RxAdvance

NEW DRUG APPROVAL

Brand Name	Bylvay™
Generic Name	odevixibat
Drug Manufacturer	Albireo Pharma, Inc.

New Drug Approval

FDA Approval Date: July 20, 2021

Review Designation: Priority; Orphan

Type of Review: Type 1 - New Molecular Entity; New Drug Application (NDA): 215498

Dispensing Restrictions: Specialty Only; Limited Distribution

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

Progressive familial intrahepatic cholestasis (PFIC) is a group of ultra-rare genetic disorders that disrupt bile formation. PFIC usually develops in infancy, although it can develop into young adulthood, and is characterized by cholestasis, jaundice, and intense pruritis. Patients typically develop fibrosis and end-stage liver disease before adulthood, which can be fatal if untreated. Most patients with PFIC require biliary diversion surgery or liver transplant by 30 years of age. PFIC is typically diagnosed using liver function tests (e.g. gamma-glutamyltransferase [GGT], aspartate aminotransferase [AST], alanine transaminase [ALT]), bile acid tests, liver biopsy, and genetic testing. While PFIC types 1–3 are the most common, new types are still being discovered. In types 1–3, benign recurrent intrahepatic cholestasis (BRIC), a transient presentation of PFIC, has occurred.

PFIC affects approximately 600 children in the United States and 15,000 individuals worldwide, according to the manufacturer. Experts estimate the incidence of PFIC to be between 1 in 50,000 and 1 in 100,000 births.

Efficacy

The efficacy of Bylvay™ was evaluated in Trial 1 (NCT03566238), a 24-week, randomized, double blind, placebo-controlled trial. Trial 1 was conducted in 62 pediatric patients, aged 6 months to 17 years, with a confirmed molecular diagnosis of PFIC type 1 or type 2, and presence of pruritus at baseline.

Table presents the results of the comparison between Bylvay™ and placebo on the mean of patients' percentage of ObsRO assessments over the 24-week treatment period that were scored as 0 (no scratching) or 1 (a little scratching). Patients treated with Bylvay™ demonstrated greater improvement in pruritus compared with placebo.

Table: Efficacy Results Over the 24-Week Treatment Period in Patients with PFIC Type 1 or 2 in Trial 1

	Placebo (n=20)	BYLVAY 40 mcg/kg/day (n=23)	BYLVAY 120 mcg/kg/day (n=19)
Mean[a] Percentage of Assessments Over the Treatment Period Scored as 0 (No Scratching) or 1 (A Little Scratching) (%)			
Mean (SE)	13.2 (8.7)	35.4 (8.1)	30.1 (9.0)
Mean Difference vs Placebo (95% CI)		22.2 (4.7, 39.6)	16.9 (-2.0, 35.7)

[a] Based on least squares means from analysis of covariance model with daytime and nighttime baseline pruritus scores as covariates and treatment group and stratification factors (i.e., PFIC type and age category) as fixed effects.

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Safety

ADVERSE EVENTS

Most common adverse reactions (>2%) are liver test abnormalities, diarrhea, abdominal pain, vomiting, and fat-soluble vitamin deficiency.

WARNINGS & PRECAUTIONS

- **Liver Test Abnormalities**: Obtain baseline liver tests and monitor during treatment. Dose reduction or treatment interruption may be required if abnormalities occur. For persistent or recurrent liver test abnormalities, consider treatment discontinuation.
- **Diarrhea**: Treat dehydration. Treatment interruption or discontinuation may be required for persistent diarrhea.
- **Fat-Soluble Vitamin (FSV) Deficiency**: Obtain baseline levels and monitor during treatment. Supplement if deficiency is observed. If FSV deficiency persists or worsens despite FSV supplementation, discontinue treatment.

CONTRAINDICATIONS

None.

Clinical Pharmacology

MECHANISMS OF ACTION

Odevixibat is a reversible inhibitor of the ileal bile acid transporter (IBAT). It decreases the reabsorption of bile acids (primarily the salt forms) from the terminal ileum. Pruritus is a common symptom in patients with PFIC and the pathophysiology of pruritus in patients with PFIC is not completely understood. Although the complete mechanism by which odevixibat improves pruritus in PFIC patients is unknown, it may involve inhibition of the IBAT, which results in decreased reuptake of bile salts, as observed by a decrease in serum bile acids.

Dose & Administration

ADULTS

Safety and efficacy have not been established.

PEDIATRICS

Capsules: Children and Adolescents weighing 19.5 kg or more.
40 mcg/kg/dose PO once daily in the morning; round to appropriate capsule strength. If no improvement after 3 months, may increase dose in 40 mcg/kg increments up to 120 mcg/kg/day.

Oral pellets: Infants 3 to 11 months and Children weighing less than 19.5 kg.
40 mcg/kg/dose PO once daily in the morning; round to appropriate oral pellet strength. If no improvement after 3 months, may increase dose in 40 mcg/kg increments up to 120 mcg/kg/day.

GERIATRICS

Safety and efficacy have not been established.

RENAL IMPAIRMENT

Specific guidelines for dosage adjustments in renal impairment are not available; it appears that no dosage adjustments are needed.

HEPATIC IMPAIRMENT

Interrupt treatment if new onset hepatic function abnormalities occur or symptoms consistent with clinical hepatitis develop. Once hepatic function returns to baseline or stabilizes at a new baseline, consider restarting odevixibat at 40 mcg/kg/day and increase as tolerated. Consider permanent discontinuation for persistent or recurrent hepatic function abnormalities. Permanently discontinue treatment if a patient progresses to portal hypertension or experiences a hepatic decompensation event (e.g., variceal hemorrhage, ascites, hepatic encephalopathy).

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

- Oral Pellets: 200 mcg, 600 mcg.
- Capsules: 400 mcg, 1200 mcg.