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Editorial

Appropriate Use Recommendations for Lecanemab

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In this issue of JPAD, Cummings et al. provide Appropriate Use Recommendations (AURs) for lecanemab (1). Lecanemab received accelerated approval from the FDA based on its phase II trial results and is expected to receive standard approval based on its phase III results. The inclusion and exclusion criteria of these trials serve as the basis for the AURs and adhering to them will help physicians safely and effectively administer lecanemab in patients with Early AD.

First and foremost, the AURs advise that all patients considered for lecanemab therapy meet clinical criteria for MCI due to AD or mild AD dementia and have biomarker confirmation (amyloid PET or CSF) of elevated brain amyloid (2). Second, the AURs warn against treatment with lecanemab in Early AD patients on anti-coagulation (e.g. warfarin, dabigatran, and others) and that patients on lecanemab not be treated with acute thrombolytics.

Just as with the AURs published for aducanumab (3), the expert panel recommends performing APOE genotyping and discussion with patients about their APOE status and risk for developing Amyloid Related Imaging Abnormalities (ARIA). The AURs include guidance on surveillance MRIs for ARIA which is similar to that used in the clinical trials of lecanemab. A total of five MRI scans is advised in the first year of treatment. An MRI scan should be performed prior to initiation of therapy, prior to the 5th, 7th, and 14th infusions, as well as at one year, particularly for APOE4 carriers or for patients with prior ARIA events. Unscheduled MRI scans may of course be performed at any time if clinically indicated. It should be kept in mind that ARIA is an MRI phenomenon that was observed in 12.6% of participants in the phase III clinical trial of lecanemab with 97.8% of cases being asymptomatic. Nevertheless, the treating physician is reminded to be vigilant for symptoms of ARIA, obtain an MRI when there is suspicion and hold treatment as per the criteria in the AURs. The AURs also suggest implementation of a protocol for the management of ARIA when establishing a therapy program with lecanemab.

The expert panel also recommends that all patients receiving lecanemab be enrolled in the Alzheimer's Network for Treatment and Diagnostics (ALZ-NET; www.alz-net.org) or similar registries as they become available. Participation in ALZ-NET is encouraged by the FDA in the prescribing information. Understanding lecanemab's long-term efficacy and safety profile in real-world settings will be critical for its successful integration into clinical practice.

Finally, the expert panel highlights that there are limitations to the clinical trial data regarding the use of lecanemab in certain populations, including under-represented minority groups as well as patients with autosomal dominant AD and those with Down syndrome. The specifics of the safety and efficacy of lecanemab in these patient populations remains to be fully understood. Therefore, the AURs advise that patients be selected for therapy based on criteria similar to those patients who have completed lecanemab clinical trials. This is the population in whom safety and efficacy have been clearly demonstrated. With this set of guidelines, we now have best practices for integrating lecanemab therapy into the clinic as we advance into a new era in AD clinical care.

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