Constipation Agents Prior Authorization with Quantity Limit Program Summary

This program applies to Medicaid formularies.

The BCBS MN Step Therapy Supplement applies to this program for Medicaid.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
02-01-2024	02-01-2017

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Amitiza®* (lubiprostone) Capsule	Treatment of chronic idiopathic constipation (CIC) in adults 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 Treatment of irritable bowel syndrome with constipation (IBS-C) in women greater than or equal to 18 years old	*generic available	1
Ibsrela® (tenapanor) Tablet	Treatment of irritable bowel syndrome with constipation (IBS-C) in adults		20
Linzess® (linaclotide) Capsule	Treatment of functional constipation (FC) in pediatric patients 6 to 17 years of age Treatment of irritable bowel syndrome with constipation (IBS-C) in adults Treatment of chronic idiopathic constipation (CIC) in adults		3
Motegrity® (prucalopride) Tablet	Treatment of chronic idiopathic constipation (CIC) in adults		11
Movantik® (naloxegol) 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		14
Relistor®	Injection/Tablet:		13

Agent(s)	FDA Indication(s)	Notes	Ref#
(methylnaltrexone) Subcutaneous injection (SC) 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		
Symproic® (naldemedine) 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		15
Trulance® (plecanatide) Tablet	Treatment of chronic idiopathic constipation (CIC) in adults. Treatment of irritable bowel syndrome with constipation (IBS-C) in adults		9
Zelnorm™ (tegaserod) Tablet	Treatment of adult women less than 65 years of age with irritable bowel syndrome with constipation (IBS-C) Limitations of Use: The safety and effectiveness of Zelnorm in men with IBS-C have not been established		18

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Irritable Bowel Syndrome with Constipation (IBS-C)	IBS is a chronic functional disorder of the gastrointestinal system. Patients experience abdominal pain and altered bowel habit, with either predominantly diarrhea (IBS-D), constipation (IBS-C), or both (IBS-M). There is no definitive investigation as no biomarker has been found, so IBS is diagnosed clinically. The Rome criteria were developed by a panel of international experts in the field of functional gastrointestinal disorders. Although initially developed to guide researchers, these criteria have undergone several revisions with the intent of making them clinically useful whereas the criteria can be applied to diagnose IBS.(19) 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:(2,19) • 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 (ACG) updated (2021) guidelines suggest that soluble (e.g., psyllium, oat bran, barley, and beans), but not insoluble (e.g., wheat bran, whole grains, and some vegetables), fiber be used to treat IBS especially when the predominant symptom is constipation. Updated guidelines recommend against the use of polyethylene glycol (PEG), probiotics and antispasmodics. However, the authors do recognize that clinicians may use PEG as a first-line treatment for constipation in IBS, given its low cost and availability.(2)

