

DRUG POLICY

Lynavoy® (linerixibat)

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

FDA-Approved Indications

Lynavoy (linerixibat) is an ileal bile acid transporter (IBAT) inhibitor for the treatment of cholestatic pruritus associated with primary biliary cholangitis (PBC) in adult patients

Limitations of Use

Avoid use of Lynavoy in patients with decompensated cirrhosis or those with prior or active hepatic decompensation events.

POLICY

Lynavoy (linerixibat) is considered **not medically necessary** for all indications, including the treatment of cholestatic pruritus associated with primary biliary cholangitis (PBC) in adult patients, due to insufficient evidence to determine meaningful clinical improvement, lack of disease-modifying benefit, and considerable adverse-event burden.

CLINICAL RATIONALE

Lynavoy (linerixibat) is the first FDA-approved therapy specifically indicated for cholestatic pruritus associated with primary biliary cholangitis (PBC) in adults. Lynavoy is a reversible ileal bile acid transporter (IBAT) inhibitor that reduces reabsorption of bile acids in the terminal ileum, increasing fecal elimination and lowering circulating bile acid-related pruritogens. However, its mechanism is directed exclusively at

symptom relief, and there is no evidence that Lynavoy improves cholestatic liver injury, disease progression, transplant-free survival, or other clinically meaningful markers of PBC activity.

PBC is a rare, chronic, autoimmune cholestatic liver disease that predominantly affects women and is characterized by progressive destruction of intrahepatic bile ducts. Pruritus is a common manifestation, affecting approximately 20% to 70% of patients, with moderate-to-severe symptoms occurring in a substantial subset. Current American Association for the Study of Liver Diseases (AASLD) guidance recommends ursodeoxycholic acid (UDCA) as foundational disease-modifying therapy for PBC. For PBC-associated pruritus, guidelines recommend off-label bile acid sequestrants (i.e., cholestyramine, colestipol, colesevelam) as first-line symptomatic treatment, followed by rifampin, opioid antagonists such as naltrexone, or sertraline for refractory symptoms.

The approval of Lynavoy was based primarily on the phase 3 GLISTEN trial (N=238), a randomized, double-blind, placebo-controlled study in adults with moderate-to-severe PBC-associated pruritus. Lynavoy demonstrated statistical superiority to placebo for the primary endpoint, producing a placebo-adjusted improvement in monthly Worst Itch Numeric Rating Scale (WI-NRS) score of only -0.72 points at week 24 (-2.86 vs -2.15; $p=0.0013$). Improvement in sleep interference was similarly modest, with a placebo-adjusted benefit of -0.53 points ($p=0.024$). Importantly, study authors identified a 3-point WI-NRS reduction as clinically meaningful to patients; therefore, the observed treatment effect versus placebo fell substantially below this threshold despite statistical significance. Additionally, the proportion of patients achieving at least a 2-point WI-NRS improvement was not significantly different between groups.

Several limitations further reduce confidence in the clinical value of Lynavoy. The trial excluded patients with hepatic decompensation, limiting external validity in more advanced disease. Nearly half of enrolled patients were already receiving concomitant antipruritic therapy, potentially confounding interpretation of efficacy. Most importantly, Lynavoy demonstrated only symptomatic benefit and lacks evidence of disease modification, unlike therapies such as Livdelzi (seladelpar), which has demonstrated improvement in both cholestatic biomarkers and pruritus. No data currently support improvements in alkaline phosphatase, bilirubin, hepatic outcomes, transplantation risk, or survival with Lynavoy.

Safety is a significant concern. In GLISTEN, adverse events occurred in approximately 92% of Lynavoy-treated patients, and treatment discontinuations due to adverse events were nearly threefold higher than placebo (14% vs 5%). Diarrhea was the predominant toxicity, occurring in 61% to 62% of patients compared with 18% on placebo, with associated abdominal pain and gastrointestinal intolerance common. Lynavoy also carries warnings for liver test elevations and fat-soluble vitamin deficiencies requiring laboratory monitoring and supplementation. Increased alanine aminotransferase (ALT), aspartate aminotransferase (AST), bilirubin elevations, hemorrhage, and potential bone health concerns related to vitamin deficiency further complicated long-term use.

While Lynavoy achieved statistical significance in GLISTEN, the magnitude of benefit was small and of questionable clinical relevance. Lynavoy offers no demonstrated disease-modifying benefit, has a substantial adverse-event burden, and enters a treatment landscape where lower-cost guideline-recommended off-label alternatives (cholestyramine, colestipol, colesevelam, rifampin, naltrexone, sertraline) are already established.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

REFERENCES

Lynavoy [package insert]. Durham, NC: GlaxoSmithKline; March 2026.

Hirschfield GM, Bowlus CL, Jones DEJ, et al. Linerixibat in patients with primary biliary cholangitis and cholestatic pruritus (GLISTEN): a randomized, multicentre, double-blind, placebo-controlled, phase 3 trial. *The Lancet*. 2026;11(1):22-33. doi:10.1016/S2468-1253(25)00192-X

Lindor KD, Bowlus CL, Boyer J, Levy C, Mayo M. Primary biliary cholangitis: 2018 Practice Guidance from the American Association for the Study of Liver Diseases. *Hepatology*. 2019;69(1):394-419. doi:10.1002/hep.30145.

European Association for the Study of the Liver (EASL). EASL clinical practice guidelines: The diagnosis and management of patients with primary biliary cholangitis. *J Hepatol*. 2017;67(1):145-172. doi:10.1016/j.jhep.2017.03.022.

POLICY HISTORY

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