Bylvay®
(odevixibat)

200 | 400 | 600 | 1200 mcg capsules

Dosage and Administration

INDICATIONS

BYLVAY is an ileal bile acid transporter (IBAT) inhibitor indicated for the treatment of:

- cholestatic pruritus in patients ≥12 months of age with Alagille syndrome (ALGS)
- pruritus in patients ≥3 months of age with progressive familial intrahepatic cholestasis (PFIC)

Limitation of Use:

BYLVAY may not be effective in a subgroup of PFIC type 2 patients with specific *ABCB11* variants resulting in non-functional or complete absence of the bile salt export pump protein.

IMPORTANT SAFETY INFORMATION

Contraindications

IBAT inhibitors, including BYLVAY, are contraindicated in patients with prior or active hepatic decompensation events (e.g., variceal hemorrhage, ascites, hepatic encephalopathy).

Preparation and Administration Instructions

Take Bylvay in the morning with a meal.

- **For patients taking bile acid binding resins, take Bylvay at least 4 hours before or 4 hours after taking a bile acid binding resin**

Oral Pellets 200 mcg |


Oral Pellets 600 mcg

Oral Pellets:

Administration Instructions:


Mix the contents of the shell containing Oral Pellets into soft food or an age-appropriate liquid, such as water, breast milk, or infant formula.


Discard the emptied shells. Do not swallow the shell containing Oral Pellets whole.

To open and mix with **soft food**:

1. Place a small amount of soft food (up to 30 mL [2 tablespoons] of apple sauce, oatmeal, banana or carrot puree, chocolate or rice pudding) in a bowl. Keep food at or below room temperature.
2. Open the shell containing Oral Pellets and empty the contents into the bowl of soft food. Gently tap the Oral Pellet shell to ensure that all contents have been dispersed.
   - If the dose requires more than one shell of Oral Pellets, repeat steps 1 and 2
3. Gently mix until well dispersed and administer the entire dose immediately.

To open Oral Pellets and mix with **liquid** (using an oral dosing syringe):

1. Open the shell containing Oral Pellets and empty the contents into a small mixing cup. Gently tap the shell containing Oral Pellets to ensure that all contents have been emptied into the mixing cup.
2. Add 1 teaspoon (5 mL) of an age-appropriate liquid (for example, breast milk, infant formula, or water).
   - If the dose requires more than one shell of Oral Pellets, repeat steps 1 and 2
3. Let the pellets sit in the liquid for about 5 minutes before administering. Note that Oral Pellets will not dissolve.
4. After 5 minutes, place the tip of the oral syringe completely into the mixing cup. Pull the plunger of the syringe up slowly to withdraw the liquid/pellet mixture into the syringe. Gently push the plunger down again to expel the liquid/pellet mixture back into the mixing cup.
   - Do this 2 to 3 times to ensure complete mixing of the pellets into the liquid
5. Withdraw the entire contents into the oral syringe by pulling the plunger on the end of the syringe.
6. Place the tip of the syringe into the front of the patient's mouth between the tongue and the side of the mouth, and then gently push the plunger down to squirt the liquid/pellet mixture between your child's tongue and the side of the mouth. Do not squirt liquid/pellet mixture in the back of the child's throat because this could cause gagging or choking.
   - Do not administer via a bottle or "sippy cup" because the Oral Pellets will not pass through the opening. The Oral Pellets will not dissolve in liquid

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS

Hepatotoxicity

BYLVAY treatment is associated with a potential for drug-induced liver injury (DILI). In the PFIC and ALGS trials, treatment-emergent elevations or worsening of liver tests occurred.

Preparation and Administration Instructions (cont'd)

Capsules 400 mcg | Capsules 1200 mcg

Capsules:

- Do not crush or chew Capsules

Administration Instructions:

Swallow the Capsule whole with a glass of water.

Alternatively, for patients unable to swallow the Capsules whole, Bylvay Capsules may be opened and then sprinkled and mixed with a small amount of soft food or age-appropriate liquid. Follow directions on previous page for Oral Pellets to prepare and administer such a mixture.

Whether mixing with soft food or liquid, follow the dose with an age-appropriate liquid and do not store mixture for future use.

Scan or click this code to view instructional videos for opening and mixing Oral Pellets with soft food or liquid.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS

Hepatotoxicity (cont'd)

Of the six patients who experienced DILI, two underwent liver transplant. Obtain baseline liver tests because some ALGS and PFIC patients have abnormal liver tests at baseline and monitor patients frequently for the first 6 to 8 months, and as clinically needed thereafter, for elevations in liver tests, for the development of liver-related adverse reactions, and for physical signs of hepatic decompensation.

