Selecting and Managing Second-line Treatment for PBC: Achieving Biochemical Disease Control and Symptom Relief



Elafibranor and Seladelpar Are Currently the Only Conditionally Approved PPAR Agonists for the Second-line Treatment of Adults with PBC with Inadequate Response to UDCA

- In practice, selection of PPAR agonists is influenced by insurance coverage and formulary access
- No clinical data to suggests superiority of one PPAR agonist over another

Monitor patients with cirrhosis for evidence of decompensation

Consider discontinuing if moderate or severe hepatic impairment

	Elafibranor	Seladelpar
MoA	Dual PPARα/δ	Selective PPARδ agonist
Dose	80 mg once daily	10 mg once daily
Efficacy (vs placebo)	■ 51% (vs 4%) biochemical response at week 52[a] ■ 15% (vs 0%) ALP normalization at week 52[b]	■ 61.7% (vs 20.0%) biochemical response at week 52[a] ■ 25% (vs 0%) ALP normalization at week 52[a]
Clinical considerations	Bone fracture (6% vs 0% in placebo)	Bone fracture risk (4% vs 0% in placebo)
	■ Risk of rhabdomyolysis/ myositis, monitor if on a concomitant statin ■ Interacts with hormonal contraception	Shown to be safe and effective in patients with PBC and compensated cirrhosis
	Some evidence for pruritus improvement	Some evidence for pruritus improvement
	Emerging evidence for fatigue improvement	
Common side effects	Weight gain, diarrhea, abdominal pain, nausea/vomiting, GERD	Headache, abdominal pain/ distension, nausea, diarrhea

[a] P<0.001. [b] P=0.002.
This table is not intended for cross-comparison between agents but rather to highlight key characteristics of each PPAR agonist.

Pruritus Management Options

In addition to evidence suggesting pruritus benefits of second-line treatment with PPAR agonists, additional therapies/interventions should be considered for targeted symptom management.

Traditional Treatments

- **Bile acid sequestrants** (e.g., cholestyramine)
- **Rifampin**
- **Opioid antagonists** (e.g., naltrexone, naloxone)
- **SSRIs**

Additional Strategies for Coping/ Managing PBC Pruritus

- ❑ UV light
- ❑ Moisturizers
- ❑ Shortened nails
- ❑ Topical cooling/anesthetic agents
- ❑ Fragrance free soaps
- ❑ Smooth, breathable clothing

New and Emerging Role for IBATis in Pruritus Management

- **MoA of IBATis**
  - ↓ Bile acids return to cholestatic liver
  - ↑ Excretion of bile acids
  - ↓ Hepatic bile acid accumulation
- Restricted to luminal intestine
  - Reduces systemic adverse effects

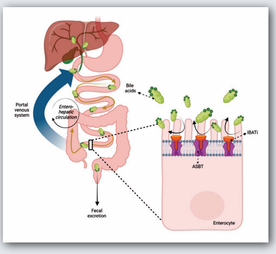
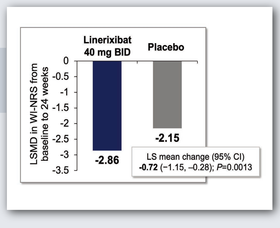


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- **Linerixibat:** first approved oral IBATi for PBC pruritus in March 2026
  - **Efficacy:** improvements in WI-NRS noted as early as 2 weeks after treatment
  - **Safety:** GI symptoms more common with linerixibat vs placebo
    - Diarrhea (61% vs 18%)
    - Abdominal pain (18% vs 3%)



ABBREVIATIONS

ALP: alkaline phosphatase
GERD: gastroesophageal reflux
GI: gastrointestinal
IBATi: ileal bile acid transporter inhibitor
LSMD: least-squares mean difference
MoA: mechanism of action
PBC: primary biliary cholangitis
PPAR: peroxisome proliferator-activated receptor
SSRI: selective serotonin reuptake inhibitor
UDCA: ursodeoxycholic acid
UV: ultraviolet
WI-NRS: Worst Itch Numeric Rating Scale

REFERENCES

Brunk D. FDA approves linerixibat for cholestatic pruritus in PBC. *GI & Hepatology News.* Published March 19, 2026. https://news.gastro.org/issues/2026/march/fda-approves-linerixibat-for-cholestatic-pruritus-in-pbc/. Accessed April 2026.

Düll MM, Kremer AE. Evaluation and management of pruritus in primary biliary cholangitis. *Clin Liver Dis.* 2022;26(4):727–745. doi:10.1016/j.cld.2022.06.009.

Efficacy and safety of seladelpar in patients with PBC and compensated cirrhosis in the phase 3 placebo-controlled RESPONSE trial. *Gastroenterol Hepatol (NY).* 2024;20(12 Suppl 12):2–3.

Elafibranor (package insert). Revised June 2024. U.S. Food and Drug Administration website. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/218860s000lbl.pdf. Accessed April 2026.

European Association for the Study of the Liver. 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.

Hirschfield GM, Bowlus CL, Jones DEJ, et al. Linerixibat in patients with primary biliary cholangitis and cholestatic pruritus (GLISTEN): a randomised, multicentre, double-blind, placebo-controlled, phase 3 trial [published correction appears in: *Lancet Gastroenterol Hepatol.* 2026;11(4):e6]. *Lancet Gastroenterol Hepatol.* 2026;11(1):22–33. doi:10.1016/S2468-1253(25)00192-X.

Hirschfield GM, Bowlus CL, Mayo MJ, et al. A phase 3 trial of seladelpar in primary biliary cholangitis. *N Engl J Med.* 2024;390(9):783–794. doi:10.1056/NEJMoa2312100.

Hirschfield GM, Kremer AE, Leby C, et al. Sustained and clinically meaningful improvements in moderate to severe pruritus patients with PBC treated with seladelpar: results from the ASSURE study up to 30 months. Abstract 5015. Presented at: American Association for the Study of Liver Diseases, The Liver Meeting 2025; November 7–11, 2025; Washington, DC.

Kowdley KV, Bowlus CL, Levy C, et al. Efficacy and safety of elafibranor in primary biliary cholangitis. *N Engl J Med.* 2024;390(9):795–805. doi:10.1056/NEJMoa2306185.

Kremer AE, Kowdley KV, Levy C, et al. LPB-028 Effect of elafibranor on pruritus in primary biliary cholangitis: symptom severity and quality of life measurements from the phase III ELATIVE trial. *J Hepatol.* 2024;80:S91–S92.

Long-term treatment with elafibranor leads to biochemical and symptomatic improvements for at least 3 years in patients with PBC. *Gastroenterol Hepatol (NY).* 2025;21(12 Suppl 10):3–4.

Martins A, Levy C. Ileal bile acid transport inhibitors for cholestatic pruritus: a primer. *Curr Hepatol Rep.* 2025;24:28.

Pate J, Gutierrez JA, Frenette CT, et al. Practical strategies for pruritus management in the obeticholic acid-treated patient with PBC: proceedings from the 2018 expert panel. *BMJ Open Gastroenterol.* 2019;6(1):e000256. doi:10.1136/bmjgast-2018-000256.

Seladelpar (package insert). Revised January 2026. U.S. Food and Drug Administration website. https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/217899s002lbl.pdf. Accessed April 2026.

Trauner M, Karpen SJ, Dawson PA. Benefits and challenges to therapeutic targeting of bile acid circulation in cholestatic liver disease. *Hepatology.* 2025;82(4):855–876. doi:10.1097/HEP.0000000000001438.