

STEPS

New Drug Reviews

Tenapanor (Ibsrela) for the Treatment of Irritable Bowel Syndrome With Constipation

Seth Curtis, MD, MPH, and Megan Curtis, MD, Reliant Medical Group, Worcester, Massachusetts

Tenapanor (Ibsrela) is labeled for the treatment of irritable bowel syndrome with constipation (IBS-C) in adults.¹ It is a sodium/hydrogen exchanger 3 inhibitor that acts on the surface of the small intestine and colon to block the absorption of dietary sodium, resulting in increased water secretion. This leads to more frequent and softer bowel movements. Tenapanor also decreases visceral hypersensitivity, leading to reduced abdominal pain.

Safety

In two randomized, double-blind, placebo-controlled trials involving 1,199 adult patients, the most concerning adverse effect was severe diarrhea, which occurred in approximately 2.5% of patients taking tenapanor, compared with 0.2% of those taking placebo.¹⁻³ Treatment with tenapanor should be discontinued if severe diarrhea occurs, and the patient should promptly rehydrate. Tenapanor should not be used in patients with suspected mechanical bowel obstruction. No adverse fetal effects have been reported in animal studies. The use of tenapanor by a small number of pregnant patients has not identified any major birth defects, miscarriages, or adverse maternal or fetal outcomes. Tenapanor should not be used in children.¹

Tolerability

The most common adverse effect with tenapanor is diarrhea (16% vs. 4% with placebo; number needed to harm = 9). Other adverse effects such

Drug	Dosage	Dose form	Cost of full course
Tenapanor (Ibsrela)	50 mg twice daily, taken immediately before first meal of the day and before dinner	50-mg tablets	Price not yet available

as flatulence, abdominal distention, and dizziness occurred in 2% to 3% of patients who received tenapanor vs. 1% who received placebo. Approximately 6% to 7% of patients will discontinue tenapanor because of adverse effects.²

Effectiveness

Tenapanor was evaluated in two randomized, double-blind, placebo-controlled studies involving a total of 1,199 patients who had irritable bowel syndrome (based on the ROME III criteria) with the IBS-C subtype (based on a mean abdominal pain score of at least 3 out of 10, fewer than five spontaneous bowel movements per week, and fewer than three complete spontaneous bowel movements per week). Each study evaluated the response to treatment over 12 weeks, with one study following patients for an additional 14 weeks. Clinical improvement, defined as at least a 30% reduction in abdominal pain and at least one additional complete spontaneous bowel movement per week for at least six out of 12 weeks, occurred in 27% to 37% of patients receiving tenapanor and 19% to 24% of those receiving placebo (number needed to treat = 8 to 12; 95% CI, 5 to 50).^{2,3}

No studies have directly compared tenapanor to other treatments for IBS-C. However, studies of other IBS-C medications followed a similar design and measured the same end points as the tenapanor studies (number needed to treat = 5 to 8 for linaclotide [Linzess]; 8 to 14 for plecanatide [Trulance]; and 13 for lubiprostone [Amitiza]).⁴⁻⁷

STEPS new drug reviews cover Safety, Tolerability, Effectiveness, Price, and Simplicity. Each independent review is provided by authors who have no financial association with the drug manufacturer.

This series is coordinated by Allen F. Shaughnessy, PharmD, assistant medical editor.

A collection of STEPS published in *AFP* is available at <https://www.aafp.org/afp/steps>.

Author disclosure: No relevant financial relationships.

Over-the-counter treatments such as psyllium (Metamucil) and polyethylene glycol (Miralax) have been shown to improve bowel movement frequency and consistency but not pain or bloating.^{8,9}

Price

Although tenapanor has been approved by the U.S. Food and Drug Administration, it is not yet available in pharmacies and prices are unknown. Linaclotide and plecanatide are approximately \$490 and \$550 per month, respectively. Lubiprostone is less expensive, costing about \$200 for a 30-day supply.

Simplicity

The recommended dosage of tenapanor is 50 mg twice daily, taken five to 10 minutes before the first meal of the day and again before dinner; missed doses should not be replaced. There are no dosing adjustments for effectiveness or patient characteristics, such as age or renal/hepatic function.¹

Bottom Line

Tenapanor provides a modest improvement in IBS-C symptoms in adults, although diarrhea will limit its use for some patients. It may be considered for patients who do not adequately respond to dietary changes and nonprescription treatments. Tenapanor performed similarly to other prescription IBS-C medications in individual clinical trials; however, direct comparison studies are still needed to make more accurate comparisons.

Address correspondence to Seth Curtis, MD, MPH, at seth.curtis@reliantmedicalgroup.org. Reprints are not available from the authors.

References

1. DailyMed. Drug label information. Ibsrela—tenapanor hydrochloride tablet. Accessed February 22, 2021. <https://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=2102da5f-a1a0-4ac7-a1f6-38698cf7273a>
2. Chey WD, Lembo AJ, Yang Y, et al. Efficacy of tenapanor in treating patients with irritable bowel syndrome with constipation: a 26-week, placebo-controlled phase 3 trial (T3MPO-2). *Am J Gastroenterol*. 2021;116(6):1294-1303.
3. Chey WD, Lembo AJ, Rosenbaum DP. Efficacy of tenapanor in treating patients with irritable bowel syndrome with constipation: a 12-week, placebo-controlled phase 3 trial (T3MPO-1). *Am J Gastroenterol*. 2020;115(2):281-293.
4. Chey WD, Lembo AJ, Lavins BJ, et al. Linaclotide for irritable bowel syndrome with constipation: a 26-week, randomized, double-blind, placebo-controlled trial to evaluate efficacy and safety. *Am J Gastroenterol*. 2012;107(11):1702-1712.
5. Rao S, Lembo AJ, Shiff SJ, et al. A 12-week, randomized, controlled trial with a 4-week randomized withdrawal period to evaluate the efficacy and safety of linaclotide in irritable bowel syndrome with constipation. *Am J Gastroenterol*. 2012;107(11):1714-1724.
6. Brenner DM, Fogel R, Dorn SD, et al. Efficacy, safety, and tolerability of plecanatide in patients with irritable bowel syndrome with constipation: results of two phase 3 randomized clinical trials. *Am J Gastroenterol*. 2018;113(5):735-745.
7. Drossman DA, Chey WD, Johanson JF, et al. Clinical trial: lubiprostone in patients with constipation-associated irritable bowel syndrome—results of two randomized, placebo-controlled studies. *Aliment Pharmacol Ther*. 2009;29(3):329-341.
8. Moayyedi P, Quigley EMM, Lacy BE, et al. The effect of fiber supplementation on irritable bowel syndrome: a systematic review and meta-analysis. *Am J Gastroenterol*. 2014;109(9):1367-1374.
9. Chapman RW, Stanghellini V, Geraint M, et al. Randomized clinical trial: macrogol/PEG 3350 plus electrolytes for treatment of patients with constipation associated with irritable bowel syndrome. *Am J Gastroenterol*. 2013;108(9):1508-1515. ■