### FDA APPROVED INDICATIONS AND DOSAGE[^1][^3][^9][^16][^18][^20][^23]

<table>
<thead>
<tr>
<th>Agent</th>
<th>Indication(s)</th>
<th>Dosage and Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitiza® (lubiprostone)³ capsules</td>
<td>Treatment of chronic idiopathic constipation (CIC) in adults.</td>
<td>CIC, OIC - 24 mcg taken twice daily orally with food and water.</td>
</tr>
<tr>
<td></td>
<td>Treatment of opioid-induced constipation (OIC) in adults with chronic, non-cancer pain including patients with chronic pain related to prior cancer of its treatment who do not require frequent (e.g. weekly) opioid dosage escalation. Limitation of Use: Effectiveness of Amitiza in the treatment of OIC in patients taking diphenylheptane opioids (e.g. methadone) has not been established.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treatment of irritable bowel syndrome with constipation (IBS-C) in women ≥ 18 years old.</td>
<td>IBS-C - 8 mcg taken twice daily orally with food and water.</td>
</tr>
<tr>
<td>Linzess® (linaclotide) capsules</td>
<td>Treatment of irritable bowel syndrome with constipation (IBS-C) in adults.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treatment of chronic idiopathic constipation (CIC) in adults.</td>
<td></td>
</tr>
<tr>
<td>Motegrity™ (prucalopride)ab Tablets</td>
<td>Treatment of chronic idiopathic constipation (CIC) in adults.</td>
<td>Adults: 2 mg once daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CrCL &lt;30 mL/min: 1 mg once daily</td>
</tr>
</tbody>
</table>

[^1]: 1, 9, 16, 18, 20, 23
| **Movantik™** (naloxegol) | Treatment of opioid-induced constipation (OIC) in adult patients with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g. weekly) opioid dosage escalation | 25 mg once daily; if not tolerated, reduce to 12.5 mg once daily
Renal Impairment (CrCl < 60 mL/min): 12.5 mg once daily; increase to 25 mg once daily if tolerated and monitor for adverse reactions
Discontinue maintenance laxative therapy before starting naloxegol; may resume laxatives if patients have OIC symptoms after taking naloxegol for 3 days
Patients receiving opioids for less than 4 weeks may be less responsive to Movantik
Discontinue if treatment with the opioid pain medication is also discontinued |
<p>| Relistor® (methylnaltrexone) | Injection/Tablet: Treatment of opioid-induced constipation (OIC) in adult patients with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation. Injection: Treatment of OIC in adult patients with advanced illness or pain caused by active cancer who require opioid dosage escalation for palliative care | 12 mg SQ once daily 450 mg orally once daily Patients receiving opioids for less than 4 weeks may be less responsive to Relistor. Discontinue maintenance laxative therapy before starting Relistor; may resume laxatives if patients have OIC symptoms after taking Relistor for 3 days. Discontinue if treatment with opioid pain medication is also discontinued. Once daily weight based administration every other day, as needed, but no more frequently than one dose in a 24 hour period. | <img src="image" alt="Table" /> | Patients receiving opioids for less than 4 weeks may be less responsive to Relistor. Discontinue maintenance laxative therapy before starting Relistor; may resume laxatives if patients have OIC symptoms after taking Relistor for 3 days. Discontinue if treatment with opioid pain medication is also discontinued. | <img src="image" alt="Table" /> |
| Symproic® (naldemedine) | Treatment of opioid-induced constipation (OIC) in adult patients with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation. | 0.2 mg once daily. Patients receiving opioids for less than 4 weeks may be less responsive to Symproic. Discontinue Symproic if treatment with the opioid pain medication is also discontinued. |</p>
<table>
<thead>
<tr>
<th><strong>Trulance®</strong> (plecanatide)</th>
<th>Treatment of chronic idiopathic constipation (CIC) in adults.</th>
<th><strong>CIC/IBS-C</strong> - The recommended adult dosage is 3 mg taken orally once daily.</th>
</tr>
</thead>
<tbody>
<tr>
<td>tablets</td>
<td>Treatment of irritable bowel syndrome with constipation (IBS-C) in adults</td>
<td></td>
</tr>
<tr>
<td><strong>Zelnorm™</strong> (tegaserod)</td>
<td>Treatment of adult women less than 65 years of age with irritable bowel syndrome with constipation (IBS-C)</td>
<td>6 mg taken twice daily orally at least 30 minutes before meals. Discontinue Zelnorm in patients who have not had adequate control of symptoms after 4 to 6 weeks of treatment</td>
</tr>
<tr>
<td>tablets</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a – effectiveness has not been established in a trial of pediatric patients 6 years and over  
b – clinical studies included individuals 17 years of age and greater  
* - The pre-filled syringe is only for patients who require a Relistor injection dose of 8 mg or 12 mg. Use the vial for patients who require other doses of Relistor injection  
± - CDC 90th percentile weight for adult males 20 years of age and over is 113.3 kg