	Tricyclic antidepressants (TCAs) are also recommended for use with global symptoms of IBS, such as patients who report abnormal bowel habits of constipation, diarrhea, or both. TCAs are believed to improve visceral pain and central pain by acting on norepinephrine, and dopaminergic receptors, thus making them attractive candidates for the treatment of IBS-related abdominal pain. A recent systematic review and meta-analysis evaluated 7 RCTs that evaluated the effect of antidepressant therapy on abdominal pain. Antidepressants were more likely to improve symptoms of abdominal pain than placebo; however, the beneficial effects were due to TCA therapy, not serotonin reuptake inhibitors (SSRIs).(2,5,8) 2021 AGA guidelines recommend lubiprostone with a strong recommendation, and with moderate quality of evidence; in addition to guanylate cyclase activators (linaclotide and plecanatide) with a strong recommendation, high quality of evidence to treat global IBS- C symptoms. Lubiprostone exhibits an appropriate safety profile and efficacy with the most common adverse events being gastrointestinal (i.e., nausea) in nature. Although there may be a delay in initial response, improvement in global symptoms is maintained or increases over time. Guanylate cyclase-C (GC-C) agonists target GC-C receptors residing in the apical membranes of intestinal epithelial cells. There are currently 2 US FDA-approved agents for the treatment of IBS-C—linaclotide 290 µg and plecanatide 3 mg. Recent comparative analyses suggest that both are comparably effective, safe, and well-tolerated. Responses develop quickly and are maintained over time. Diarrhea is the most common adverse event experienced, but discontinuation rates due to diarrhea are low and both are well-tolerated. The 5-HT4 agonist tegaserod is also suggested to be used to treat IBS-C symptoms in women younger than 65 years with ≤1 cardiovascular risk factors who have not adequately responded to secretagogues, but the recommendation is conditional (weak) with a low quality of evidence.(2,5,8)
Chronic Idiopathic Constipation (CIC)	Rome IV diagnostic criteria for functional constipation requires the presence of the following for at least 3 months:(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) According to 2021 American College of Gastroenterology (ACG) guidelines, polyethylene glycol (PEG) is a relatively inexpensive, widely available, nonprescription osmotic laxative that is US FDA-approved for occasional constipation based on several RCT studies. Four trials in chronic idiopathic have yielded improvement in stool frequency and stool consistency. 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 (PEG)). 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.10 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.(5)
Pediatric Functional Constipation	Rome IV defines functional constipation separately for infants and children greater than 4 years of age. For children greater than 4 years, must include 2 or more of the following occurring at least once per week for a minimum of 1 month with insufficient criteria for a diagnosis of irritable bowel syndrome: • 2 or fewer defecations in the toilet per week in a child of a developmental age of at least 4 years • At least 1 episode of fecal incontinence per week • History of retentive posturing or excessive volitional stool retention • History of painful or hard bowel movements • Presence of a large fecal mass in the rectum • History of large diameter stools that can obstruct the toilet Polyethylene glycol (PEG 3350) has become the first line treatment of functional constipation due to its efficacy, safety profile, and because it is well tolerated. There are variations in the amount of PEG 3350 recommended for the cleanout phase of the treatment regime, but a reasonable dose would be 1 to 1.5 grams per kilogram PEG 3350 mixed with 6 to 8 oz. water or juice. Significantly higher doses have been used, especially in the hospital setting. Patients should be encouraged to drink this over 3 hours, if possible. If there has not been a significant response to this treatment, the patient can repeat the dose the next day. If there is no response after two days of treatment or significant abdominal discomfort, persistent vomiting, or any other concerns, the family should present for follow-up and reevaluation. In the second phase of treatment, maintenance therapy, the goal is to keep the stool very soft, preventing reaccumulation of hard stool while the colon returns to normal size and function. Drugs in this phase are oral medications: • Osmotic laxatives: polyethylene glycol (PEG) 3350 at 0.2-0.8 g/kg/day, lactulose at 1- 3 mL /kg/day or magnesium hydroxide at 0.5-3 mL/kg/day • Stool Softeners: docusate sodium at 5 mg/kg/day or mineral oil (lubricant) at 1-3 mL/kg/day • Stimulant laxative for rescue therapy in addition or alone (duration less than 30 days): senna at 2.5-7.5 mL/day or bisacodyl at 5-10 mg/day Normal fiber and fluid intake are recommended for children with constipation, along with an average amount of physical activity. There is no evidence to support the routine use of intensive behavioral protocolized therapy programs or biofeedback in addition to conventional treatment. There is no evidence to suggest the use of prebiotics or probiotics in the treatment of constipation. Among patients referred to pediatric gastroenterologists, 50 percent will recover as defined by 3 or more bowel movements per week without fecal incontinence and be without laxatives after 6 to 12 months. Approximately an additional 10 percent are well while taking laxatives, and 40 percent will still be symptomatic despite laxatives.(21)
Opioid-Induced Constipation (OIC)	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.(6) National Comprehensive Cancer Network (NCCN) guidelines on adult cancer pain include the following recommendations on OIC. Preventative measures include prophylactic medications such as a stimulant laxative (e.g., senna and polyethylene

