Aducanumab: A Summary Guide for Primary Care Clinicians

The Alzheimer's Association® provides information and strategies to support clinicians and health systems, and improve how Alzheimer's and all other dementia are addressed in clinical practice. This summary guide is designed to help you understand aducanumab (Aduhelm™), including how it is designed to work and its implications for your patients.

BACKGROUND

More than 6 million Americans are living with Alzheimer's. By 2050, this number is projected to rise to nearly 13 million. In addition, dementia is one of the costliest conditions to society. In 2021, total payments for caring for Americans aged 65 and older with Alzheimer's or other dementias are estimated to reach $355 billion and could rise as high as $1.1 trillion by 2050. Alzheimer's adds to the difficulty and cost of managing care for adults, resulting in more expensive hospitalizations, additional emergency department visits and complicated management of other conditions.

In June 2021, the Food and Drug Administration (FDA) granted accelerated approval to aducanumab, an anti-amyloid intravenous infusion therapy for Alzheimer's disease. While existing therapies may temporarily address some symptoms, this is the first approved treatment to address the underlying biology of the disease.

ROLE OF PRIMARY CARE CLINICIANS

Primary care clinicians play an important role in understanding the overall picture of a patient's health. For all patients, regardless of whether they are candidates for aducanumab, primary care clinicians can maximize outcomes by regularly monitoring the patient's health and cognition; educating and supporting patients and their families; initiating pharmacologic and nonpharmacologic treatments as appropriate; and evaluating the patient and/or family's interest in clinical trials. Primary care clinicians may not be able to prescribe aducanumab, but play a key role in ensuring early and accurate diagnosis, access to treatment and quality care so that individuals who may benefit from all available treatments can do so at the earliest point possible.

The Alzheimer's Association offers a number of tools to help primary care clinicians with this process, including a Cognitive Assessment Toolkit and our Alzheimer's Disease Pocketcard Mobile App and Online Portal. Visit **alz.org/clinicalcare** to access these tools or to learn more.

Individuals whose cognitive assessment indicates that their memory or cognition is consistent with mild cognitive impairment (MCI) or early Alzheimer's

dementia should be evaluated further or referred to a specialist for follow-up. This may include additional biomarker assessments such as imaging and biofluid analysis to determine a definitive diagnosis and appropriate treatment.

OVERVIEW OF THE EVIDENCE

In the Phase III clinical trials, EMERGE and ENGAGE, aducanumab was administered intravenously once every four weeks over a period of 78 weeks using titration protocols. The clinical trials for aducanumab exclusively enrolled participants with MCI due to Alzheimer's disease and early Alzheimer's dementia, and abnormal amyloid buildup confirmed through positron emission tomography (PET) imaging. This allowed researchers to monitor participants' amyloid levels and measure changes over the course of the trial to determine whether the treatment reduced amyloid. Researchers used a variety of cognitive assessments, participant and caregiver reports, as well as medical examinations to learn whether aducanumab would provide a clinical benefit.

Data collected during the EMERGE trial suggest that exposure to the highest dose of aducanumab over 18 months led to reduced levels of amyloid in the brain. Researchers also saw reduced symptoms of cognitive and functional decline, along with reduced decline associated with activities of daily living.

Based on their review, the FDA determined that there is substantial evidence that aducanumab reduces amyloid plaques, one of the hallmarks of Alzheimer's, and that the reduction in these plaques is reasonably likely to reduce cognitive and functional decline in people living with early Alzheimer's.

As with all drug therapies, this drug may work differently for everyone who takes it, and may not work for some individuals.

INDICATIONS AND USAGE

ADUHELM is an amyloid beta-directed antibody indicated for the treatment of Alzheimer's disease. Treatment with ADUHELM 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 ADUHELM. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trial(s).

WARNINGS AND PRECAUTIONS

In the FDA label, the most common side effects include amyloid-related imaging abnormalities (ARIA), headache and fall. Another potentially serious side effect is allergic reaction.

ARIA is a common side effect that does not usually cause any symptoms but can be serious. It is typically a temporary swelling in areas of the brain that usually resolves over time. Some people may also have small spots of bleeding in or on the surface of the brain with the swelling, although most people with swelling in areas of the brain do not have symptoms. Some may have symptoms of ARIA such as headache, dizziness, nausea, confusion and vision changes.

As part of the treatment and monitoring for risk of ARIA in patients receiving this therapy, MRI scans are required by the FDA prior to beginning treatment and before the seventh and 12th infusion. Enhanced clinical vigilance for ARIA is also recommended during the first eight doses of treatment with aducanumab, particularly during titration. If a patient experiences symptoms which could be suggestive of ARIA, clinical evaluation should be performed, including MRI testing if indicated.

POINTS TO DISCUSS WITH YOUR PATIENTS

When considering any treatment, it is important for patients and clinicians to have a conversation to determine if the patient is a candidate, and make an informed decision to determine if the treatment is an option. Not all patients with amyloid will be good candidates for the treatment, depending on the stage of the disease and other risk factors.

Review the benefits and risks of aducanumab with your patients and consider discussing the following additional points:

- Aducanumab is not a cure for Alzheimer's disease. It is the first treatment approved for the disease since 2003 and the first to address its underlying biology. According to the FDA, this reduction in amyloid plaques, one of the hallmarks found in the brains of individuals with Alzheimer's, is reasonably likely to lead to a reduction in the clinical decline due to Alzheimer's disease.
    - This could mean more time for individuals to actively participate in daily life, have sustained independence and hold on to memories longer.
    - There is no evidence that aducanumab can restore lost memories or cognitive function.
- Aducanumab was studied in people living with early Alzheimer's disease and mild cognitive impairment (MCI) due to Alzheimer's who showed evidence of a buildup of amyloid plaques in the brain. The therapy has not yet been tested on people with more advanced cases of dementia due to Alzheimer's disease or those without clinical symptoms.
- The label says aducanumab is indicated for the treatment of Alzheimer's, based on reduction in amyloid beta plaques, one of the hallmarks of the disease and required for an Alzheimer's diagnosis. This means that a physician should confirm the presence of amyloid plaques in the brain before prescribing this anti-amyloid plaque treatment.
    - Confirmatory tests like cerebrospinal fluid (CSF) analysis or amyloid positron emission tomography (PET) imaging should be a part of the diagnostic process to determine eligibility for the treatment.
    - MRI will also be required before and during the treatment process to monitor for side effects.
- The progression of Alzheimer's disease is different in each individual, and therefore treatment responses may also vary. The drug's benefit to the patient will need to be assessed over time.

PATIENT RESOURCES

The following resources may be helpful to your patients living with Alzheimer's and their families. For additional support, encourage them to call the Alzheimer's Association's free 24/7 Helpline at **800.272.3900** or visit **alz.org**.

- Aducanumab FAQs
- I Have Alzheimer's
- Caregiving
- Downloadable Resources
- Clinical Trials Recruiting

To learn more about aducanumab or to access additional resources for clinicians and health systems, visit **alz.org/clinicalcare**.