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Advanced Imaging Digest

MRI and Aduhelm™ treatment for Alzheimer's disease

The anti-amyloid drug aducanumab, sold under the brand name Aduhelm, recently received approval from the US Federal Drug Administration (FDA) using its accelerated approval pathway. It is the first novel therapy approved since 2003 for Alzheimer's disease (AD) and the only one that targets the underlying pathophysiology of AD, the presence of amyloid beta plaques in the brain. Studies on patients treated with aducanumab have shown a reduction in the number of amyloid plaques in the brain. However, the results of EMERGE and ENGAGE, recent Phase 3 clinical trials, have caused controversy, and uncertainty still exists about the clinical benefits of aducanumab.

The ENGAGE trial showed no benefit in disease course. The EMERGE trial, which used a higher dose of aducanumab, showed no initial benefit, but demonstrated significant positive benefit with prolonged follow-up. The current FDA approval is based on a surrogate clinical endpoint (reduction of amyloid plaque in the brain) and not on clinical outcomes and potential benefits versus risk. Reduction of amyloid plaque is expected to result in reduced clinical decline. However, there is little known correlation between the number and size of plaques and symptoms.

In both studies, participants included patients with early symptomatic AD who were positive for brain amyloid pathology as assessed by positron emission tomography (PET). Other inclusion criteria were baseline Mini-Mental State Exam score of 24 to 30 (inclusive) and a Clinical Dementia Rating global score of 0.5. The ε4 allele of apolipoprotein E (ApoE) is the strongest genetic risk factor for AD and associated with increased risk for both early- and late-onset AD. ApoE ε4 carriers and ApoE ε4 noncarriers were both enrolled. Exclusion criteria included comorbid medical condition, cerebrovascular disease, psychiatric illness, and unstable disease.

Magellan Healthcare clinical leaders continually review imaging trends and needs in light of current medical concerns, available literature, and society and Centers for Disease Control and Prevention recommendations and guidelines. This document is a summary of our latest findings. Please consult references for detailed information.

The FDA has approved aducanumab for the early stages of AD, mild cognitive impairment and mild dementia. The treatment is administered intravenously through infusion over a one-hour period every four weeks for an indefinite period of time. Monitoring using magnetic resonance imaging (MRI) is required by the FDA, including obtaining a brain MRI that was conducted within one year of treatment commencement, and prior to the seventh and twelfth infusions. When ten or more new incident microhemorrhages or > 2 focal areas of superficial siderosis (radiographic severe ARIA-H) are observed, treatment may be continued with caution only after a clinical evaluation and a follow-up MRI demonstrate radiographic stabilization. Repeat MRI is also indicated for changes in clinical status.

PET scan with amyloid disposition was an inclusion criterion in the Phase 3 studies. Current approval is based on a reduction in amyloid plaques on follow-up PET scans as a surrogate endpoint, as the clinical benefit is still unclear. The FDA prescribing information does not include PET as an inclusion criterion or as a required method of follow-up. The Society of Nuclear Medicine and Molecular Imaging has engaged the Centers for Medicare and Medicaid Services to provide paid coverage of beta-amyloid PET imaging in prospective patients.

Although minimal evidence suggests that aducanumab has improved clinical endpoints in some patients who have mild dementia, it is appropriate for patients being administered the medication or those meeting medical necessity for this treatment to receive the FDA-required initial brain MRI and MRIs after the seventh and twelfth infusions of the drug.

About the authors

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Dr. Khalid joined Magellan in 2014. As a board-certified diagnostic radiologist with a career spanning more than twenty years, he has a thorough understanding of the complexities of the U.S. healthcare system and current standards of care. In his current role, Dr. Khalid is involved in training new physicians, auditing, continuing education and policy development.

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