENNSYLVANIA**	**TEXAS**
Other known causes of dementia have been ruled out (i.e., vascular dementia, Parkinson's disease, dementia, etc.)	All other causes of cognitive impairment have been excluded such as the following: • Vascular Dementia (for example, stroke, transient ischemic attack) • Lewy body dementia • Frontotemporal dementia	Other conditions mimicking, but of non-Alzheimer's dementia etiology, have been ruled out (e.g., vascular dementia, dementia with Lewy bodies [DLB], frontotemporal dementia [FTD], normal pressure hydrocephalus)	Adult does NOT have any medical or neurological condition (other than Alzheimer's Disease) that might be a contributing cause of the subject's cognitive impairment, specifically ruling out ALL of the following: vascular dementia; and lewy body dementia; and frontotemporal dementia; and dementia in Down's syndrome; and Parkinson's disease dementia	Prescriber states on the request that other causes of cognitive impairment have been ruled out (including, but not limited to, alcohol/substance abuse, frontotemporal dementia (FTD), Lewy body dementia (LBD), Parkinson's disease dementia, unstable psychiatric illness, and vascular dementia)	[Not mentioned]	Patient has undergone a complete physical and neurological exam to comprehensively rule out all other possible causes of neurocognitive decline including but not limited to: • Any medication potentially causing cognitive impairment must have been stopped for at least 4 weeks with continued cognitive symptoms • Currently uncontrolled psychiatric condition (including alcohol or substance abuse) • Parkinson's disease • Lewy body dementia • Vascular dementia (such as from a stroke)	Provider has ruled out any other medical or neurological conditions (other than Alzheimer's Disease) that may be contributing to member's cognitive impairment, including any medications that can substantially contribute to cognitive impairment (see Beer's List).	Prescribers must attest that the patient does not have evidence of any medical or neurological condition other than Alzheimer's Disease that could be contributing to the patient's cognitive impairment	Beneficiary has undergone testing to rule out reversible causes of dementia (ex. CBC, CMP, TSH, B12, urine drug screen, RPR/VDRL, (folate (if alcohol abuse is present), HIV (if risk present) and has had an assessment including a review of current medications as a cause of intellectual decline.	Does not have any of the following: a. A medical or neurological condition (other than Alzheimer's disease) that might be a significant contributing cause of the beneficiary's cognitive impairment b. A history of stroke or transient ischemic attack (TIA) or unexplained loss of consciousness in the past year.	The prescriber attests that other forms of dementia except Alzheimer's disease have been ruled out by appropriate lab or other diagnostic testing.

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