**CLINICAL RATIONALE**

**Chronic Idiopathic Constipation (CIC):**

Rome IV diagnostic criteria for functional constipation requires the presence of the following for at least 3 months:\(^\text{12}\)

- Must include two or more of the following:
  - Straining during more than 25 percent of defecations
  - Lumpy or hard stools (Bristol Stool Scale Form 1-2) in more than 25 percent of defecations
  - Sensation of incomplete evacuation for more than 25 percent of defecations
  - Manual maneuvers to facilitate more than 25 percent of defecations (e.g., digital evacuation, support of the pelvic floor)
  - Fewer than three spontaneous bowel movements per week
- Loose stools are rarely present without the use of laxatives
- There are insufficient criteria for Irritable Bowel Syndrome (IBS)

The American College of Gastroenterology (ACG) (2014) states that although linaclotide and lubiprostone are effective in CIC and are well tolerated, there have been no comparative studies. As both were evaluated in comparison with placebo rather than “standard therapy,” a recommendation regarding their precise position in a CIC treatment algorithm (i.e., for those who have failed fiber, osmotic, or stimulant laxatives, or as primary therapy) cannot be made at this time.\(^\text{5}\)

American Gastroenterology Association recommends a gradual increase in fiber intake, as both foods included in the diet and as supplements and/or an inexpensive osmotic agent (e.g., milk of magnesia or polyethylene glycol). Depending on stool consistency, the next step may be to supplement the osmotic agent with a stimulant laxative (e.g., bisacodyl or glycerol suppositories), preferably administered 30 minutes after a meal to synergize the pharmacologic agent with the gastrocolonic response. A newer agent (e.g., linaclotide, lubiprostone) should be considered when symptoms do not respond to other laxatives.\(^\text{11}\)

UpToDate states that for initial management, suggest dietary fiber and bulk-forming laxatives (e.g., psyllium or methylcellulose), together with adequate fluids. For patients who do not tolerate bulk-forming laxatives or respond poorly to fiber, osmotic laxatives, stool softeners, or stimulant laxatives may be tried. For patients who have failed the above options, additional options, including pharmaceutical options of linaclotide, plecanatide, lubiprostone, misoprostol, or prucalopride, may be tried.\(^\text{10}\)
**Irritable Bowel Syndrome with Constipation (IBS-C):**
Rome IV defines IBS as recurrent abdominal pain, on average, at least one day per week in the last three months associated with two or more of the following:\(^{13}\)
- Related to defecation
- Associated with a change in stool frequency
- Associated with a change in stool form (appearance)

The goal of treatment of IBS-C is to improve symptoms such as abdominal bloating, discomfort, and constipation. The American College of Gastroenterology states that in some patients, lifestyle modifications, high fiber diets, over-the-counter laxatives (including bulking agents such as psyllium and polyethylene glycol [PEG]), tricyclic antidepressants and SSRIs, or antispasmodics may be effective treatment. In more severe cases of IBS-C, lubiprostone may be effective.\(^{2}\) The guideline states that lubiprostone has not been studied in men and that more data is needed before lubiprostone can be recommended in men with IBS-C.\(^{2}\)

The American College of Gastroenterology monograph (2014) on the management of IBS and CIC states that although linaclotide and lubiprostone are effective in constipation-predominant IBS, these agents were evaluated vs. placebo rather than “standard therapy”. Their position in an IBS treatment algorithm (i.e., for those who have failed other treatments or as primary therapy) is difficult to define and complicated by lack of consensus on what “standard” therapy should be in IBS, given the limitations of data on other agents.\(^{5}\) A 2018 updated monograph lists lubiprostone, linaclotide, and plecanatide as strong recommendations for treatment in IBS-C.\(^{21}\)

A review (2015) states relatively small response rates, higher costs, and adverse effects associated with lubiprostone and linaclotide will likely render these agents suitable as second-line therapies in the treatment of IBS-C and CIC.\(^{7}\)