	glycol) in addition to maintaining adequate fluid intake, maintaining adequate dietary fiber, and exercise if feasible. Supplemental medicinal fiber (e.g., psyllium) is unlikely to control OIC and may worsen constipation. Docusate does 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, rectal suppository, lactulose, sorbitol, magnesium citrate, or 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 such as methylnaltrexone or naloxegol; 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.(16)
Safety (1,3,9,11,13-15,18,20)	Amitiza carries the following contraindication: • Known or suspected mechanical gastrointestinal obstruction Ibsrela carries the following contraindications: • Pediatric patients less than 6 years of age • Patients with known of suspected mechanical gastrointestinal obstruction Linzess carries the following contraindications: • Known or suspected mechanical gastrointestinal obstruction • Patients under 6 years of age Movantik carries the following contraindications: • 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 carries the following contraindications: • 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 carries the following contraindication: • Patients with known or suspected mechanical gastrointestinal obstruction and at increased risk of recurrent obstruction Symproic carries the following contraindications: • Patients with known or suspected gastrointestinal obstruction at increased risk of recurrent obstruction • Patients with a history of a hypersensitivity reaction to naldemedine Trulance carries the following contraindications: • Patients less than 6 years of age due to the risk of serious dehydration. • Patients with known or suspected mechanical gastrointestinal obstruction Zelnorm carries the following contraindications: • 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

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Number	Reference
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3	Linzess Prescribing Information. Forest Pharmaceuticals, Inc. June 2023.
4	National Comprehensive Cancer Network (NCCN) Clinical Practice guidelines in oncology. Adult Cancer Pain. Version 1.2023.
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6	Argoff C, Brennan M, Camilleri M, et al. Review Article: Consensus recommendations on initiating prescription therapies for opioid-induced constipation. Pain Med. 2015;16(12):2324-2337. DOI: 10.1111/pme.12937.
7	Chang, Lin, et al. American Gastroenterological Association-American College of Gastroenterology Clinical Practice Guideline: Pharmacological Management of Chronic Idiopathic Constipation. Gastroenterology, vol. 164, no. 7, 1 June 2023, pp. 1086–1106. https://doi.org/10.1053/j.gastro.2023.03.214.
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Number	Reference
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10	American Gastroenterological Association Medical Position Statement on Constipation. Gastroenterology. 2013;144:211–217. https://www.gastrojournal.org/article/s0016-5085(12)01545-4/fulltext.
11	Motegrity prescribing information. Shire US, Inc. November 2020.
12	Crockett SD, Greer KB, Heidelbaugh JJ, et al. American Gastroenterological Association Institute guideline on the medical management of opioid-induced constipation. Gastroenterology 2019;156:218-226.
13	Relistor prescribing information. Salix Pharmaceuticals. March 2018.
14	Movantik prescribing information. Astra Zeneca Pharmaceutical LP. April 2020.
15	Symproic prescribing information. Purdue Pharma LP. January 2018.
16	American College of Gastroenterology monograph on management of irritable bowel syndrome. American Journal of Gastroenterology. 2018; 113:1–18. https://journals.lww.com/ajg/fulltext/2018/06002/american_college_of_gastroenterology_monograph_on.1.aspx
17	Reference no longer used.
18	Zelnorm prescribing information. US WorldMeds LLC. July 2019.
19	Lacy BE, Patel NK. Rome Criteria and a Diagnostic Approach to Irritable Bowel Syndrome. *Journal of Clinical Medicine*. 2017; 6(11):99. https://doi.org/10.3390/jcm6110099.
20	Ibsrela prescribing information. Ardelyx, Inc. April 2022.
21	Allen P, Setya A, Lawrence VN. Pediatric Functional Constipation. Updated 2022 Aug 19. In: StatPearls. StatPearls Publishing; 2023 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK537037/

