Irritable Bowel Syndrome (IBS) Drug Comparison

The chart below compares drugs approved for irritable bowel syndrome (IBS). Treatment is determined by the predominant symptom, **constipation (IBS-C)** or **diarrhea (IBS-D)**, and symptom severity.[6,11] It is generally okay to hold these IBS meds on hospital admission if not on formulary. See our chart, *Irritable Bowel Syndrome FAQs*, for more about managing IBS including use of other symptomatic treatments (e.g., laxatives, antidiarrheals, antispasmodics) and the role of fiber and probiotics.

--Information in the chart below is from product labeling unless otherwise noted.--

Medication	MOA/Adult Dosing/ Effectiveness[a]	Adverse Effects[a]	Other Considerations[a]
FDA- and/or Health Canada-Approved Medications for IBS-C			
Linaclotide • U.S.: *Linzess* • Canada: *Constella*	• **MOA**: guanylate cyclase-c agonist. Also known as a secretagogue.[11] • 290 mcg PO once daily (at least 30 minutes before the first meal of the day)[b,j] • Improves global symptoms (e.g., abdominal pain, stool consistency, IBS quality of life) more than placebo (NNT ~8) [Evidence Level A-2].[1,3,6]	• Adverse effects (≥2% of patients): o abdominal pain and distension o flatulence o diarrhea ▪ If severe diarrhea occurs, patients should hold linaclotide and rehydrate.	• Recommended treatment option for IBS.[6,11] • FDA- and Health Canada-approved for use in **ADULTS** with IBS-C. • Avoid in patients between 6 and 18 years old. • **Contraindicated** in: o children younger than six years old (due to risk of dehydration). o patients with known or suspected mechanical GI obstruction. • No known drug interactions.
Lubiprostone U.S.: *Amitiza*; generics Cancelled before marketing in Canada.	• **MOA**: chloride channel activator. Referred to as a secretagogue.[11] • 8 mcg PO BID[b] (with food and water) • Improves global symptoms (e.g., abdominal pain, stool consistency, IBS quality of life) more than placebo (NNT ~13) [Evidence Level A-2].[1,4,7]	• Adverse effects (>4% of patients): o abdominal pain o nausea (taking with food may reduce nausea) o diarrhea ▪ If severe diarrhea occurs, patients should hold lubiprostone and contact their prescriber.	• Recommended[11] treatment option for IBS (suggested[6] treatment option in Canadian guidelines [though currently not available]). • FDA-approved in **adult females** with IBS-C. In Canada, *Amitiza* was only approved for the treatment of chronic idiopathic constipation. • **Contraindicated** in patients with known or suspected mechanical GI obstruction. • Effectiveness may be reduced in patients also taking methadone.

Medication	MOA/Adult Dosing/ Effectiveness[a]	Adverse Effects[a]	Other Considerations[a]
FDA- and/or Health Canada-Approved Medications for IBS-C, continued			
Plecanatide *Trulance* • U.S.: • Canada:	• **MOA**: guanylate cyclase-c agonist. Referred to as a secretagogue.[11] • 3 mg PO once daily (with or without food)[b,j] • Reduces abdominal pain and improves constipation more than placebo over 12 weeks (NNT ~10) [Evidence Level A-1].[9]	• Adverse effect (≥2% of patients) is diarrhea. o If severe diarrhea occurs, patients should hold plecanatide and rehydrate.	• Recommended treatment option in U.S. IBS guidelines.[11,e] • FDA- and Health Canada-approved for use in **ADULTS** with IBS-C. • **Contraindicated** in patients with known or suspected mechanical GI obstruction, as well as children younger than six years. • No known drug interactions. • If doses are missed, do NOT double up. Restart when able, at next scheduled dose.
Tegaserod U.S.: *Zelnorm*	• **MOA**: serotonin-type-4 (5-HT_4) agonist. • 6 mg PO BID (at least 30 minutes before meals) • Discontinue in patients who do NOT achieve adequate symptom control after four to six weeks of therapy. • Reduces abdominal pain and improves constipation more than placebo (NNT ~17) [Evidence Level B-2].[10,13,14]	• Adverse effects (≥2% of patients): o headache o abdominal pain/dyspepsia o nausea o diarrhea ▪ If severe diarrhea occurs, hold tegaserod and contact prescriber o flatulence o dizziness • There are reports of: o CV ischemic events[c] o ischemic colitis o suicidal ideation and behavior[d]	• Recommended treatment option in females <65 years with ≤1 CV risk factor who have not responded to a secretogogue (e.g., linaclotide, lubiprostone, plecanatide) in IBS guidelines.[11] • FDA-approved for use in **adult females <65 years old** with IBS-C. • **Contraindicated** in patients with a history of: o myocardial infarction, stroke, transient ischemic attack, or angina. o ischemic colitis or other intestinal ischemia. o bowel obstruction, symptomatic gallbladder disease, suspected sphincter of Oddi dysfunction, or abdominal adhesions. **OR** o with severe kidney disease (eGFR <15 mL/min/1.73 m^2) or end-stage kidney disease. o with moderate or severe liver disease (Child-Pugh Class B or C). • Coadministration with p-glycoprotein inhibitors may increase tegaserod levels, but the clinical significance of this is unknown.

