Livdelzi® (seladelpar) – New orphan drug approval

- On August 14, 2024, Gilead announced the FDA approval of Livdelzi (seladelpar), for the treatment of primary biliary cholangitis (PBC) in combination with ursodeoxycholic acid (UDCA) in adults who have had an inadequate response to UDCA, or as monotherapy in patients unable to tolerate UDCA.
    - This indication is approved under accelerated approval based on a reduction of alkaline phosphatase (ALP). Improvement in survival or prevention of liver decompensation events have not been demonstrated. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).
    - Livdelzi is not recommended in patients who have or develop decompensated cirrhosis (eg, ascites, variceal bleeding, hepatic encephalopathy).
- PBC is a rare, chronic inflammatory liver disease primarily affecting women. PBC is characterized by impaired bile flow and the accumulation of toxic bile acids in the liver, leading to inflammation and destruction of the bile ducts within the liver. Progression of PBC is associated with an increased risk of liver-related mortality.
- Livdelzi is a PPAR-delta agonist. PPAR-delta has been shown to regulate critical metabolic and liver disease pathways.
- The efficacy of Livdelzi was established in a randomized, double-blind, placebo-controlled study in 193 adult patients with PBC with an inadequate response or intolerance to UDCA. Patients were randomized to Livdelzi or placebo. The primary endpoint was biochemical response at month 12, defined as achieving ALP less than 1.67x upper limit of normal (ULN), an ALP decrease of greater than or equal to 15% from baseline, and total bilirubin less than or equal to ULN.
    - Biochemical response was achieved in 62% of patients with Livdelzi vs. 20% with placebo (treatment difference 42, 95% CI: 28, 53; $p < 0.0001$).
- Warnings and precautions for Livdelzi include fractures, liver test abnormalities, and biliary obstruction.
- The most common adverse reactions (≥ 5% and higher compared to placebo) with Livdelzi use were headache, abdominal pain, nausea, abdominal distension, and dizziness.
- The recommended dose of Livdelzi is 10 mg orally once daily.
- Livdelzi will be priced at $151,000 per year.
- Gilead's launch plans for Livdelzi are pending. Livdelzi will be available as a 10 mg capsule.