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Linzess	linaclotide cap	145 MCG ; 290 MCG ; 72 MCG	M ; N ; O ; Y	N		1. Preferred
Amitiza	Lubiprostone Cap 24 MCG	24 MCG	M ; N ; O ; Y	O ; Y		1. Preferred
Amitiza	Lubiprostone Cap 8 MCG	8 MCG	M ; N ; O ; Y	O ; Y		1. Preferred
Relistor	methylnaltrexone bromide inj	12 MG/0.6ML ; 8 MG/0.4ML	M ; N ; O ; Y	N		2. Non-Preferred
Relistor	methylnaltrexone bromide tab	150 MG	M ; N ; O ; Y	N		2. Non-Preferred
Symproic	naldemedine tosylate tab	0.2 MG	M ; N ; O ; Y	N		2. Non-Preferred
Movantik	naloxegol oxalate tab	12.5 MG ; 25 MG	M ; N ; O ; Y	N		2. Non-Preferred
Trulance	plecanatide tab	3 MG	M ; N ; O ; Y	N		2. Non-Preferred
Motegrity	prucalopride succinate tab	1 MG ; 2 MG	M ; N ; O ; Y	N		2. Non-Preferred
Zelnorm	tegaserod maleate tab	6 MG	M ; N ; O ; Y	N		2. Non-Preferred
Ibsrela	tenapanor hcl tab	50 MG	M ; N ; O ; Y	N		2. Non-Preferred

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Amitiza	Lubiprostone Cap 24 MCG	24 MCG	60	Capsules	30	DAYS			
Amitiza	Lubiprostone Cap 8 MCG	8 MCG	120	Capsules	30	DAYS			
Relistor	methylnaltrexone bromide inj	12 MG/0.6 ML	60	Vials	30	DAYS	Quantity Limit allows for dosing for individuals at least 90th percentile weight		65649055102
Relistor	methylnaltrexone bromide inj	12 MG/0.6 ML	30	Syringes	30	DAYS			65649055103 ; 65649055107
Relistor	Methylnaltrexone Bromide Inj 8 MG/0.4ML (20 MG/ML)	8 MG/0.4 ML	30	Syringes	30	DAYS			
Zelnorm	Tegaserod Maleate Tab 6 MG (Base Equivalent)	6 MG	60	Tablets	30	DAYS			
Linzess	Linaclotide Cap 145 MCG	145 MCG	30	Capsules	30	DAYS			
Linzess	Linaclotide Cap 290 MCG	290 MCG	30	Capsules	30	DAYS			
Linzess	Linaclotide Cap 72 MCG	72 MCG	30	Capsules	30	DAYS			
Ibsrela	Tenapanor HCl Tab	50 MG	60	Tablets	30	DAYS			
Motegrity	Prucalopride Succinate Tab 1 MG (Base Equivalent)	1 MG	30	Tablets	30	DAYS			
Motegrity	Prucalopride Succinate Tab 2 MG (Base Equivalent)	2 MG	30	Tablets	30	DAYS			
Movantik	Naloxegol Oxalate Tab 12.5 MG (Base Equivalent)	12.5 MG	30	Tablets	30	DAYS			
Movantik	Naloxegol Oxalate Tab 25 MG (Base Equivalent)	25 MG	30	Tablets	30	DAYS			
Relistor	Methylnaltrexone Bromide Tab 150 MG	150 MG	90	Tablets	30	DAYS			
Symproic	Naldemedine Tosylate Tab 0.2 MG (Base Equivalent)	0.2 MG	30	Tablets	30	DAYS			
Trulance	Plecanatide Tab 3 MG	3 MG	30	Tablets	30	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Amitiza	Lubiprostone Cap 24 MCG	24 MCG	Medicaid
Amitiza	Lubiprostone Cap 8 MCG	8 MCG	Medicaid
Linzess	linaclotide cap	145 MCG ; 290 MCG ; 72 MCG	Medicaid
Ibsrela	tenapanor hcl tab	50 MG	Medicaid