The World Gastroenterology Organization (2015) states there is no general agreement on the cause of IBS, and no single treatment is currently regarded throughout the world as being universally applicable to the management of all IBS patients. Lubiprostone and linaclotide are considered safe and effective for treatment of IBS-C. However, nausea has been the major side effect limiting use of lubiprostone. Diarrhea is the major adverse effect of linaclotide; and further studies are needed to evaluate its long-term efficacy and safety.\(^{8}\)

UpToDate recommends that for treating IBS-C, soluble fiber should be tried first, followed by osmotic laxatives for those who fail soluble fiber. Those who have persistent constipation with osmotic laxatives are treated with lubiprostone, or a guanylate cyclase agonist (linaclotide or plecanatide).\(^{15}\)

**Opioid-Induced Constipation (OIC):**
OIC Consensus Recommendations (2015): In anticipation of potential OIC development with long-term opioid use, treatment guidelines recommend initiation of a prophylactic bowel regimen that may involve increased fluid and fiber intake, stool softeners, and/or laxatives. When a diagnosis of OIC is suspected despite prophylactic treatment, clinicians should confirm that initiation of opioid therapy has led to a change from baseline in the patient’s typical bowel habits, before consideration of further or alternative interventions. First line approaches to intervention also include dietary changes, OTC treatments, and exercise. The panel believes that the accessibility and relatively low risk of dietary and OTC options justify their prophylactic and first-line use for OIC.\(^{6}\)

National Comprehensive Cancer Network (NCCN, 2019) guidelines on adult cancer pain include the following recommendations on OIC. Preventative measures include prophylactic medications (stimulant laxative, polyethylene glycol), maintaining adequate fluid intake, maintaining adequate dietary fiber, and exercise if feasible. Supplemental medicinal fiber is...
unlikely to control OIC and may worsen constipation. Docusate may not provide benefit. If constipation develops, pharmacological recommendations include titrating stool softeners/laxatives as needed to achieve one non-forced bowel movement every 1-2 days. Consider adjuvant analgesics to allow reduction of opioid dose. If constipation persists, pharmacological recommendations include the consideration of adding another agent (magnesium hydroxide, bisacodyl, lactulose, sorbitol, magnesium citrate, polyethylene glycol). When response to laxative therapy has not been sufficient for OIC in patients with advanced illness, then consider peripherally acting mu opioid receptor antagonists; other second line agents include lubiprostone and linaclotide.\(^4\)

The American Gastroenterological Association Institute 2019 guideline for OIC recommends that patients with OIC, first line agents are traditional laxatives which include osmotic, stimulant, detergent/surfactant stool softener, and lubricant agents. In patients with laxative refractory OIC, naldemedine, naloxegol, and methylnaltrexone are recommended over no therapy. No recommendations are made on lubiprostone or prucalopride. Fiber or bulk forming agents have limited role in OIC. Enemas may occasionally be prescribed as rescue therapy, but are not used regularly due to inconvenience, patient preference, and safety concerns.\(^17\)

UpToDate states that prevention is preferred over management of OIC. For all patients with predisposing factors, suggest prophylactic therapy when opioid treatment is initiated. This is accomplished with a contact cathartic (e.g., senna), with or without a stool softener (e.g., docusate), or daily administration of an osmotic laxative (polyethylene glycol or lactulose), except if lactose intolerant. All patients should be encouraged to increase fluid intake, mobility, and dietary fiber (unless severely debilitated with limited oral fluid intake, or bowel obstruction is suspected). For patients who develop OIC despite a prophylactic regimen, before proceeding to an approach typically considered for refractory cases, the conventional starting strategies can be switched (e.g., from a contact cathartic to an osmotic cathartic or vice versa), and dose escalation can be considered. Some patients also are able to improve bowel function by dietary modifications (increased consumption of fluids and soluble dietary fiber) and increased physical activity. Fiber should not be increased if the patient is debilitated, bowel obstruction is suspected, or hydration has been difficult to maintain. For refractory cases, opioid receptor antagonist therapy and lubiprostone, which are specifically approved for this indication, are available.\(^14\)

### Safety

Linzess (linaclotide) carries a black box warning that it is contraindicated in pediatric patients up to 6 years of age. Linaclotide caused deaths due to dehydration in young juvenile mice. Avoid use of linaclotide in pediatric patients 6 through 17 years of age. The safety and efficacy of linaclotide has not been established in pediatric patients under 18 years of age. It also carries an additional contraindication in patients with known or suspected mechanical gastrointestinal obstruction.\(^3\)

Trulance (plecanatide) carries the following black box warnings:\(^9\)

- Plecanatide is contraindicated in patients less than 6 years of age; in young juvenile mice, plecanatide caused death due to dehydration.
- Avoid use of plecanatide in patients 6 years to less than 18 years of age.
- The safety and effectiveness of plecanatide have not been established in patients less than 18 years of age.

