Albireo Pharma appreciates the time your team has dedicated to reviewing Bylvay (odevixibat) post approval.

PFIC Disease Burden

Progressive familial intrahepatic cholestasis (PFIC) is a spectrum of rare, heterogeneous, genetic liver disorders, characterized by early onset cholestasis which leads to rapidly progressive liver failure and early mortality

The hallmark symptom of PFIC is pruritus, which has been described as intractable and debilitating. Severe itching may lead to cutaneous mutilation and scarring, loss of sleep, irritability, poor attention, and impaired school performance

Pruritus is cited as the indication for surgical biliary diversion (SBD) in the majority of patients with PFIC and for liver transplant in 50% of patients with PFIC1. Patients with PFIC experience progressive liver manifestations and deterioration.

The FDA recognized there remained a significant unmet medical need in the treatment of PFIC when they granted Bylvay Fast Track status, Rare Pediatric Disease, and Orphan Drug Designations in the United States despite availability of surgical interventions. In addition, the FDA has granted orphan drug designation to odevixibat for the treatment of Alagille syndrome, biliary atresia, and primary biliary cholangitis (PBC).

Bylvay

Bylvay is the first medication approved by the FDA for the treatment of pruritus in patients 3 months of age and older **with all types** of PFIC. Limitation of Use: Bylvay may not be effective in PFIC type 2 patients with ABCB11 variants resulting in non-functional or complete absence of bile salt export pump protein (BSEP-3). It is also the first ileal bile acid transporter inhibitor (IBATi) to be approved in the United States, offering a novel mechanism of action for treating patients with PFIC.

Bylvay has been studied in two phase 3 clinical trials, placebo-controlled PEDFIC 1 and ongoing open-label extension PEDFIC 2, in which it demonstrated an improvement in pruritus, decrease in serum bile acids (sBA), and a tolerable safety profile. PEDFIC 1 is the largest PFIC clinical trial and the only phase 3, placebo-controlled trial completed in PFIC.

Currently, no other drugs are FDA-approved for the treatment of pruritus in PFIC. Although several medications have been used off-label to treat PFIC, patients often still require surgery due to intractable pruritus, growth failure, and nutritional deficiencies. Requiring time to step patients through non-FDA approved medications delays time to initiation of the only proven therapy indicated to treat the significant pruritis associated with PFIC

As of 19 November 2021, BYLVAY is the only product with a compendia-listed use for pruritus in PFIC.

We respectfully seek Bylvay coverage to FDA indicated label.