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Motegrity	prucalopride succinate tab	1 MG ; 2 MG	Medicaid
Movantik	naloxegol oxalate tab	12.5 MG ; 25 MG	Medicaid
Relistor	methylnaltrexone bromide inj	12 MG/0.6ML ; 8 MG/0.4ML	Medicaid
Relistor	methylnaltrexone bromide tab	150 MG	Medicaid
Symproic	naldemedine tosylate tab	0.2 MG	Medicaid
Trulance	plecanatide tab	3 MG	Medicaid
Zelnorm	tegaserod maleate tab	6 MG	Medicaid

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Amitiza	Lubiprostone Cap 24 MCG	24 MCG	Medicaid
Amitiza	Lubiprostone Cap 8 MCG	8 MCG	Medicaid
Relistor	methylnaltrexone bromide inj	12 MG/0.6ML	Medicaid
Relistor	methylnaltrexone bromide inj	12 MG/0.6ML	Medicaid
Relistor	Methylnaltrexone Bromide Inj 8 MG/0.4ML (20 MG/ML)	8 MG/0.4ML	Medicaid
Zelnorm	Tegaserod Maleate Tab 6 MG (Base Equivalent)	6 MG	Medicaid
Linzess	Linaclotide Cap 145 MCG	145 MCG	Medicaid
Linzess	Linaclotide Cap 290 MCG	290 MCG	Medicaid
Linzess	Linaclotide Cap 72 MCG	72 MCG	Medicaid
Ibsrela	Tenapanor HCl Tab	50 MG	Medicaid
Motegrity	Prucalopride Succinate Tab 1 MG (Base Equivalent)	1 MG	Medicaid
Motegrity	Prucalopride Succinate Tab 2 MG (Base Equivalent)	2 MG	Medicaid
Movantik	Naloxegol Oxalate Tab 12.5 MG (Base Equivalent)	12.5 MG	Medicaid
Movantik	Naloxegol Oxalate Tab 25 MG (Base Equivalent)	25 MG	Medicaid
Relistor	Methylnaltrexone Bromide Tab 150 MG	150 MG	Medicaid
Symproic	Naldemedine Tosylate Tab 0.2 MG (Base Equivalent)	0.2 MG	Medicaid
Trulance	Plecanatide Tab 3 MG	3 MG	Medicaid

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
Through Preferred	**TARGET AGENT(S)** **Preferred Agent(s)** **Amitiza** (lubiprostone)* **Linzess** (linaclotide) **Nonpreferred Agent(s)** **Ibsrela** (tenapanor) **Motegrity** (prucalopride) **Movantik** (naloxegol) **Relistor** (methylnaltrexone) **Symproic** (naldemedine) **Trulance** (plecanatide) **Zelnorm** (tegaserod) *-generic available

Module	Clinical Criteria for Approval
	Initial Evaluation **Target Agent(s)** 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: 1. The patient has had IBS-C symptoms for greater than or equal to 3 months **AND** 2. ONE of the following: A. The requested agent is Trulance (plecanatide), Linzess (linaclotide) OR Ibsrela (tenapanor) **OR** B. The requested agent is Amitiza (lubiprostone) OR Zelnorm (tegaserod) AND ONE of the following: 1. The patient's sex is female **OR** 2. The prescriber has provided information that the requested agent is medically appropriate for the patient's sex and the intended diagnosis **AND** 3. ONE of the following: A. The patient's medication history includes at least 2 standard laxative therapy classes (e.g., bulk-forming, stimulant, enema, osmotic, or stool softener) AND ONE of the following: 1. The patient has had an inadequate response to at least 2 standard laxative therapy classes **OR** 2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over at least 2 standard laxative therapy classes **OR** B. The patient has an intolerance or hypersensitivity to at least 2 standard laxative therapy classes **OR** C. The patient has an FDA labeled contraindication to ALL standard laxative therapy classes **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that ALL standard laxative therapy classes (e.g., bulk-forming, stimulant, enema, osmotic, or stool softener) 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 **OR** B. The patient has a diagnosis of chronic idiopathic constipation (CIC) AND ALL of the following: 1. The patient has had CIC symptoms for greater than or equal to 3 months **AND** 2. The requested agent is Amitiza (lubiprostone), Linzess (linaclotide), Motegrity (prucalopride), or Trulance (plecanatide) **AND** 3. ONE of the following: A. The patient's medication history includes at least 2 standard laxative therapy classes (e.g., bulk-forming, stimulant, enema, osmotic, or stool softener) AND ONE of the following:

