Jesduvroq (daprodustat) – New drug approval

- On February 1, 2023, the FDA announced the approval of GSK's Jesduvroq (daprodustat), for the treatment of anemia due to chronic kidney disease (CKD) in adults who have been receiving dialysis for at least four months.
    - Jesduvroq has not been shown to improve quality of life, fatigue, or patient well-being.
    - Jesduvroq is not indicated for use as a substitute for red blood cell transfusions in patients who require immediate correction of anemia or for treatment of anemia of CKD in patients who are not on dialysis.
- Over a half million adults in the U.S. have CKD requiring dialysis. Kidneys produce a hormone called erythropoietin, which signals the body to make red blood cells. In a person with CKD on dialysis, the kidneys cannot produce enough erythropoietin, leading to reduced numbers of red blood cells.
- Jesduvroq is an oral, first-in-class hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI). Inhibition of oxygen-sensing prolyl hydroxylase enzymes stabilizes hypoxia-inducible factors, which can lead to transcription of erythropoietin and other genes involved in the correction of anemia.
    - The other FDA-approved treatments for CKD-associated anemia are injectable erythropoietin stimulating agents (ESAs) (eg, epoetin alfa, darbepoetin alfa).
- The efficacy of Jesduvroq was established in ASCEND-D, a randomized, sponsor-blind, active-controlled, event-driven clinical trial in 2,964 adults with anemia due to CKD on dialysis and receiving an ESA at the time of study entry. Patients on hemodialysis were randomized to receive oral Jesduvroq or intravenous epoetin alfa while patients on peritoneal dialysis were randomized to receive oral Jesduvroq or subcutaneous darbepoetin alfa. The co-primary endpoints were the mean change in hemoglobin from baseline to the Evaluation Period (weeks 28 to 52) and time to first adjudicated MACE (defined as all-cause mortality, non-fatal myocardial infarction, or non-fatal stroke), using a non-inferiority comparison to rhEPO (epoetin alfa and darbepoetin alfa) for both endpoints.
    - The lower limit of the 95% CI for the overall hemoglobin treatment difference was greater than the pre-specified non-inferiority margin of -0.75 g/dL, demonstrating non-inferiority of Jesduvroq to rhEPO with respect to the mean change in hemoglobin between baseline and over the Evaluation Period. Results were similar in patients receiving either hemodialysis or peritoneal dialysis.
    - The hazard ratio for the time to first occurrence of MACE, comparing Jesduvroq to rhEPO was 0.93 (95% CI: 0.81, 1.07). Non-inferiority of Jesduvroq to rhEPO on MACE was achieved because the upper limit of the 95% CI for the MACE hazard ratio was less than the pre-specified non-inferiority margin of 1.25.
    - Refer to the Jesduvroq drug label for complete trial results.
- Jesduvroq carries a boxed warning for increased risk of death, myocardial infarction, stroke, venous thromboembolism, and thrombosis of vascular access.
- Jesduvroq is contraindicated in patients:
    - Receiving a strong CYP2C8 inhibitor such as gemfibrozil
    - With uncontrolled hypertension.

Continued . . .

- Additional warnings and precautions for Jesduvroq include risk of hospitalization for heart failure, hypertension, gastrointestinal erosion, serious adverse events in patients with anemia due to CKD and not on dialysis, and malignancy.

- The most common adverse reactions (≥ 10%) with Jesduvroq use were hypertension, thrombotic vascular events, and abdominal pain.

- Jesduvroq is administered orally once daily. For adults not being treated with an ESA, the starting dose of Jesduvroq (1 mg to 4 mg) is based on the hemoglobin level. For adults being switched from an ESA to Jesduvroq, the starting dose of Jesduvroq (4 mg to 12 mg) is based on the dose regimen of the ESA at the time of substitution.

    - Jesduvroq dosing should be individualized and the lowest dose sufficient to reduce the need for red blood cell transfusions should be use. A hemoglobin higher than 11 g/dL should not be targeted.
    - Refer to the Jesduvroq drug label for complete dosing and administration, including monitoring response to therapy and dose adjustment recommendation.

- GSK's launch plans for Jesduvroq are pending. Jesduvroq will be available as 1 mg, 2 mg, 4 mg, 6 mg, and 8 mg tablets.

Optum