Leqembi® (lecanemab-irmb) – Accelerated approval converted to traditional approval

- On July 6, 2023, the FDA announced the traditional approval of Eisai/Biogen's Leqembi (lecanemab-irmb), for the treatment of Alzheimer's disease. Treatment with Leqembi 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.
    - Leqembi was previously approved for this indication via the accelerated approval pathway.
- The conversion of the accelerated approval to traditional approval was based on the findings of CLARITY AD, a randomized, double-blind, placebo-controlled study in 1,795 patients with Alzheimer's disease. Patients were randomized to receive placebo or Leqembi. The primary endpoint was the change from baseline at 18 months in the Clinical Dementia Rating Scale Sum of Boxes (CDR-SB) score.
    - Leqembi treatment met the primary endpoint and reduced clinical decline on the CDR-SB compared with placebo at 18 months (-0.45 [-27%], $p < 0.0001$).
- In addition to the traditional approval, the FDA added a boxed warning for Leqembi for amyloid related imaging abnormalities (ARIA).
    - Patients treated with beta amyloid targeted therapies, including Leqembi, who are ApoE ε4 homozygotes have a higher incidence of ARIA, including symptomatic and serious ARIA, compared to heterozygotes and noncarriers. Testing for ApoE ε4 status should be performed prior to initiation of treatment to inform the risk of developing ARIA. Prior to testing, prescribers should discuss with patients the risk of ARIA across genotypes and the implications of genetic testing results.
    - The benefit of Leqembi and potential risk of serious adverse events associated with ARIA should be considered when deciding to initiate treatment with Leqembi.
- The recommended dose of Leqembi is 10 mg/kg via intravenous infusion over approximately one hour, once every two weeks.
- CMS also announced that Medicare coverage for Leqembi, as outlined in the National Coverage Determination (NCD) guidance, is through enrollment in a registry-based study.
    - Prior to the traditional approval, coverage for Leqembi was restricted to patients enrolled in a randomized clinical trial.