Medication	MOA/Adult Dosing/ Effectiveness[a]	Adverse Effects[a]	Other Considerations[a]
FDA- and/or Health Canada-Approved Medications for IBS-C, continued			
Tenapanor *Ibsrela* • Canada	• **MOA**: locally acting sodium/hydrogen exchanger 3 (NHE3) inhibitor. • 50 mg PO BID[b] (immediately before breakfast and the evening meal) • Reduces abdominal pain and improves stool frequency more than placebo over 12 weeks (NNT ~12) [Evidence Level A-1].[12]	• Adverse effects (≥2% of patients): o abdominal distension o flatulence o dizziness o diarrhea ▪ If severe diarrhea occurs, patients should hold tenapanor and rehydrate.	• Health Canada-approved for use in **ADULTS** with IBS-C.[e] Though previously approved by the FDA, the U.S. manufacturer is not planning to market tenapanor for IBS-C in the U.S.[15] • Avoid in patients between the ages of six and 18 years. • **Contraindicated** in: o children younger than six years old. o patients with known or suspected mechanical GI obstruction. • If doses are missed, do NOT double up. Restart when able, at next scheduled dose.
FDA- and/or Health Canada-Approved Medications for IBS-D			
Alosetron U.S.: *Lotronex*, generics (1 mg BID:	• **MOA**: selective serotonin type-3 ($5\text{-}HT_3$) antagonist • Start with 0.5 mg PO BID. May increase to 1 mg PO BID after four weeks if well tolerated for additional symptom control. • Improves pain and global symptoms (e.g., abdominal pain, stool consistency, IBS quality of life); NNT ~8 [Evidence Level B-2].[1,4,5]	• Adverse effects (≥2% of patients): o abdominal discomfort or pain o nausea o constipation (If constipation or symptoms of ischemic colitis [e.g., pain, tenderness, cramping] develop, patients should hold alosetron and contact their prescriber.) Do NOT restart after ischemic colitis.	• Recommended in IBS guidelines and FDA-approved **for use in adult females** with severe, chronic IBS-D who have failed conventional therapy.[11,g] • **Contraindicated** in patients with: o constipation. o history of GI conditions (e.g., obstruction, Crohn's disease, ulcerative colitis). **See product labeling for complete list.** o severe liver disease (use with caution in mild or moderate liver disease). o concomitant use of fluvoxamine.

Medication	MOA/Adult Dosing/ Effectiveness[a]	Adverse Effects[a]	Other Considerations[a]
FDA- and/or Health Canada-Approved Medications for IBS-D, continued			
Eluxadoline *Viberzi* 100 mg BID • U.S.: • Canada: Class IV (C-IV) controlled substance (U.S.)	• **MOA**: dual mechanism (peripherally acting mu- and kappa-opioid agonist and delta-opioid antagonist). • 100 mg PO BID (with food) • 75 mg BID (with food) in patients: o with mild to moderate liver disease (contraindicated at all levels of liver disease [Canada]). o with moderate or severe kidney disease (eGFR <60 mL/min/m^2) or end-stage kidney disease not on dialysis (eGFR <15 mL/min/m^2). o taking an OATP1B1 inhibitor[h] (contraindicated [Canada]). o unable to tolerate 100 mg dosing o consider in elderly patients (U.S.). In Canada, start patients 65 years and older on 75 mg BID, increasing if tolerated and increased efficacy needed. • Improves abdominal pain and loose stools (100 mg BID over about six months [NNT ~8]) [Evidence Level B-2].[2,4,5] o Improves loose stool more effectively than abdominal pain.	• Adverse effects (≥2% of patients): o abdominal pain o nausea o constipation ▪ If severe constipation occurs, patients should hold eluxadoline and contact their prescriber.	• Suggested treatment option in IBS guidelines.[6,11] • FDA- and Health Canada-approved for use in **ADULTS** with IBS-D. • **Contraindicated** in patients with: o alcoholism or daily intake of more than three alcoholic beverages. o biliary duct obstruction. o history of chronic or severe constipation, or GI obstruction. o history of pancreatitis or pancreatic obstruction. o no gallbladder. o severe liver disease (Child-Pugh Class C [U.S.]; Child-Pugh Class A, B, or C [Canada]). o sphincter of Oddi dysfunction. o taking an OATP1B1 inhibitor[h] (Canada only). • Avoid concomitant use of meds that can cause constipation (e.g., opioids, anticholinergics, alosetron). Loperamide may be used occasionally for severe acute diarrhea, but chronic use should be avoided. • If coadministered with rosuvastatin, use the lowest effective rosuvastatin dose, as eluxadoline can increase rosuvastatin levels increasing the risk of myopathy. • If doses are missed, do NOT double up. Restart when able, at next scheduled dose.