<table>
<thead>
<tr>
<th>Agent</th>
<th>Contraindication(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitiza (lubiprostone)</td>
<td>• Known or suspected mechanical gastrointestinal obstruction</td>
</tr>
<tr>
<td>Linzess (linaclotide)</td>
<td>• Known or suspected mechanical gastrointestinal obstruction</td>
</tr>
<tr>
<td></td>
<td>• Patients under 6 years of age</td>
</tr>
</tbody>
</table>
### Contraindication(s)

<table>
<thead>
<tr>
<th>Agent</th>
<th>Contraindication(s)</th>
</tr>
</thead>
</table>
| Movantik (naloxegol) | - Patients with known or suspected gastrointestinal obstruction and patients at increased risk of recurrent obstruction  
- Concomitant use with strong CYP3A4 inhibitors (e.g., clarithromycin, ketoconazole)  
- Known serious or severe hypersensitivity reaction to naloxegol or any of its excipients |
| Motegrity (prucalopride) | - A history of hypersensitivity to Motegrity. Reactions including dyspnea, rash, pruritus, urticaria, and facial edema have been observed  
- Intestinal perforation or obstruction due to structural or functional disorder of the gut wall, obstructive ileus, severe inflammatory conditions of the intestinal tract such as Crohn’s disease, ulcerative colitis, and toxic megacolon/megarectum. |
| Relistor (methylnaltrexone) | - Patients with known or suspected mechanical gastrointestinal obstruction and at increased risk of recurrent obstruction |
| Sympioic (naldemedine) | - Patients with known or suspected gastrointestinal obstruction at increased risk of recurrent obstruction  
- Patients with a history of a hypersensitivity reaction to naldemedine. |
| Trulance (plecanatide) | - Patients less than 6 years of age due to the risk of serious dehydration.  
- Patients with known or suspected mechanical gastrointestinal obstruction. |
| Zelnorm (tegaserod) | - A history of myocardial infarction, stroke, transient ischemic attack, or angina.  
- A history of ischemic colitis or other forms of intestinal ischemia.  
- Severe renal impairment (eGFR < 15 mL/min/1.73 m2) or end-stage renal disease.  
- Moderate or severe hepatic impairment (Child-Pugh B or C).  
- A history of bowel obstruction, symptomatic gallbladder disease, suspected sphincter of Oddi dysfunction, or abdominal adhesions.  
- Hypersensitivity to tegaserod. |

For additional clinical information see the Prime Therapeutics Formulary Chapters 7.1: Laxatives and 7.7E: Irritable Bowel Syndrome Agents and Formulary Monograph: Linaclotide.

**REFERENCES**

Constipation Agents Prior Authorization with Quantity Limit

TARGET PREFERRED AGENTS
Symproic® (naldemedine)
Trulance® (plecanatide)

TARGET NON-PREFERRED AGENTS
Amitiza® (lubiprostone)
Linzess® (linclotide)
Motegrity™ (prucalopride)
Relistor® (methylnaltrexone)
Movantik™ (naloxegol)
Zelnorm™ (tegaserod)

