



Indian Health Service

National Pharmacy and Therapeutics Committee

Formulary Brief: Chronic Constipation Treatment

-November 2025-



Background:

The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) reviewed chronic constipation and available treatment options. This is the first NPTC review of chronic constipation, though in May 2018, Irritable Bowel Syndrome (IBS) was reviewed and dicyclomine, loperamide, and polyethylene glycol (PEG) were added to the National Core Formulary (NCF). Following this comprehensive clinical review, the NPTC voted to add (1) **any sennoside -or- bisacodyl product**, (2) **any psyllium product**, and (3) **lubiprostone** to the NCF.

Constipation is defined as stool frequency of less than three bowel movements per week which may be associated with difficulty passing stools, hard stools, feeling of incomplete evacuations, straining, or painful bowel movements.^{1,2} Chronic constipation occurs when symptoms are present for at least six months and is classified into primary and secondary types.^{1,4,19} Constipation-predominant IBS (IBS-C) and Chronic Idiopathic Constipation (CIC) are primary constipation subtypes classified as functional gastrointestinal disorders whose etiology is unclear. Although symptoms of abdominal pain or bloating may be seen in both IBS-C and CIC, the predominant symptom of pain distinguishes IBS-C from CIC.⁶ The underlying etiology of secondary constipation is disease or medication use such as opioids [e.g., opioid-induced constipation (OIC)].^{1,2,5} The standard for diagnosing bowel disorders are the Rome I-IV criteria, of which the Rome IV criteria is the most current.⁷

Discussion:

Preliminary evaluation of constipation involves ruling out underlying biological conditions requiring immediate attention (i.e. colorectal cancer, inflammatory bowel disease).⁸ Initial management of constipation involves optimizing diet and lifestyle factors such as ensuring adequate dietary fiber intake (20-35 grams) and hydration (at least 1.5 Liters of water daily), regular physical aerobic activity (at least 140 minutes per week), defecation posture modification with use of a squat assist device if needed.⁸ The squat posture relaxes the puborectalis muscle contributing to defecation. Fiber intake should be taken with an adequate amount of fluids and gradually increased in order to decrease bloating.

Pharmacologic management includes over-the-counter (OTC) and prescription medications. OTC treatments such as bulk forming laxatives (psyllium), osmotic laxatives (PEG, lactulose, magnesium sulfate, magnesium citrate and magnesium hydroxide) and stimulant laxatives (bisacodyl, senna) are considered first line.³⁻⁵ Docusate calcium and docusate sodium, an OTC stool softener or surfactant agent, is considered less effective than other OTC agents and should not be used as monotherapy.^{9,10} More current studies show docusate is no different than placebo in increasing bowel movements.^{9,10}

According to the [American Academy of Family Physicians](#), first-line treatment for pediatric management of CIC is PEG. Second-line considerations include lactulose, milk of magnesia, stimulants (bisacodyl, senna) or mineral oil.¹² A Cochrane review of 25 randomized controlled trials (RCTs) of pediatric patients ages 0 months to 18 years-old with chronic constipation, showed that PEG was associated with greater number of stools per week compared to lactulose (Mean Difference [MD]: 0.70, 95% CI: 0.10 to 1.31, $I^2=69\%$).¹² PEG was also associated with greater number of stools per week compared to milk of magnesia [MD 0.69 stools, 95% CI: 0.48 to 0.89, $I^2=0\%$].¹² Bowel retraining should be considered in conjunction with maintenance laxative use in order to encourage positive association with bowel movements and prevent stool leakage or fecal incontinence.

Prescription laxatives are second line for CIC in adults and include secretagogues (linaclotide, plecanatide, and lubiprostone), 5-HT₄ agonist (prucalopride) and sodium/hydrogen exchanger inhibitor (tenapanor). For OIC, peripherally acting mu-opioid receptor antagonists (PAMORA) are second line and include naldemedine, naloxegol, and methylnaltrexone.

