IOWA | Health and Human Services

New Drug Overview

Lynavoy (linerixibat)
PDL Category: GI - MISC

Introduction

Disease Background:

- Primary biliary cholangitis (PBC) is a chronic, autoimmune cholestatic condition. It is an antimitochondrial antibody-positive, disease of the liver that incurs gradual damage of intrahepatic bile ducts, chronic cholestasis, portal inflammation, and fibrosis that leads to cirrhosis and liver failure if not treated (*Tapper et al 2026*).
  - Specifically, it is described as a T-lymphocyte-mediated attack on small intralobular bile ducts, and a persistent attack on the cells of the bile duct leads to damage and eventually disappearance (*Poupon 2025*).
  - It was formerly known as primary biliary cirrhosis.
- PBC is rare, with a prevalence of 19 to 402 cases per million people (*Poupon 2025*); it mainly affects women, with diagnosis generally made at 40 to 60 years of age (*Tapper et al 2026*).
- Risk factors for PBC includes family history, infections, environmental toxic agents, positive antimitochondrial antibody (AMA), or other autoimmune disease (*Tapper et al 2026*).
- The most frequent symptom that occurs with PBC is fatigue, which is reported in more than 75% of patients. In addition, pruritus (focal or diffuse) may be reported (*Tapper et al 2026*).
  - Assess patients for symptoms, especially pruritus (itching), fatigue, and sicca; however, note that the severity of symptoms is not related to the stage of disease.
  - While more than half of patients have no symptoms when PBC is diagnosed, symptoms generally start to occur within 2 to 4 years.
- Goals for therapy should address preventing end-stage liver disease complications and managing associated symptoms (*Tapper et al 2026*).
  - All should avoid alcohol and be vaccinated against hepatitis A and hepatitis B.
  - Ursodeoxycholic acid (UDCA) is recommended for PBC patients and abnormal liver enzymes.
  - Pruritus should be managed in a step-wise approach, including starting with conservative methods such as emollients and allergen avoidance.
- Lynavoy was FDA approved in 2026.

Pharmacology/Usage

- Lynavoy (linerixibat) is a reversible inhibitor of the ileal bile acid transporter (IBAT). It decreases the reabsorption of bile acids in the terminal ileum leading to their increased fecal elimination.
  - Cholestatic pruritus is a common symptom in patients with PBC, and the pathophysiology of pruritus in patients with PBC is not completely understood. Although the complete mechanism by which linerixibat improves pruritus in PBC patients is not known, it may involve inhibition of the IBAT as observed by a decrease in mediators of pruritus including serum bile acids.

Indications

Table 1. Food and Drug Administration Approved Indications

Indication	Lynavoy (linerixibat)
• For the treatment of cholestatic pruritus associated with primary biliary cholangitis (PBC) in adult patients. [a]	✔

[a] Limitations of use includes to avoid use of Lynavoy in patients with decompensated cirrhosis or those with prior or active hepatic decompensation events (eg, variceal hemorrhage, ascites, hepatic encephalopathy).

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(Prescribing information: Lynavoy 2026)

- Information on indications, mechanism of action, pharmacokinetics, dosing, safety, and clinical efficacy summary has been obtained from the prescribing information for the individual products, except where noted otherwise.

Dosing and administration

Table 2. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Lynavoy (linerixibat)	Film-coated Tablets: 40mg.	PO	Take 40mg PO BID. -Swallow tablets whole at least 30 minutes before any food or beverage (other than water).	• If a dose is missed, take the missed dose as soon as possible and at least 30 minutes before your next meal, then resume the original dosing schedule. If a dose is missed by more than 6 hours, skip the dose and resume the original dosing schedule. Do not take a double dose to make up for a missed dose. • Administer Lynavoy at least 4 hours before or 4 hours after taking a bile acid binding resin. • The safety and efficacy of Lynavoy have not been studied in patients with severe renal impairment, including those on hemodialysis. • The efficacy and safety of Lynavoy have not been evaluated in patients with moderate and severe hepatic impairment with decompensated cirrhosis or those with decompensation events. Avoid use in patients with

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Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
				decompensated cirrhosis or those with prior or active decompensation events.