<table>
<thead>
<tr>
<th>Brand (generic)</th>
<th>GPI (NDC)</th>
<th>Multisource Code</th>
<th>Quantity Limit (per day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitiza (lubiprostone)</td>
<td></td>
<td>M, N, O, or Y</td>
<td></td>
</tr>
<tr>
<td>8 mcg capsule</td>
<td>52450045000110</td>
<td></td>
<td>4 capsules</td>
</tr>
<tr>
<td>24 mcg capsule</td>
<td>52450045000120</td>
<td></td>
<td>2 capsules</td>
</tr>
<tr>
<td>Linzess (linclotide)</td>
<td></td>
<td>M, N, O, or Y</td>
<td></td>
</tr>
<tr>
<td>72 mcg capsule</td>
<td>52557050000110</td>
<td></td>
<td>1 capsule</td>
</tr>
<tr>
<td>145 mcg capsule</td>
<td>52557050000120</td>
<td></td>
<td>1 capsule</td>
</tr>
<tr>
<td>290 mcg capsule</td>
<td>52557050000140</td>
<td></td>
<td>1 capsule</td>
</tr>
<tr>
<td>Motegrity (prucalopride)</td>
<td></td>
<td>M, N, O, or Y</td>
<td></td>
</tr>
<tr>
<td>1 mg tablet</td>
<td>52560060200320</td>
<td></td>
<td>1 tablet</td>
</tr>
<tr>
<td>2 mg tablet</td>
<td>52560060200330</td>
<td></td>
<td>1 tablet</td>
</tr>
<tr>
<td>Movantik (naloxegol)</td>
<td></td>
<td>M, N, O, or Y</td>
<td></td>
</tr>
<tr>
<td>12.5 mg tablet</td>
<td>52580060300320</td>
<td></td>
<td>1 tablet</td>
</tr>
<tr>
<td>25 mg tablet</td>
<td>52580060300330</td>
<td></td>
<td>1 tablet</td>
</tr>
<tr>
<td>Relistor (methylnaltrexone)</td>
<td></td>
<td>M, N, O, or Y</td>
<td></td>
</tr>
<tr>
<td>12 mg/0.6 mL (20 mg/mL) injection syringe</td>
<td>52580050106420</td>
<td></td>
<td>1 syringe</td>
</tr>
<tr>
<td>8 mg/0.4 mL (20 mg/mL) injection syringe</td>
<td>52580050102015</td>
<td></td>
<td>1 syringe (0.4 mL)</td>
</tr>
<tr>
<td>12 mg/0.6 mL (20 mg/mL) injection syringe</td>
<td>52580050102020 (65649-0551-07)</td>
<td></td>
<td>1 syringe (0.6 mL)</td>
</tr>
<tr>
<td>12 mg/6 mL (20 mg/mL) injection vials</td>
<td>52580050102020 (65649-0551-02)</td>
<td></td>
<td>2 vials (1.2 mL)</td>
</tr>
<tr>
<td>150 mg tablet</td>
<td>52580050100320</td>
<td></td>
<td>3 tablets</td>
</tr>
<tr>
<td>Symproic (naldemedine)</td>
<td></td>
<td>M, N, O, or Y</td>
<td></td>
</tr>
<tr>
<td>0.2 mg tablet</td>
<td>52580057200320</td>
<td></td>
<td>1 tablet</td>
</tr>
<tr>
<td>Trulance (plecanatide)</td>
<td></td>
<td>M, N, O, or Y</td>
<td></td>
</tr>
<tr>
<td>3 mg tablet</td>
<td>52543060000320</td>
<td></td>
<td>1 tablet</td>
</tr>
<tr>
<td>Zelnorm (tegaserod)</td>
<td></td>
<td>M, N, O, or Y</td>
<td></td>
</tr>
<tr>
<td>6 mg tablet</td>
<td>52555060200320</td>
<td></td>
<td>2 tablets</td>
</tr>
</tbody>
</table>

*a - Quantity Limit allows for dosing for individuals at least 90th percentile weight

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
Target Agents will be approved when ALL of the following are met:
1. ONE of the following:
   a. The patient has a diagnosis of irritable bowel syndrome with constipation (IBS-C) AND ALL of the following:
      i. The patient has documentation of IBS-C symptoms for ≥3 months
ii. ONE of the following:
   1. The requested agent is Trulance (plecanatide) OR Linzess (linaclotide)
      OR
   2. The requested agent is Amitiza (lubiprostone) OR Zelnorm (tegaserod) AND ONE of the following:
      a. The patient is female
      OR
      b. The prescriber has provided documentation that the requested agent is medically appropriate for the patient’s gender and the intended diagnosis

iii. The patient is 18 years of age or over

iv. ONE of the following:
   1. The patient has tried and had an inadequate response to at least 2 standard laxative therapy classes (bulk forming, stimulant, enema, osmotic, or stool softener)
      OR
   2. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to at least 2 standard laxative therapy classes (bulk forming, stimulant, enema, osmotic, or stool softener)

b. The patient has a diagnosis of chronic idiopathic constipation (CIC) AND ALL of the following:
   i. The patient has documentation of CIC symptoms for ≥3 months
   AND
   ii. ONE of the following:
       1. The requested agent is Trulance (plecanatide), Amitiza (lubiprostone), OR Linzess (linaclotide); AND the patient is 18 years of age or over
       OR
       2. The requested agent is Motegrity (prucalopride)
   AND
   iii. ONE of the following:
       1. The patient has tried and had an inadequate response to at least 2 standard laxative therapy classes (bulk forming, stimulant, enema, osmotic, or stool softener)
       OR
       2. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to at least 2 standard laxative therapy classes (bulk forming, stimulant, enema, osmotic, or stool softener)