Module	Clinical Criteria for Approval
	1. The patient has had an inadequate response to at least 2 standard laxative therapy classes **OR** 2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over at least 2 standard laxative therapy classes **OR** B. The patient has an intolerance or hypersensitivity to at least 2 standard laxative therapy classes **OR** C. The patient has an FDA labeled contraindication to ALL standard laxative therapy classes **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that ALL standard laxative therapy classes (e.g., bulk-forming, stimulant, enema, osmotic, or stool softener) 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 **OR** C. The patient has a diagnosis of opioid-induced constipation (OIC) AND ALL of the following: 1. ONE of the following: A. BOTH of the following: 1. ONE of the following: A. The requested agent is Symproic (naldemedine), Movantik (naloxegol), OR Relistor (methylnaltrexone) tablet **OR** B. The requested agent is Amitiza (lubiprostone), AND the patient is not currently receiving a diphenylheptane opioid (e.g., methadone) **AND** 2. ONE of the following: A. The patient has chronic non-cancer pain **OR** B. The patient has chronic pain related to prior cancer or its treatment **OR** C. The patient has active cancer pain **OR** B. The requested agent is Linzess (linaclotide) AND the patient has active cancer pain **OR** C. The request is for Relistor (methylnaltrexone) injection and the patient is receiving palliative care AND ONE of the following: 1. The patient has advanced illness **OR** 2. The patient has pain caused by active cancer **AND** 2. The patient has chronic use of an opioid agent in the past 30 days **AND** 3. ONE of the following: A. The patient's medication history includes at least 2 standard laxative therapy classes (e.g., stimulant, enema, osmotic, or stool softener, but not including fiber or bulking agents) AND ONE of the following: 1. The patient has had an inadequate response to at least 2 standard laxative therapy classes **OR** 2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over at least 2 standard laxative therapy classes **OR** B. The patient has an intolerance or hypersensitivity to at least 2 standard laxative therapy classes **OR**

Module	Clinical Criteria for Approval

C. The patient has an FDA labeled contraindication to ALL standard laxative therapy classes **OR**
D. The patient is currently being treated with the requested agent as indicated by ALL of the following:
1. A statement by the prescriber that the patient is currently taking the requested agent **AND**
2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND**
3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR**
E. The prescriber has provided documentation that ALL standard laxative therapy classes (e.g., stimulant, enema, osmotic, or stool softener, but not including fiber or bulking agents) 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 **OR**

D. The patient has a diagnosis of pediatric functional constipation and ONE of the following:
1. The patient's medication history includes at least 2 standard laxative therapy classes (e.g., bulk-forming, stimulant, enema, osmotic, or stool softener) AND ONE of the following:
1. The patient has had an inadequate response to at least 2 standard laxative therapy classes **OR**
2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over at least 2 standard laxative therapy classes **OR**
2. The patient has an intolerance or hypersensitivity to at least 2 standard laxative therapy classes **OR**
3. The patient has an FDA labeled contraindication to ALL standard laxative therapy classes **OR**
4. The patient is currently being treated with the requested agent as indicated by ALL of the following:
1. A statement by the prescriber that the patient is currently taking the requested agent **AND**
2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND**
3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR**
5. The prescriber has provided documentation that ALL standard laxative therapy classes (e.g., bulk-forming, stimulant, enema, osmotic, or stool softener) 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 **AND**