See the current prescribing information for full details.

Clinical Efficacy Summary

- The efficacy of Lynavoy was assessed in Study 1 (GLISTEN), a randomized, double-blind, placebo-controlled trial that included adults (N = 238) with a confirmed diagnosis of PBC and presence of pruritus at baseline.
  - Patients were randomized to Lynavoy 40mg BID (N = 119) or placebo (N = 119) for 24 weeks.
    - At baseline, 97% of patients were receiving UDCA and 47% of patients were receiving concomitant antipruritic drugs. In addition, 11% of Lynavoy-treated and 10% of placebo-treated patients had compensated liver cirrhosis (Child-Pugh A).
    - The mean age of patients was 55.8 years (range 30 to 80), while 95% were female and 62% were White.
      - Patients were excluded from the study if they had hepatic decompensation, chronic viral hepatitis, symptomatic cholelithiasis, active cholecystitis, primary sclerosing cholangitis, alcoholic liver disease, bariatric surgery with ileal bypass, clinically significant diarrhea, or severe renal impairment.
  - Efficacy assessment included itch severity and sleep interference.
    - Patients rated their worst itch severity twice daily using the 11-point Worst Itch Numeric Rating Scale (NRS), with possible scores ranging from 0 (no itching) to 10 (worst imaginable itching).
      - The Worst Daily Itch Score was computed as the worst (highest) of the two scores recorded in a day.
      - The Weekly Itch Score was computed as the average of the Worst Daily Itch Scores across the 7 days in a week.
      - The Monthly Itch Score was computed at the worst (highest) Weekly Itch Score within a 4-week period.
      - Patients were included in this study if their Monthly Itch Score in the 4 weeks preceding randomization was 4 or greater. The mean Monthly Itch Score at baseline was 7.3.
    - Sleep interference due to pruritus was assessed each morning using the 11-point Sleep Interference NRS, with possible scores ranging from 0 (did not interfere) to 10 (completely interfered).
      - The Weekly Sleep Score was computed as the average of the daily sleep scores recorded over the 7 days in a week.
      - The Monthly Sleep Score was computed as the worst (highest) Weekly Sleep Score within a 4-week period.
      - The mean Monthly Sleep Score at baseline was 6.3.
  - Efficacy results for the primary endpoint of change from baseline in Monthly Itch Score over 24 weeks included that patients who received Lynavoy demonstrated a greater improvement from baseline in pruritus compared with placebo over 24 weeks of treatment.
    - Results are presented in the table below, which was adapted from the prescribing information.

Table 3. Efficacy results

	Lynavoy (N = 119)	Placebo (N = 118)
Baseline Monthly Itch Score mean	7.33	7.36
Change from baseline in Monthly Itch Score over 24 weeks		

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	Lynavoy (N = 119)	Placebo (N = 118)
Change from baseline least squares (LS) mean	-2.86	-2.15
LS mean difference vs placebo	-0.72	
p-value	0.001	

- There was greater improvement from baseline in pruritus measured by weekly itch score at week 2 for patients who received Lynavoy compared with placebo (LS mean difference -0.71, $p < 0.001$).
- Efficacy results for Lynavoy and placebo treatment groups based on the secondary endpoint, change from baseline in Monthly Sleep Score over 24 weeks, included that patients who received Lynavoy demonstrated greater improvement in pruritus-related sleep interference compared with placebo over 24 weeks of treatment.
  - Results are presented in the table below, which was adapted from the prescribing information.