OR

c. The patient has a diagnosis of opioid-induced constipation (OIC) AND ALL of the following:
   i. ONE of the following:
      1. ALL of the following:
         a. ONE of the following:
            i. The requested agent is Symproic (naldemedine), Movantik (naloxegol), OR Relistor (methylnaltrexone) tablet
            OR
ii. The requested agent is Amitiza (lubiprostone), AND BOTH of the following:
   1. The patient is not currently receiving a diphenylheptane opioid (e.g. methadone) AND
   2. The patient is 18 years of age or over

b. ONE of the following:
   i. The patient has chronic non-cancer pain
   OR
   ii. The patient has chronic pain related to prior cancer or its treatment
   OR
   iii. The patient has active cancer pain
   OR

2. The requested agent is Linzess (linaclotide) AND BOTH of the following:
   a. The patient has active cancer pain
   AND
   b. The patient is 18 years of age or over
   OR

3. The request is for Relistor (methylnaltrexone) injection AND The patient has advanced illness receiving palliative care OR pain caused by active cancer receiving palliative care

   ii. The patient has chronic use of an opioid agent in the past 30 days
   AND

   iii. ONE of the following:
       1. The patient has tried and had an inadequate response to at least 2 standard laxative therapy classes (stimulant, enema, osmotic, or stool softener, but not including fiber or bulking agents)
       OR
       2. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to at least 2 standard laxative therapy classes (stimulant, enema, osmotic, or stool softener, but not including fiber or bulking agents)

   AND

2. The patient does NOT have any FDA labeled contraindications to the requested agent

AND

3. ONE of the following:
   a. The request is for Symproic (naldemedine), Trulance (plecanatide), OR Relistor (methylnaltrexone) injection
   OR
   b. The requested agent is for use in IBS-C or CIC AND ONE of the following:
      i. The patient has tried and had an inadequate response to Trulance (plecanatide)
      OR
      ii. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to Trulance (plecanatide) that is not expected to occur with the requested agent
   OR
   c. The requested agent is for use in OIC AND ONE of the following:
      i. The patient has tried and had an inadequate response to Symproic (naldemedine)
      OR
ii. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to Symproic (naldemedine) that is not expected to occur with the requested agent

**AND**

4. **ONE** of the following:
   a. The requested quantity (dose) does not exceed the program quantity limit
   **OR**
   b. **ALL** of the following:
      i. The requested quantity (dose) is greater than the program quantity limit
      **AND**
      ii. The requested quantity (dose) does not exceed the maximum FDA labeled dose for the requested indication
      **AND**
      iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit
   **OR**
   c. **ALL** of the following:
      i. The requested quantity (dose) is greater than the program quantity limit
      **AND**
      ii. The requested quantity (dose) is greater than the maximum FDA labeled dose for the requested indication
      **AND**
      iii. The prescriber has submitted documentation in support of therapy with a higher dose for the requested indication

**Length of approval:** 12 months
Step Therapy Supplement

This program applies to FlexRx Closed, FlexRx Open, GenRx Closed, GenRx Open, Health Insurance Marketplace, FocusRx and KeyRx formularies.

Please note, this does not include or apply to quantity limit questions.

STEP THERAPY SUPPLEMENT

OBJECTIVE
The intent of the Step Therapy Supplement is to provide additional questions, to ensure compliance to MN Statute 62Q.184. These questions will apply if the step therapy component within a Prior Authorization or Step Therapy program is not able to be approved.

CONDITIONS FOR APPROVAL
The requested agent will be approved when ONE of the following are met:

1. The patient is currently being treated with the requested agent as indicated by ALL of the following:
   a. A statement by the prescriber that the patient is currently taking the requested agent  
      **AND**
   b. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent  
      **AND**
   c. The prescriber states that a change in therapy is expected to be ineffective or cause harm

   **OR**

2. The patient’s medication history include the required prerequisite/preferred agent(s) as indicated by:
   a. Evidence of a paid claim(s) within the past 999 days  
      **OR**
   b. The prescriber has stated that the patient has tried the required prerequisite/preferred agent(s) in the past 999 days **AND** the required prerequisite/preferred agent(s) was discontinued due to lack of effectiveness or an adverse event  
      **OR**

   **OR**

3. The prescriber has provided documentation that the required prerequisite/preferred agent(s) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm

**Length of Approval:** As per program specific criteria