Medication	MOA/Adult Dosing/ Effectiveness[a]	Adverse Effects[a]	Other Considerations[a]
FDA- and/or Health Canada-Approved Medications for IBS-D, continued			
Rifaximin Cost/14-day course: • U.S.: *Xifaxan* • Canada: *Zaxine*	• **MOA**: changes GI tract microbiome.[11] • 550 mg PO TID[b] for 14 days o Can be repeated up to a total of three 14-day courses. • Improves global symptoms (e.g., abdominal pain, stool consistency, IBS quality of life) and reduces bloating (NNT ~10) [Evidence Level B-2].[1,4,5]	• Adverse effects (≥2% of patients): o nausea o increased alanine transaminate (ALT) • Can cause tears, sweat, and urine to be a reddish color.	• Recommended treatment option in IBS guidelines.[11,f] • FDA- and Health Canada-approved for use in **ADULTS** with IBS-D. • Over half of patients who respond will relapse within six months.[8] • **Contraindicated** in patients who are allergic to any of the rifamycin antimicrobials (e.g., rifampin) • Interacts with warfarin. Monitor INR and adjust warfarin doses to maintain target INR.

Abbreviations: ACG = American College of Gastroenterology; BID = twice daily; CV = cardiovascular; eGFR = estimated glomerular filtration rate; GI = gastrointestinal; IBS = irritable bowel syndrome; IBS-C = constipation-dominant IBS; IBS-D = diarrhea-dominant IBS; INR = international normalized ratio; NNT = number needed to treat; OATP1B1 = organic anion transporting polypeptide 1B1; PO = orally; TID = three times daily

a. **U.S. product labeling** used in the above chart: *Linzess* (September 2020); *Amitiza* (November 2020); *Trulance* (October 2020); *Zelnorm* (June 2020); *Ibsrela* (April 2020); *Lotronex* (July 2016); *Viberzi* (June 2020); *Xifaxan* (October 2020). **Canadian product labeling** used in the above chart: *Constella* (August 2018); *Trulance* (March 2021); *Ibsrela* (April 2020); *Viberzi* (April 2019); *Zaxine* (February 2019).
b. Tablets/capsules should be swallowed whole.[a]
c. All CV events were in patients with a history of CV ischemic disease and/or more than one CV risk factor.[a]
d. Risk may be increased in the first few months of treatment and in patients taking an antidepressant. Monitor patients for worsening depression and suicidal thoughts or behavior.[a]
e. Not included in current IBS guidelines (Canadian [plecanatide]; U.S. and Canadian [tenapanor]), due to timing of guideline publication and drug approval.
f. No recommendation for or against made in current Canadian guidelines.[6]
g. Restricted-access drug due to severe GI adverse effects (e.g., ischemic colitis). More information available at https://www.lotronex.com/PrescribingProgramForLotronex.aspx.
h. Examples of some OATP1B1 inhibitors include cyclosporine, gemfibrozil, and rifampin.
i. Pricing, for generic when available, based on wholesale acquisition cost (WAC). U.S. medication pricing by Elsevier, accessed February 2021.
j. Crush only if necessary and give immediately in applesauce or water (can give via nasogastric tube). See product labeling for specific instructions.[a]

Levels of Evidence

In accordance with our goal of providing Evidence-Based information, we are citing the **LEVEL OF EVIDENCE** for the clinical recommendations we publish.

Level	Definition	Study Quality
A	Good-quality patient-oriented evidence.*	1. High-quality randomized controlled trial (RCT) 2. Systematic review (SR)/Meta-analysis of RCTs with consistent findings 3. All-or-none study
B	Inconsistent or limited-quality patient-oriented evidence.*	1. Lower-quality RCT 2. SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings 3. Cohort study 4. Case control study
C	Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening.	

***Outcomes that matter to patients** (e.g., morbidity, mortality, symptom improvement, quality of life).

[Adapted from Ebell MH, Siwek J, Weiss BD, et al. Strength of Recommendation Taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. *Am Fam Physician* 2004;69:548-56. http://www.aafp.org/afp/2004/0201/p548.pdf.]

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