Table 4. Efficacy results

	Lynavoy (N = 119)	Placebo (N = 118)
Baseline Monthly Sleep Score mean	6.29	6.33
Change from baseline in Monthly Sleep Score over 24 weeks		
Change from baseline least squares (LS) mean	-2.77	-2.24
Mean difference vs placebo	-0.53	
p-value	0.024	

Clinical guidelines

- **Primary Biliary Cholangitis: 2018 Practice Guidance from the American Association for the Study of Liver Diseases** (*Lindor et al 2019*).
  - Guidance statements for therapy include:
    - UDCA dosed at 13 to 15 mg/kg/day PO is recommended for PBC patients with abnormal liver enzyme values regardless of histologic stage.
    - For patients needing bile acid sequestrants, UDCA should be given at least 1 hour before or 4 hours after the bile acid sequestrant.
    - Assess biochemical response to UDCA at 12 months after the start of treatment to determine if patients should be considered for second-line therapy.
    - If there is no adequate response to UDCA then patients should consider treatment with OCA (obeticholic acid) starting at 5 mg/day.
    - Fibrates can be considered with PBC patients and inadequate response to UDCA, with the understanding that this is considered an off-label alternative.
    - Use of OCA and fibrates is discouraged with decompensated liver disease.
  - Managing pruritus symptoms:
    - Anion-exchange resins should be utilized as initial treatment for pruritus in patients with PBC.

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- The following can be used for pruritus if refractory to anion-exchange resins:
  - Rifampicin 150 to 300mg BID.
  - Oral opiate antagonists such as naltrexone.
  - Sertraline 75mg to 100mg QD.

- **Primary biliary cholangitis: 2021 practice guidance update from the American Association for the Study of Liver Diseases** (*Lindor et al 2022*).
  - This update provided revised guidance statements that were published in the 2018 practice guidance on PBC.
    - Fibrates can be considered as off-label alternatives for PBC patients who have an inadequate response to UDCA, although fibrate use is discouraged in patients with decompensated liver disease.
    - OCA is contraindicated in patients with advanced cirrhosis. In addition, careful monitoring is recommended in patients with cirrhosis, even if not advanced, receiving OCA.
- **European Association for the Study of the Liver (EASL) Clinical Practice Guidelines: The diagnosis and management of patients with primary biliary cholangitis** (*EASL 2017*).
  - UDCA 13-15 mg/kg/day is recommended as first-line treatment for all with PBC, and is usually continued for life.
  - Oral OCA has been conditionally approved for PBC in combination with UDCA in patients that have an inadequate response to UDCA or as monotherapy if intolerant to UDCA, and EASL suggests considering it for this use in such patients.
  - EASL suggests a recommendation for budesonide and bezafibrate cannot be made.
  - EASL recommends that all patients be assessed for symptoms, especially pruritus, sicca complex, and fatigue.
  - EASL recommends a stepwise approach for treating pruritus.
    - Cholestyramine is recommended as first-line treatment for pruritus and rifampicin is recommended as second-line treatment for pruritus.

Safety summary

- **Contraindications:** None.

- **Box Warning:** None.

- **Warnings and precautions:**
  - In study 1, liver test elevations were observed more commonly in Lynavoy-treated patients compared to placebo-treated patients.
    - Obtain baseline liver tests (alanine aminotransferase [ALT], aspartate aminotransferase [AST], total bilirubin [TB], direct bilirubin [DB], alkaline phosphatase [ALP]) prior to starting treatment with Lynavoy and monitor the levels per standard clinical practice for PBC patients during Lynavoy treatment. If new liver test elevations occur, monitor ALT, AST, TB, DB, and ALP more frequently. If liver test elevations persist, discontinue Lynavoy.
  - Diarrhea was reported as the most common adverse reaction in patients treated with Lynavoy.
    - If diarrhea occurs, advise patients to monitor for dehydration. Consider interrupting or discontinuing Lynavoy treatment if diarrhea persists.
  - Lynavoy may adversely affect absorption of fat-soluble vitamins (FSV). FSV include vitamins A, D, E, and K.
    - Obtain serum FSV levels (vitamins A, D, and E) and INR prior to starting Lynavoy and monitor the levels periodically during treatment, along with any clinical manifestations of FSV deficiency. Supplement with FSV if FSV deficiency is diagnosed. Consider discontinuing Lynavoy if FSV deficiency persists or worsens despite adequate FSV supplementation.

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- Bleeding was observed more frequently in Lynavoy-treated patients compared to placebo-treated patients. If bleeding occurs, interrupt Lynavoy treatment and assess for potential FSV deficiency. Lynavoy can be restarted if FSV deficiency is corrected, levels are maintained, and bleeding has resolved.
- IBAT inhibitors have been associated with bone fractures. Monitor bone health and ensure adequate FSV levels.

