

**Company**

Albireo Pharma, Inc.

**Drug or Device Name**

Bylvay®

**Category**

Biotechnology

**Compound/Technical Name**

Odevixibat

**Trade Name**

Bylvay®

**Date of Approval**

07/20/2021

**Therapeutic Categories**

Progressive familial intrahepatic cholestasis (PFIC)

**Indications**

Bylvay® (odevixibat) is the first drug approved in the U.S. for the treatment of pruritus in patients 3 months of age and older in all types of progressive familial intrahepatic cholestasis (PFIC). Bylvay is a potent, once-daily, non-systemic ileal bile acid transport (IBAT) inhibitor and acts locally in the small intestine. Bylvay can be taken as a capsule for patients that are able to swallow capsules, or opened and sprinkled onto food, which is a factor of key importance for adherence in a pediatric patient population. The most common adverse reactions for Bylvay are diarrhea, liver test abnormalities, vomiting, abdominal pain, and fat-soluble vitamin deficiency. The medicine can only be obtained with a prescription. 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). The European Commission (EC) and UK Medicines and Healthcare Products Regulatory Agency (MHRA) have also granted marketing authorization of Bylvay for the treatment of PFIC in patients aged 6 months or older. Bylvay is available in Germany and the UK and will be available for sale in other European countries following pricing and reimbursement approval. See full Prescribing Information for U.S. and Summary of Product Characteristics for the EU and UK attached.

**Background**

Progressive familial intrahepatic cholestasis (PFIC) is a rare, pediatric, genetic disease of cholestasis, characterized by inadequate bile secretion, often requiring liver transplantation, and leading to liver failure and early death. Patients have impaired bile flow, or cholestasis, and the resulting bile build-up in liver cells causes liver disease and symptoms including intense itching, poor sleep and diminished quality of life. The estimated incidence of PFIC ranges from 1 in 50,000 to 100,000 live births. Subtypes

PFIC1, PFIC2 and PFIC3 are most common, and other rare forms of PFIC exist with varying phenotypes, all presenting with cholestasis. The body naturally makes bile acids that help with digestion, including absorption fats and some vitamins. In PFIC, the normal flow of bile acids is disrupted, building up in the body and damaging the liver. A debilitating symptom of PFIC is pruritus (insatiable itching) which may be so severe that it leads to skin mutilation, loss of sleep, irritability, poor attention and impaired school performance. Up to 80% of PFIC patients have pruritus graded as severe (associated with abrasions, skin mutilation, hemorrhage or scarring). Survival analysis showed that at 18 years, only 44% of PFIC1 patients and 32% of PFIC2 patients were alive with their native liver. Pruritus is a primary cause of surgical treatments and transplant, cited as the indication for surgical diversion in the majority of PFIC patients and for transplant in 50% of patients with PFIC1. Surgical treatment options for PFIC all have significant risks. Prior to Bylvay's approval, there were no medical treatments approved for pruritus in PFIC and non-invasive treatments were needed to help avoid surgeries and transplantation, the only options available despite nearly a quarter of liver transplants in children failing within the first six months, almost a third within five years and almost half within 20 years.

### Development

Bylvay is the first drug approved in the U.S. for the treatment of pruritus in patients 3 months of age and older in all types of progressive familial intrahepatic cholestasis (PFIC). The European Commission (EC) and UK Medicines and Healthcare Products Regulatory Agency (MHRA) have also granted marketing authorization of Bylvay for the treatment of PFIC in patients aged 6 months or older. Bylvay is available in Germany and the UK. Bylvay is an oral medicine that is taken once a day (taken in the morning with a meal). Before Bylvay, no medicine could effectively relieve the intense, severe itching caused by PFIC. Bylvay may provide itch relief without surgery. The journey to the approval of Bylvay is supported by over a decade of gold standard research and development stemming from Albireo's expertise in bile acid modulation. In July 2021, Bylvay was approved in the U.S. and Europe just four days apart. The approval of Bylvay was supported by data from PEDFIC 1 and PEDFIC 2, the largest, global, Phase 3 clinical trials ever conducted in PFIC. PEDFIC 1 evaluated the efficacy and tolerability of Bylvay in reducing pruritus and serum bile acids in a randomized, double-blind, placebo-controlled trial, and PEDFIC 2 was a long-term, open-label Phase 3 extension study. A pooled analysis of data from PEDFIC 1 and PEDFIC 2 evaluating the long-term clinical benefit of Bylvay showed that Bylvay was associated with large, sustained improvements in mean serum bile acids and pruritus scores, as well as improvement in pruritus assessments, growth and other markers of liver function, in patients treated up to 128 weeks. Across both studies, Bylvay was consistently well tolerated with diarrhea/frequent stools being the most common treatment-related gastrointestinal adverse events. There were no serious treatment-related adverse events. Since Bylvay's approval, Albireo has driven patient access and expansion of Bylvay globally, with data (presented at conferences) showing measurable impact on the quality of life for both patients and their families.