Guidelines recommend dietary fiber (psyllium preferred) as first line for CIC in patients who have low fiber intake, normal colonic transit times, and can maintain adequate hydration.³⁻⁵ However, patients with slow colonic transit or outlet obstruction may not benefit.^{1,2,8} If there is an inadequate response with trial of fiber, PEG is strongly recommended next as it is better tolerated than lactulose and is safe for chronic use with a durable response of over 6 months.³⁻⁵ However, lactulose may be considered an alternative to PEG if it is not tolerated. Magnesium-based laxatives are considered second-line and should be avoided in those with renal impairment due to risk of hypermagnesemia.³ Stimulant laxatives (senna, bisacodyl) may be considered for as needed rescue therapy or as a short-term add on (< 4 weeks) as they have a rapid effect, but long-term daily use can cause possible tolerance and abdominal cramping.³

There is moderate certainty of evidence for the use of lubiprostone, linaclotide and plecanatide for CIC treatment.³⁻⁵ Plecanatide is considered an alternative to linaclotide and may be particularly useful if bloating/pain is present.³ In a 2024 systematic review and meta-analysis of 24 studies of adults with chronic constipation, linaclotide and lubiprostone showed similar efficacy profiles. There was a significant mean change from baseline in spontaneous bowel movement (SBM) with lubiprostone compared to placebo at week 1 (MD: 3.64, 95% CI: 0.83–6.46, $p=0.011$; $I^2=82\%$).¹¹ Lubiprostone (24mcg BID) has an NNT=3 for ≥ 4 SBMs per week and NNT=5 for ≥ 3 SBMs per week.¹¹ Linaclotide 500mcg showed significantly improved change from baseline in SBM frequency at week 1 (MD: 2.24, 95% CI: 1.65-2.83, $p< 0.0001$); $I^2=0\%$; NNT=5.¹¹

For IBS-C, PEG may be considered to improve stool output, but is not recommended for use in relieving global IBS symptoms which include abdominal pain, bloating, and cramping.^{13,14} Lubiprostone is FDA-approved for treating IBS-C in women ages ≥ 18 years-old and can improve global symptoms, but dose-dependent nausea is a common side effect.^{13,14} Guidelines consider linaclotide as the preferred prescription laxative as it is effective for pain, bloating and stool normalization.^{13,14} Plecanatide is considered an alternative to linaclotide. Tenapanor is considered for global IBS-C symptom relief especially when visceral pain and constipation are both prominent and if linaclotide or plecanatide is ineffective or poorly tolerated.¹³

In a systematic review and meta-analysis of 15 placebo-controlled trials in patients >16 years of age with IBS-C, linaclotide 290mcg achieved a better abdominal pain response vs. placebo (RR=0.79, 95% CI: 0.73-0.85, P-score 0.88).²⁰ Linaclotide 290mcg also was associated with achieving complete SBMs vs. placebo (RR=0.76, 95% CI: 0.65-0.88, P-score 0.76).²⁰ However, linaclotide 290mcg daily was associated with greater dropout rates due to diarrhea. Lubiprostone was associated with a significant increase in the incidence of nausea.

For OIC, the [American Gastroenterological Association](#) (AGA) strongly recommends PEG as a first-line laxative and is preferred over lactulose for its efficacy and tolerability.¹⁵ Stimulant laxatives (senna, bisacodyl) are recommended for scheduled use in combination with PEG or other osmotic laxatives.¹⁵ Naldemedine is the preferred oral PAMORA for adults with laxative refractory OIC as it is well tolerated.^{15,16} Naloxegol can also be considered for laxative refractory OIC.¹⁵ Methylnaltrexone is considered when rapid relief is needed especially in those with advance illness (e.g., palliative care, inpatient).¹⁵ The European Society for Medical Oncology considers methylnaltrexone clinically effective in advanced cancer.¹⁷ Lubiprostone and prucalopride are not recommended for OIC due to insufficient evidence.¹⁵

In a meta-analysis of 27 RCTs of adults with or without cancer pain and with or without a history of laxative use, naldemedine compared to placebo was more effective in achieving ≥ 3 complete SBMs per week (RR=0.65, 95% CI: 0.52-0.82, $p=0.011$; $I^2=79.6\%$); NNT=5 (95% CI: 4-8).¹⁸ Methylnaltrexone was significantly better than placebo in achieving ≥ 3 complete SBMs per week (RR=0.62, 95% CI: 0.50-0.76, $p<0.001$; $I^2=77.2\%$); NNT=3.4 (95% CI: 3-6). Naloxegol was also considered to be effective (RR=0.77, 95% CI: 0.61-0.97, $p<0.026$; $I^2=86.4\%$); NNT=7 (95% CI: 4-26). Lubiprostone showed a modest benefit compared to placebo (RR=0.90, 95% CI 0.83-0.97, $p<0.005$; $I^2=0.0\%$); NNT=15 (95% CI: 9-51).

Findings:

Chronic constipation is complex and should be managed in a stepwise approach. OTC pharmacologic therapy is generally considered first-line, whereas prescription medications should be considered after adequate OTC options have been exhausted. Docusate is no more effective than placebo and should not be included in initial OTC considerations.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov. For more information about the NPTC, please visit the [NPTC website](#).

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