Medical Information

ADUHELM™ (aducanumab-avwa): Use in Persons with Down Syndrome (Trisomy 21)

For a copy of the full prescribing information, please click **here**.

The information provided herein is done so as an educational resource for healthcare providers in response to an unsolicited request and should be considered current as of the date listed herein. It is not intended to be a substitute for consultation and review of reference materials and medical literature pertaining to individual clinical circumstances. Healthcare providers should make all treatment decisions based on the context of the situation and their clinical judgment.

Aducanumab-avwa is Not Indicated for Use in Persons with Down Syndrome

Aducanumab-avwa has not been studied in persons with Down Syndrome associated Alzheimer's disease (DS-AD), and there are no data on the efficacy and safety in this population. Aducanumab-avwa is indicated for the treatment of Alzheimer's disease. Treatment with aducanumab-avwa should be initiated in patients with mild cognitive impairment or mild dementia stage of disease, the population in which treatment was initiated in clinical trials. There are no safety or effectiveness data on initiating treatment at earlier or later stages of the disease than were studied. This indication is approved under accelerated approval based on reduction in amyloid beta plaques observed in patients treated with aducanumab-avwa. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trial(s) (1). Any use of aducanumab-avwa outside of the labeled indication is done at the discretion of the treating clinician and cannot be recommended by Biogen.

Biogen has been involved with the research community in discussions around the supplemental evidence needed in DS-AD should a drug be approved for sporadic AD (most recently in the Critical Path Innovation Meeting [CPIM] organized by LuMIND. Biogen welcomes input to advance research and potential treatments for people with DS-AD.

Several Relevant Exclusion Criteria were Applied in Phase 3 Clinical Trials

In the Phase 3 studies of aducanumab-avwa, EMERGE and ENGAGE[1], the mean age at study entry was 70 years (range from 50 to 85) (1). Patients meeting any of the following relevant exclusion criteria were excluded from study entry (2, 3):

- Any uncontrolled medical or neurological/neurodegenerative condition (other than AD) that, in the opinion of the Investigator, might be a contributing cause of the subject's cognitive impairment;

[1] EMERGE (N = 1638) and ENGAGE (N = 1647) were Phase 3, multicenter, randomized, double-blind, placebo-controlled, parallel-group studies designed to evaluate the efficacy and safety of two dosing regimens of aducanumab-avwa versus placebo in patients with early Alzheimer's Disease (AD).

- Brain MRI performed at Screening (per centrally read MRI) that shows evidence of any finding that, in the opinion of the Investigator, might be a contributing cause of a subject's dementia, might pose a risk to the patient, or might prevent a satisfactory MRI assessment for safety monitoring.

Guidance from Expert Groups Recommend Against the Use of Aducanumab-avwa in Persons with Down Syndrome and Suggest Continued Research

In a recent publication by Cummings et al. an expert panel reviewed appropriate use recommendations for aducanumab-avwa in clinical practice. Authors acknowledge that there are many differences between Down syndrome and late onset AD and as such, recommend against treating persons with Down syndrome with aducanumab-avwa until more data are available. According to Cummings et al., persons with Down syndrome may become eligible for treatment when additional studies have been conducted and additional data are accrued in this population (4).

According to a consensus statement released by the National Task Group on Intellectual Disabilities and Dementia Practices, several issues were noted related to Down syndrome and the use of aducanumab-avwa. The group raises concerns regarding a lack of data in adults with Down syndrome, lack of protocols for use by clinicians, and an unknown efficacy profile with early presence of high amyloid pathology. Recommendations from the group are focused around including participants with Down syndrome in further research efforts, enhanced screening efforts, patient/caregiver involvement and developing protocols to coordinate treatment (5).

References

1. ADUHELM (aducanumab-avwa) Prescribing Information. Cambridge, MA: Biogen Inc; July 2021.
2. Biogen Data on File: Aducanumab (1).
3. Biogen Data on File: Aducanumab (2).
4. Cummings J, Aisen P, Apostolova LG, et al. Aducanumab: Appropriate Use Recommendations. *J Prev Alzheimers Dis*. 2021.
5. National Task Group on Intellecutal Disabilities and Dementia Practices. An Issues Consesus Statement Aducanumab and Persons with Down Syndrome: What Do we Do Now?