Kisunla™ (donanemab-azbt) – New drug approval

- On July 2, 2024, Eli Lilly announced the FDA approval of Kisunla (donanemab-azbt), for the treatment of Alzheimer's disease. Treatment with Kisunla should be initiated in patients with mild cognitive impairment or mild dementia stage of disease, the population in which treatment was initiated in the clinical trials.

- Kisunla is the third FDA approved amyloid beta-directed antibody for Alzheimer's disease. Other approved drugs in the class include Aduhelm® (aducanumab-avwa) and Leqembi® (lecanemab-irmb).

    - Biogen has discontinued the commercialization and sale of Aduhelm. Aduhelm will no longer be available for purchase after November 1, 2024.

- The efficacy of Kisunla was established in a randomized, double-blind, placebo-controlled, study in 1,736 patients with Alzheimer's disease (patients with confirmed presence of amyloid pathology and mild cognitive impairment or mild dementia stage of disease). Patients were randomized to Kisunla every 4 weeks or placebo for a total of up to 72 weeks. The treatment was switched to placebo based on amyloid PET levels measured at week 24, week 52, and week 76. If the amyloid plaque level was < 11 Centiloids on a single PET scan or 11 to < 25 Centiloids on 2 consecutive PET scans, the patient was eligible to be switched to placebo. The primary endpoint was change in the integrated Alzheimer's Disease Rating Scale (iADRS) score from baseline to 76 weeks. The total score ranges from 0 to 144, with lower scores reflecting worse cognitive and functional performance. A key secondary endpoint was the Clinical Dementia Rating Scale – Sum of Boxes (CDR-SB) score.

    - In the overall population, patients treated with Kisunla demonstrated a statistically significant reduction in clinical decline on iADRS compared to placebo at week 76 (2.92, $p < 0.0001$).
    - Similarly, patients treated with Kisunla demonstrated a statistically significant reduction in clinical decline on CDR-SB compared to placebo at week 76 (-0.70, $p < 0.0001$).

- Kisunla carries a boxed warning for amyloid related imaging abnormalities (ARIA).

- Additional warnings and precautions for Kisunla include hypersensitivity reactions and infusion-related reactions.

- The most common adverse reactions (≥ 10% and higher incidence compared to placebo) with Kisunla use were ARIA with edema E (ARIA-E), ARIA with hemosiderin deposition (ARIA-H) microhemorrhage, ARIA-H superficial siderosis, and headache.

- The recommended dosage of Kisunla is 700 mg every four weeks for three doses, then 1,400 mg every four weeks. Kisunla is administered every four weeks as an intravenous infusion over approximately 30 minutes.

    - The presence of amyloid beta pathology should be confirmed prior to initiating treatment.
    - Kisunla dosing can be stopped based on reduction of amyloid plaques to minimal levels on amyloid PET imaging.

- The wholesale acquisition cost (WAC) for one vial of Kisunla is $695.65. The total cost of Kisunla will vary by patient based on when they complete treatment.

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— In TRAILBLAZER-ALZ 2, people were able to complete treatment and switch to placebo at 6, 12, or 18 months after they achieved one of the study's treatment goals, minimal levels of amyloid plaque consistent with a visually negative amyloid PET scan. In the overall population of people receiving Kisunla, 17% completed treatment at 6 months, 47% at 12 months, and 69% at 18 months based on an assessment of amyloid levels via an amyloid PET scan.

Length of treatment	6 months	12 months	18 months
30-minute infusions	6	13	19
Course of therapy cost	$12,522	$32,000	$48,696

- Eli Lilly's launch plans for Kisunla are pending. Kisunla will be available as a 350 mg/20 mL (17.5 mg/mL) single-dose vial.