

Policy Type: PA/SP

Pharmacy Coverage Policy: EOCCO170

Description

Tenapanor (Ibsrela) is an orally administered sodium/hydrogen exchange 3 (NHE3) inhibitor.

Length of Authorization

- Initial: Three months
- Renewal: 12 months

Quantity limits

Product Name	Dosage Form	Indication	Quantity Limit
tenapanor (Ibsrela)	50 mg tablets	Irritable bowel syndrome with constipation (IBS-C)	60 tablets/30 days

Initial Evaluation

- I. **Tenapanor (Ibsrela)** may be considered medically necessary when the following criteria below are met:
 - A. The member is 18 years of age or older; **AND**
 - B. The medication is prescribed by, or in consultation with, a gastroenterologist; **AND**
 - C. A diagnosis of **irritable bowel syndrome with constipation (IBS-C)** when the following are met:
 1. The member has had an inadequate response, or intolerance to, ALL of the following, unless all are contraindicated (*Please note: These agents may be subject to additional prior authorization review):
 - i. Dietary and lifestyle modifications (e.g., removal of offending foods, increased fiber intake) and increased physical activity; **AND**
 - ii. At least one osmotic laxative (e.g., polyethylene glycol); **AND**
 - iii. plecanatide (Trulance); **AND**
 - iv. linaclotide (Linzess)*; **AND**
 - v. lubiprostone (Amitiza)*
- II. Tenapanor (Ibsrela) is considered investigational when used for all other conditions, including but not limited to:
 - A. Hyperphosphatemia
 - B. Chronic kidney disease
 - C. Irritable bowel syndrome with diarrhea
 - D. Mixed irritable bowel syndrome

- E. Chronic idiopathic constipation
- F. Opioid-induced constipation

Renewal Evaluation

- I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
- II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
- III. The member has exhibited response to the treatment (e.g., improvement in complete spontaneous bowel movements per week from baseline, reduction in abdominal pain)

Supporting Evidence

- I. Tenapanor (Ibsrela) is approved by the US Food and Drug Administration (US-FDA) for the treatment of irritable bowel syndrome with constipation (IBS-C) in adults.
- II. Given the complexities involved in diagnosis and management of IBS-C, as well as required monitoring for adverse events and therapy response, therapy decisions regarding initiation of tenapanor (Ibsrela) must be made by, or under the supervision of, a specialist practicing in this setting (e.g., gastroenterologist).
- III. Tenapanor (Ibsrela) is a sodium/hydrogen exchange 3 (NHE3) inhibitor acting specifically in the GI tract, with minimal systemic availability following oral administration. Inhibition of NHE3 leads to a reduction in dietary sodium absorption and an increase in intracellular protons across membranes in the GI tract, which results in reduction of phosphate absorption from the small intestine and colon. Additionally, consequent increase in sodium and phosphorus content in the stool, decreased urinary sodium and phosphorus excretion, and increased water secretion into the intestinal lumen and the increased stool water content leads to loosened stool consistency and increased bowel movement frequency.
- IV. Tenapanor (Ibsrela) has a Black Box Warning for serious dehydration in pediatric patients and has not been evaluated in any pediatric population to date. It is contraindicated in those less than six years of age and comes with a recommendation to avoid use in those less than 12 years of age due to animal studies showing cause of death to be dehydration in young juvenile rats. Additionally, tenapanor (Ibsrela) is also contraindicated in patients with known or suspected mechanical gastrointestinal obstruction.
- V. Tenapanor (Ibsrela) was evaluated in two double-blind, placebo-controlled, randomized trials in adult patients –T3MPO-2 and T3MPO-1. The majority of subjects were female (83%), white, and all met Rome III criteria for IBS-C. This requires a pain score of at least three on a 0-10 scale, less than three complete spontaneous bowel movements (CSBMs) per week, and less than five spontaneous bowel movements (SBMs) per week.