- **Common adverse drug reactions**:
  - Listed % incidence for adverse drug reactions= reported % incidence for drug (Lynavoy) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the same as or less than placebo.
    - The most frequently reported adverse events included diarrhea (44%), abdominal pain (16%), nausea (1%), increased alanine aminotransferase (ALT; 6%), hemorrhage (6%), increased aspartate aminotransferase (AST; < 8%), headache (5%), dyspepsia (< 8%), gastroesophageal reflux disease (3%), abdominal distension (2%), dizziness (3%), and arthralgia (1%).

- **Drug interactions:**
  - Instruct patients to take Lynavoy at least 4 hours before or 4 hours after taking a bile acid binding resin. Based on in vitro data, bile acid resins may bind linerixibat in the gut. Concomitant use of bile acid binding resins with Lynavoy can potentially inhibit the effects of Lynavoy on the ileal bile acid transporter.

- **Special populations:**
  - There is no pregnancy category for this medication; however, the risk summary indicates that there are no data on use in pregnant women to inform a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. Use of Lynavoy during pregnancy is expected to result in minimal fetal exposure because systemic absorption following oral administration is low.
    - Linerixibat may inhibit the absorption of FSV. FSV are essential for normal fetal growth and development. Monitor pregnant patients for FSV deficiency and supplement as needed. Increased supplementation of FSVs may be needed during pregnancy.
    - There is a pregnancy safety study that monitors pregnancy exposures and outcomes in women who have taken Lynavoy during pregnancy. Pregnant women exposed to Lynavoy, or their healthcare providers, should report Lynavoy exposure by contacting Intercept Pharmaceuticals at 1-844-782-4278.
  - The safety and efficacy of use in the pediatric population have not been established.

Conclusion

- Primary biliary cholangitis (PBC) is a chronic, autoimmune cholestatic condition. It is an antimitochondrial antibody-positive, disease of the liver that incurs gradual damage of intrahepatic bile ducts, chronic cholestasis, portal inflammation, and fibrosis that leads to cirrhosis and liver failure if not treated (*Tapper et al 2026*).
- Lynavoy is an IBAT inhibitor indicated for the treatment of cholestatic pruritus associated with primary biliary cholangitis (PBC) in adult patients.
  - A limitation of use includes to avoid use of Lynavoy in patients with decompensated cirrhosis or those with prior or active hepatic decompensation events (eg, variceal hemorrhage, ascites, hepatic encephalopathy).
- As liver test elevations were observed more commonly in Lynavoy-treated patients compared to placebo-treated patients, it is recommended to obtain baseline liver tests prior to starting treatment and monitor the levels per standard clinical practice for PBC patients during Lynavoy treatment.
- Lynavoy may adversely affect absorption of FSV.

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- Obtain serum FSV levels and INR prior to starting Lynavoy and monitor the levels periodically during treatment, along with any clinical manifestations of FSV deficiency. Supplement with FSV if FSV deficiency is diagnosed. Consider discontinuing Lynavoy if FSV deficiency persists or worsens despite adequate FSV supplementation.

- The efficacy of Lynavoy was assessed in a randomized, double-blind, placebo-controlled trial that included adults with a confirmed diagnosis of PBC and presence of pruritus at baseline.
  - Based on the primary endpoint of change from baseline in Monthly Itch Score over 24 weeks, patients who received Lynavoy demonstrated a greater improvement from baseline in pruritus compared with placebo over 24 weeks.
- Guidelines were published prior to Lynavoy being FDA approved; however, guidelines recommend a stepwise approach to managing pruritus. Recommended first-line treatment includes anion-exchange resins/cholestyramine. Note that Lynavoy is the first FDA-approved medication for cholestatic pruritus in patients with PBC.

- It is recommended that Lynavoy should be non-preferred in order to confirm the appropriate diagnosis and clinical parameters for use.

- **PDL Placement:**
  - ☐ Preferred
  - ☒ Non-Preferred

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