Vafseo® (vadadustat) – New drug approval

- On March 27, 2024, Akebia announced the FDA approval of Vafseo (vadadustat), for the treatment of anemia due to chronic kidney disease (CKD) in adults who have been receiving dialysis for at least three months.

- Anemia commonly occurs in people with CKD because their kidneys do not produce enough erythropoietin, a hormone that helps regulate production of red blood cells. Anemia due to CKD can cause fatigue, dizziness, shortness of breath and cognitive dysfunction. Anemia is associated with increased mortality in people with CKD.

    — Approximately 500,000 adult patients in the U.S. on dialysis have anemia due to CKD.

- Vafseo is a hypoxia-inducible factor prolyl hydroxylase inhibitor that activates the physiologic response to hypoxia to stimulate endogenous production of erythropoietin to manage anemia.

- The efficacy and safety of Vafseo was established in two randomized, active-controlled, non-inferiority, open-label studies in patients with dialysis-dependent CKD (DD-CKD), INNO$_2$VATE-1 (N = 369) and INNO$_2$VATE-2 (N = 3,554). Patients in each study were randomized to receive Vafseo or darbepoetin alfa for 52 weeks. The primary endpoint in each study was the difference in mean change of hemoglobin from baseline to the primary evaluation period (weeks 24 to 36). A secondary endpoint was the difference in mean change of hemoglobin from baseline to the secondary evaluation period (weeks 40 to 52). After 52 weeks, patients continued the study medication to assess long-term safety until the event-driven major adverse cardiovascular event (MACE) endpoints were reached. MACE was defined as all-cause mortality, non-fatal myocardial infarction, and non-fatal stroke.

    — The mean differences between the Vafseo and darbepoetin alfa groups in the change in hemoglobin were -0.3 g/dL (95% CI: -0.5 to -0.1) at weeks 24 to 36 and -0.1 g/dL (95% CI: -0.3 to 0.2) at weeks 40 to 52 in INNO$_2$VATE-1 and -0.2 g/dL (95% CI: -0.2 to -0.1) and -0.2 g/dL (95% CI: -0.3 to -0.1), respectively, in INNO$_2$VATE-2.
    — Vafseo was non-inferior to darbepoetin alfa on the time to first occurrence of MACE (hazard ratio 0.96, 95% CI: 0.83, 1.11). An analysis of the U.S. region (N = 2,361 of 3,902 total patients globally) for MACE and the individual MACE components, where patients were treated to a hemoglobin target of 10 to 11 g/dL, showed a similar risk of MACE compared to darbepoetin alfa. The results were consistent for the individual components of the MACE endpoint.

- Vafseo carries a boxed warning increased risk of death, myocardial infarction, stroke, venous thromboembolism, and thrombosis of vascular access.

- Vafseo is contraindicated in patients with uncontrolled hypertension.

- Additional warnings and precautions include hepatotoxicity; hypertension; seizures; gastrointestinal erosion; serious adverse reactions in patients with anemia due to CKD and not on dialysis; and malignancy.

- The most common adverse reactions (≥ 10%) with Vafseo use were hypertension and diarrhea.

- The recommended starting dose of Vafseo is 300 mg orally once daily, with or without food.

Continued . . .

  - Hemoglobin levels should be monitored when initiating or adjusting dose and then monthly.
  - The dose should be increased no more than once every 4 weeks. Decreases in dose can occur more frequently.
  - The dose should be adjusted in increments of 150 mg to achieve or maintain hemoglobin levels of 10 g/dL to 11 g/dL. Doses may range from 150 mg to a maximum of 600 mg.

- Akebia plans to launch Vafseo in January 2025. Vafseo will be available in 150 mg, 300 mg, and 450 mg tablets.