Recommended Dosing for Bylvay® (odevixibat)

Dosage Forms and Strengths

Bylvay is currently available in 200 mcg and 600 mcg Oral Pellets, and 400 mcg and 1200 mcg Capsules.

Recommended starting dose for PFIC: 40 mcg/kg/day
Maximum total daily dose for PFIC: 6 mg

Recommended starting dose for Alagille syndrome: 120 mcg/kg/day
Maximum total daily dose for Alagille syndrome: 7.2 mg

Recommended Dosage of Bylvay for 40 mcg/kg/day

Body Weight (kg)	Total Daily Dose (mcg)	Number of Oral Pellets or Capsules
7.4 and below	200	1 (200 mcg Oral Pellet)
7.5 to 12.4	400	2 (200 mcg Oral Pellets)
12.5 to 17.4	600	1 (600 mcg Oral Pellet)
17.5 to 19.4	800	4 (200 mcg Oral Pellets)
19.5 to 25.4	800	2 (400 mcg Capsules)
25.5 to 35.4	1200	1 (1200 mcg Capsule)
35.5 to 45.4	1600	4 (400 mcg Capsules)
45.5 to 55.4	2000	5 (400 mcg Capsules)
55.5 and above	2400	2 (1200 mcg Capsules)

For patients with PFIC, if there is no improvement in pruritus after 3 months, the dosage may be increased in 40 mcg/kg increments up to 120 mcg/kg once daily not to exceed a total daily dose of 6 mg.

Oral Pellets are intended for use by patients weighing less than 19.5 kilograms. Capsules are intended for use by patients weighing 19.5 kilograms or above.

How Supplied/Storage and Handling

Bylvay Capsules are supplied in bottles of 30 with child-resistant closure.
Store at 20°C to 25°C (68°F to 77°F).

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS

Hepatotoxicity (cont'd)

If liver test abnormalities or signs of clinical hepatitis occur in the absence of other causes, consider dose reduction or treatment interruption. Permanently discontinue BYLVAY if a patient experiences the following: persistent or recurrent liver test abnormalities, or upon rechallenge, signs and symptoms consistent with clinical hepatitis, or a hepatic decompensation event.

Recommended Dosing for Bylvay® (odevixibat) (cont'd)

Recommended Dosage of Bylvay for 80 mcg/kg/day

Body Weight (kg)	Total Daily Dose (mcg)	Number of Oral Pellets or Capsules
7.4 and below	400	2 (200 mcg Oral Pellets)
7.5 to 12.4	800	4 (200 mcg Oral Pellets)
12.5 to 17.4	1200	1 (1200 mcg Capsule)
17.5 to 19.4	1600	8 (200 mcg Oral Pellets)
19.5 to 25.4	1600	4 (400 mcg Capsules)
25.5 to 35.4	2400	2 (1200 mcg Capsules)
35.5 to 45.4	3200	8 (400 mcg Capsules)
45.5 to 55.4	4000	10 (400 mcg Capsules)
55.5 and above	4800	4 (1200 mcg Capsules)

Maximum total daily dose for PFIC: 6 mg

Recommended Dosage of Bylvay for 120 mcg/kg/day

Body Weight (kg)	Total Daily Dose (mcg)	Number of Oral Pellets or Capsules
7.4 and below	600	1 (600 mcg Oral Pellet)
7.5 to 12.4	1200	1 (1200 mcg Capsule)
12.5 to 17.4	1800	3 (600 mcg Oral Pellets)
17.5 to 19.4	2400	2 (1200 mcg Capsules)
19.5 to 25.4	2400	2 (1200 mcg Capsules)
25.5 to 35.4	3600	3 (1200 mcg Capsules)
35.5 to 45.4	4800	4 (1200 mcg Capsules)
45.5 to 55.4	6000	5 (1200 mcg Capsules)
55.5 and above	7200	6 (1200 mcg Capsules)

Maximum total daily dose for PFIC: 6 mg
Maximum total daily dose for Alagille syndrome: 7.2 mg

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS

Hepatotoxicity (cont'd)

The safety and effectiveness of BYLVAY have not been established in patients with decompensated cirrhosis. Monitor patients with compensated cirrhosis or portal hypertension more frequently and discontinue if hepatic decompensation occurs. IBAT inhibitors, including BYLVAY, are contraindicated in patients with prior or active hepatic decompensation events.

IMPORTANT SAFETY INFORMATION

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IBAT inhibitors, including BYLVAY, are contraindicated in patients with prior or active hepatic decompensation events (e.g., variceal hemorrhage, ascites, hepatic encephalopathy).