- The primary outcome was proportion of responders, defined as achieving both of the following for at least six of the first 12 weeks of the trials: an increase of at least one CSBM per week on average and a reduction of 30% in weekly average abdominal pain score compared to baseline.
 - T3MPO-2: 620 subjects were evaluated for 26 weeks of treatment. Responders active vs. placebo: 37% vs. 24% (CI 6-20%). Difference from placebo 13%.
 - T3MPO-1: 606 subjects were evaluated for 12 weeks and then were re-randomized to active drug or placebo for a 4-week withdrawal period. Responders active vs. placebo: 27% vs. 19% (CI: 2-15%). Difference from placebo 8%.
- VI. The quality of the evidence is considered low given the invalidated subjective endpoints used to determine efficacy and the short duration of therapy evaluated for safety and efficacy.
- VII. First-line treatment options for the treatment of IBS-C include dietary modifications, increased fiber intake, and physical activity. Adjunctive pharmacotherapy includes over-the-counter osmotic laxatives. When lifestyle modifications and osmotic laxatives fail to produce sufficient relief of constipation, further pharmacological interventions are indicated. The 2021 American College of Gastroenterology (ACG) clinical guidelines for management of IBS-C recommend use of guanylate cyclase activators (e.g., linaclotide [Linzess], plecanatide [Trulance]) and chloride channel activator (e.g., lubiprostone [Amitiza]) as recommended therapeutic options based on high and moderate quality of clinical evidence, respectively. As of March 2022, the ACG guidelines do not include tenapanor (Ibsrela) as a recommended agent for the treatment of IBS-C. Based on the clinical evidence showing limited treatment effect and lack of place in therapy information, usability of tenapanor (Ibsrela) is uncertain at this time. Thus, use of non-pharmacologic agents and other established therapies are warranted prior to payment consideration for tenapanor (Ibsrela).

Investigational or Not Medically Necessary Uses

- I. Safety and efficacy have not yet been sufficiently established and/or clinical trials are currently underway for the following indications:
- A. Hyperphosphatemia
 - B. Chronic kidney disease
 - i. Tenapanor (Ibsrela) was evaluated for the treatment of hyperphosphatemia associated with chronic kidney disease (CKD). On July 29, 2021, the US-FDA issued a complete response letter (CRL) regarding the New Drug Application (NDA) for tenapanor for the control of serum phosphorus levels in patients with CKD on dialysis. In the CRL, while the FDA agreed that “the submitted data provide substantial evidence that tenapanor is effective in reducing serum phosphorus in CKD patients on dialysis,” the agency found the treatment effect was “small and of unclear significance.” Additionally, the FDA indicated to the need to “conduct an additional adequate and well-controlled trial demonstrating a clinically

relevant treatment effect on serum phosphorous or an effect on the clinical outcome thought to be caused by hyperphosphatemia in CKD patients on dialysis”. It is unclear if or when the US-FDA approval for tenapanor (Ibsrela) may be granted for this indication.

- II. Tenapanor (Ibsrela) has not been evaluated and/ or approved for the treatment of following indications:
- A. Irritable bowel syndrome with diarrhea
 - B. Mixed irritable bowel syndrome
 - C. Chronic idiopathic constipation
 - D. Opioid-induced constipation

References

1. Ibsrela [Prescribing Information]. Ardelyx, Inc. Fremont, CA. 2019.
2. Zelnorm [Prescribing Information]. Sloan Pharma/WorldMeds LLC. Louisville, KY. 2019.
3. Moayyedi P, Mearin F, Azpiroz F, et al. Irritable bowel syndrome diagnosis and management: A simplified algorithm for clinical practice. United European Gastroenterol J. 2017;5(6):773-788.
4. 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 Feb;115(2):281-293.
5. Chey WD, Lembo AJ, Yang Y, Rosenbaum DP. 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 Jun 1;116(6):1294-1303.
6. Weinberg D.S., Smalley W. Heidelbaugh J.J., et al. American Gastroenterological Association institute guidelines on the pharmacological management of irritable bowel syndrome. Gastroenterology. 2014;144: 1146-1148.
7. Lacy BE, Pimentel M, Brenner DM, Chey WD, Keefer LA, Long MD, Moshiree B. ACG Clinical Guideline: Management of Irritable Bowel Syndrome. Am J Gastroenterol. 2021 Jan 1;116(1):17-44.

Related Policies

Policies listed below may be related to the current policy. Related policies are identified based on similar indications, similar mechanisms of action, and/or if a drug in this policy is also referenced in the related policy.

Policy Name	Disease state
tegaserod (Zelnorm) Policy	Irritable bowel syndrome with constipation (IBS-C)
Opioid-Induced Constipation Policy	Opioid-induced constipation

Policy Implementation/Update:

Action and Summary of Changes	Date
Policy updated to include pre-requisites of trial of current formulary and preferred agents; removed criteria requiring documentation of pain scores and stool frequency; updated supporting evidence	03/2022
Policy created	02/2020