2. If the patient has an FDA approved indication, then ONE of the following:
A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR**
B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND**
3. If the request is for one of the following brand agents with an available generic equivalent (listed below), then ONE of the following:

Brand	**Generic**
Amitiza	lubiprostone

1. The patient's medication history includes the generic equivalent AND ONE of the following:

Module	Clinical Criteria for Approval
	1. The patient has had an inadequate response to the generic equivalent that is not expected to occur with the brand agent **OR** 2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the generic equivalent over the brand agent **OR** B. The patient has an intolerance or hypersensitivity to generic equivalent that is not expected to occur with the brand agent **OR** C. The patient has an FDA labeled contraindication to generic equivalent that is not expected to occur with the brand agent **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that generic equivalent 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 **AND** 4. ONE of the following: A. The request is for Linzess (linaclotide) for use in pediatric functional constipation **OR** B. The requested agent is for use in IBS-C AND ONE of the following: 1. The patient's sex is female and ONE of the following: 1. The requested agent is lubiprostone **OR** 2. The patient's medication history includes lubiprostone AND ONE of the following: 1. The patient has had an inadequate response to lubiprostone **OR** 2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over lubiprostone **OR** C. The patient has an intolerance or hypersensitivity to lubiprostone that is not expected to occur with the requested agent **OR** D. The patient has an FDA labeled contraindication to lubiprostone that is not expected to occur with the requested agent **OR** E. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** F. The prescriber has provided documentation that lubiprostone 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 **OR** 2. The patient's sex is male and ONE of the following: 1. The requested agent is Linzess (linaclotide) **OR** 2. The patient's medication history includes Linzess (linaclotide) AND ONE of the following: 1. The patient has had an inadequate response to Linzess (linaclotide) **OR**

Module	Clinical Criteria for Approval
	2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over lubiprostone **OR** C. The patient has an intolerance or hypersensitivity to Linzess (linaclotide) that is not expected to occur with the requested agent **OR** D. The patient has an FDA labeled contraindication to Linzess (linaclotide) that is not expected to occur with the requested agent **OR** E. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** F. The prescriber has provided documentation that Linzess (linaclotide) 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 **OR** C. The requested agent is for use in CIC or OIC AND ONE of the following: 1. The requested agent is lubiprostone **OR** 2. The patient's medication history includes lubiprostone AND ONE of the following: 1. The patient has had an inadequate response to lubiprostone **OR** 2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over lubiprostone **OR** 3. The patient has an intolerance or hypersensitivity to lubiprostone that is not expected to occur with the requested agent **OR** 4. The patient has an FDA labeled contraindication to lubiprostone that is not expected to occur with the requested agent **OR** 5. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** 6. The prescriber has provided documentation that lubiprostone 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 **AND** 5. The patient will NOT be using the requested agent in combination with another constipation agent in this program for the requested indication **AND** 6. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria. **Renewal Evaluation**

Module	Clinical Criteria for Approval
	Target Agent(s) will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process **AND** 2. If the patient has an FDA approved indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND** 3. The patient has had clinical benefit with the requested agent **AND** 4. The patient will NOT be using the requested agent in combination with another constipation agent in this program for the requested indication **AND** 5. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Quantity Limit for the Target Agent(s) will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. ALL of the following: 1. The requested quantity (dose) exceeds the program quantity limit **AND** 2. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** 3. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does NOT exceed the program quantity limit **OR** 3. ALL of the following: 1. The requested quantity (dose) exceeds the program quantity limit **AND** 2. The requested quantity (dose) exceeds the maximum FDA labeled dose for the requested indication **AND** 3. The prescriber has provided information in support of therapy with a higher dose for the requested indication **Length of Approval**: 12 months