WARNINGS AND PRECAUTIONS

Hepatotoxicity
BYLVAY treatment is associated with a potential for drug-induced liver injury (DILI). In the PFIC and ALGS trials, treatment-emergent elevations or worsening of liver tests occurred. Of the six patients who experienced DILI, two underwent liver transplant. Obtain baseline liver tests because some ALGS and PFIC patients have abnormal liver tests at baseline and monitor patients frequently for the first 6 to 8 months, and as clinically needed thereafter, for elevations in liver tests, for the development of liver-related adverse reactions, and for physical signs of hepatic decompensation. If liver test abnormalities or signs of clinical hepatitis occur in the absence of other causes, consider dose reduction or treatment interruption. Permanently discontinue BYLVAY if a patient experiences the following: persistent or recurrent liver test abnormalities, or upon rechallenge, signs and symptoms consistent with clinical hepatitis, or a hepatic decompensation event.

The safety and effectiveness of BYLVAY have not been established in patients with decompensated cirrhosis. Monitor patients with compensated cirrhosis or portal hypertension more frequently and discontinue if hepatic decompensation occurs. IBAT inhibitors, including BYLVAY, are contraindicated in patients with prior or active hepatic decompensation events.

Diarrhea
In the PFIC and ALGS clinical trials, diarrhea was reported more frequently in BYLVAY-treated patients compared to placebo. In the PFIC clinical trials, treatment interruption due to diarrhea occurred in 2 patients with 3 events. Treatment interruption due to diarrhea ranged between 3 to 7 days. One patient withdrew from the trial. In the ALGS clinical trial, no patients interrupted or discontinued treatment due to diarrhea.

If diarrhea occurs, monitor for dehydration and treat promptly. Interrupt dosing if a patient experiences persistent diarrhea. Restart BYLVAY at 40 mcg/kg/day when diarrhea resolves and increase the dose as tolerated if appropriate. If diarrhea persists and no alternate etiology is identified, stop treatment.

Fat-Soluble Vitamin (FSV) Deficiency
Fat-soluble vitamins (FSV) include vitamin A, D, E, and K. PFIC and ALGS patients can have FSV deficiency at baseline. BYLVAY may affect absorption of FSVs. In clinical trials, new onset or worsening of existing FSV deficiency was reported more frequently in BYLVAY-treated patients compared to placebo.

Obtain baseline INR and FSV levels and monitor during treatment along with any clinical manifestations. If FSV deficiency is diagnosed, supplement with FSV. Discontinue BYLVAY if FSV deficiency persists or worsens despite adequate FSV supplementation and consider restarting once the patient is clinically stable.

If bleeding occurs, interrupt treatment with BYLVAY. Optimize treatment of FSV deficiency and consider restarting BYLVAY once the patient is clinically stable..

Adverse Reactions
The most common adverse reactions for BYLVAY in patients with PFIC are diarrhea, liver test abnormalities, vomiting, abdominal pain, and FSV deficiency.

The most common adverse reactions for BYLVAY patients with ALGS are diarrhea, abdominal pain, hematoma, and decreased weight.

Drug Interactions
For patients taking bile acid binding resins, take BYLVAY at least 4 hours before or 4 hours after taking a bile acid binding resin.

Use in Specific Populations
There are no human data on BYLVAY use in pregnant persons to establish a drug-associated risk of major birth defects, miscarriage, or adverse developmental outcomes. Based on findings from animal reproduction studies, BYLVAY may cause cardiac malformations when a fetus is exposed during pregnancy. There is a pregnancy exposure registry that monitors pregnancy outcomes in persons exposed to BYLVAY during pregnancy. For more information, please call 1-855-463-5127.

To report SUSPECTED ADVERSE REACTIONS, contact Ipsen Biopharmaceuticals, Inc. at 1-855-463-5127 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see full Prescribing Information.

Dedicated Support for Your Patients Prescribed Bylvay

The **IPSEN CARES** patient support program helps patients get access to their Bylvay prescription with the information and support they need

Personalized Support Services

Financial & Insurance Assistance

Continuity of Care

Dedicated, Individualized Support

Educational Materials & Programs

Visit **IPSENCARES.com** or call (866) 435-5677
Monday-Friday, 8:00 AM – 8:00 PM ET
support@ipsencares.com

Bylvay®
(odevixibat)

200 | 400 | 600 | 1200 mcg capsules

Find instructional videos and other tips on taking Bylvay at **Bylvay.com** or by scanning this code

Please see Important Safety Information throughout, and the full Prescribing Information.