### Innovation

Bylvay's U.S. and global regulatory approvals underscore its importance and innovation in treating rare liver disease, receiving U.S. FDA Fast Track, Rare Pediatric Disease and Orphan Drug Designations, as well as several ex-U.S. designations: NICE Highly Specialised Technologies (HST) in England & Wales, Scottish Medicines Consortium (SMC) Ultra-orphan Pathway in Scotland, the HAS Transparency Committee's Fast-Track in France and the Highly Innovative Technology status in Poland. We also continue to coordinate pricing and reimbursement in countries around the globe. Prior to Bylvay's approval, there was an immense unmet need for PFIC patients for a non-invasive drug treatment option to help manage the insatiable itching (pruritus) associated with cholestatic liver disease, versus

surgeries that pose significant risks. Patients may also experience symptoms like jaundice, fatigue, cirrhosis and more. As the first drug approved for PFIC patients, Bylvay is a ground-breaking treatment for patients with this rare disease. The ability to offer a non-surgical treatment option that does not require refrigeration and is easily administered as a once-daily capsule for older children or opened and sprinkled onto soft foods provides this patient population with a much-needed treatment alternative that improves treatment adherence.<sup>1</sup> Dosing is customizable per weight and guidance from a physician, allowing it to be adjusted over time. Albireo's pioneering research on enterohepatic circulation and bile acid show they are involved in more than just digestion. Most people are unaware that bile acids interact with receptors throughout the body and are responsible for many different things, leaving a gap in today's market for exploration. Modulation is important because too much bile acid is highly toxic. As the leader in bile acid science, Albireo is investing its expertise in bile acid modulation to bring novel, potentially transformative medicines to patients.

### Pubmed

Baumann U, Sturm E, Lacaille F, et al. Effects of odeixibat on pruritus and bile acids in children with cholestatic liver disease: Phase 2 study. *Clin Res Hepatol Gastroenterol*. 2021;45(5):101751. doi:10.1016/j.clinre.2021.101751. <https://pubmed.ncbi.nlm.nih.gov/34182185/> Slavetinsky C, Sturm E. Odeixibat and partial external biliary diversion showed equal improvement of cholestasis in a patient with progressive familial intrahepatic cholestasis. *BMJ Case Rep*. 2020;13(6):e234185. Published 2020 Jun 29. doi:10.1136/bcr-2019-234185. <https://pubmed.ncbi.nlm.nih.gov/32601135/> Mighiu C, O'Hara S, Ferri Grazi E, et al. Impact of progressive familial intrahepatic cholestasis on caregivers: caregiver-reported outcomes from the multinational PICTURE study. *Orphanet J Rare Dis*. 2022;17(1):32. Published 2022 Feb 2. doi:10.1186/s13023-022-02177-0. <https://pubmed.ncbi.nlm.nih.gov/35109890/> Baker A, Kerkar N, Todorova L, Kamath BM, Houwen RHJ. Systematic review of progressive familial intrahepatic cholestasis [published correction appears in *Clin Res Hepatol Gastroenterol*. 2020 Feb;44(1):115]. *Clin Res Hepatol Gastroenterol*. 2019;43(1):20-36. doi:10.1016/j.clinre.2018.07.010. <https://pubmed.ncbi.nlm.nih.gov/30236549/>

### Attachments

- 1656516075Bylvay\_Patient\_Brochure\_R14-64.pdf
- 1656514924Background.pdf
- 1656519576Development\_Pack.pdf
- 1656514737Indications.pdf

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