Washington State Health Care Authority

Chronic GI Motility Agents

Medical policy no. 52.55.00-2 Effective Date: July 1, 2018

Note: *New-to-market drugs included in this class based on the Apple Health Preferred Drug List are non-preferred and subject to this prior authorization (PA) criteria. Non-preferred agents in this class require an inadequate response or documented intolerance due to severe adverse reaction or contraindication to at least TWO preferred agents. If there is only one preferred agent in the class documentation of inadequate response to ONE preferred agent is needed. If a drug within this policy receives a new indication approved by the Food and Drug Administration (FDA), medical necessity for the new indication will be determined on a case-by-case basis following FDA labeling.*

To see the list of the current Apple Health Preferred Drug List (AHPDL), please visit: https://www.hca.wa.gov/assets/billers-and-providers/apple-health-preferred-drug-list.xlsx

Background:

Chronic constipation is infrequent bowel movements or difficult passage of stools that persist for several weeks or longer. There are many possible causes such as blockage in the colon or rectum, problems with nerves around the colon or rectum, and difficulty with the muscles involved in elimination. Symptoms of diarrhea may consist of loose, watery, bowel movements that are more frequent, greater volume of stool, and abdominal cramps. The multiple causes of chronic diarrhea include celiac disease, colon cancer, Crohn's disease, inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), and ulcerative colitis.

Medical necessity

Drug	Medical Necessity
Alosetron (**LOTRONEX®**)	Alosetron may be considered medically necessary when used to treat: • Women with severe diarrhea-predominant irritable bowel syndrome (IBS)
Eluxadoline (**VIBERZI™**)	Eluxadoline may be considered medically necessary when used to treat: • irritable bowel syndrome with diarrhea (IBS-D)
Linaclotide (**LINZESS®**)	Linaclotide may be considered medically necessary when used to treat: • irritable bowel syndrome with constipation (IBS-C) • chronic idiopathic constipation (CIC)
Lubiprostone (**AMITIZA®**)	Lubiprostone may be considered medically necessary when used to treat: • irritable bowel syndrome with constipation (IBS-C); • chronic idiopathic constipation (CIC) • opioid-induced constipation (OIC) for non-cancer pain
Methylnaltrexone (**RELISTOR®**)	Methylnaltrexone may be considered medically necessary when used to treat: • opioid-induced constipation (OIC) for non-cancer pain

	• opioid induced constipation (OIC) in patients with advanced illness or pain caused by active cancer requiring opioid dosage escalation for palliative care (injection)
Naldemadine (**SYMPROIC®**)	Naldemadine may be considered medically necessary when used to treat: • opioid-induced constipation (OIC) for non-cancer pain, including chronic pain related to prior cancer that does not require frequent (e.g. weekly) opioid dosage escalation • Opioid-induced constipation (OIC) in patients with cancer
Naloxegol (**MOVANTIK®**)	Naloxegol may be considered medically necessary when used to treat: • opioid-induced constipation (OIC) for non-cancer pain
Plecanatide (**TRULANCE™**)	Plecanatide may be considered medically necessary when used to treat: • irritable bowel syndrome with constipation (IBS-C) • chronic idiopathic constipation (CIC)
Prucalopride (**MOTEGRITY™**)	Prucalopride may be considered medically necessary when used to treat: • chronic idiopathic constipation (CIC)
Tegaserod (**ZELNORM™**)	Tegaserod may be considered medically necessary when used to treat: • Women with irritable bowel syndrome with constipation (IBS-C)

Clinical policy:

Clinical Criteria (Initial Approval)	
Irritable bowel syndrome with constipation (IBS-C)	1. Diagnosis of irritable bowel syndrome with constipation; **AND** 2. History of failure, contraindication or intolerance to ≥ 2 week trial of at least **TWO** of the following conventional therapies: a. Bulk-forming laxative (e.g. psyllium) b. Stool softener (e.g. docusate sodium) c. Osmotic agents (e.g. lactulose, polyethylene glycol) d. Stimulant laxative (e.g. sennoside); **AND** 3. Patient does not have history of known or suspected GI obstruction; **AND** 4. Patient is greater than or equal to (≥) 18 years of age; **AND** 5. <u>Lubiprostone only</u>: patient must be biologically female 6. <u>Tegaserod only:</u> a. Patient must be biologically female; **AND** b. Patient is less than 65 years of age; **AND** c. No history of myocardial infarction, stroke, transient ischemic attack, or angina; **AND** d. No history of abdominal adhesions, ischemic colitis or other forms of intestinal ischemia; **AND** e. No history of symptomatic gallbladder disease; **AND** f. eGFR greater than 15 mL/min

	If ALL criteria are met, the request may be approved for **12 months** If all criteria are not met, but there are documented medically necessary or situational circumstances, based on the professional judgement of the clinical reviewer, requests may be approved on a case-by-case basis up to the initial authorization duration.
Chronic idiopathic constipation (CIC)	1. Diagnosis of chronic idiopathic constipation; **AND** 2. History of failure, contraindication or intolerance to ≥ 2 week trial of **TWO** of the following conventional therapies: a. Bulk-forming laxative (e.g. psyllium) b. Stool softener (e.g. docusate sodium) c. Osmotic agents (e.g. lactulose, polyethylene glycol) d. Stimulant laxative (e.g. sennoside); **AND** 3. Patient does not have history of known or suspected GI obstruction; **AND** 4. Patient is greater than or equal to (≥) 18 years of age If ALL criteria are met, the request may be approved for **12 months** If all criteria are not met, but there are documented medically necessary or situational circumstances, based on the professional judgement of the clinical reviewer, requests may be approved on a case-by-case basis up to the initial authorization duration.
Opioid-induced constipation (OIC) 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	1. Diagnosis of opioid-induced constipation; **AND** 2. History of failure, contraindication or intolerance to ≥ 2 week trial of **TWO** of the following conventional therapies: a. Bulk-forming laxative (e.g. psyllium) b. Stool softener (e.g. docusate sodium) c. Osmotic agents (e.g. lactulose, polyethylene glycol) d. Stimulant laxative (e.g. sennoside); **AND** 3. Patient does not have history of known or suspected GI obstruction; **AND** 4. Patient is greater than or equal to (≥) 18 years of age If ALL criteria are met, the request may be approved for **12 months** If all criteria are not met, but there are documented medically necessary or situational circumstances, based on the professional judgement of the clinical reviewer, requests may be approved on a case-by-case basis up to the initial authorization duration.

Irritable bowel syndrome with diarrhea (IBS-D)	1. Diagnosis of irritable bowel syndrome with diarrhea (IBS-D); **AND** 2. Patient does not have history of known or suspected GI obstruction and has been ruled out; **AND** 3. No history of the following: a. Cholecystectomy b. Alcoholism or consumption of more than 3 alcoholic drinks daily c. Biliary duct obstruction d. Chronic or severe constipation e. Severe hepatic impairment (Child-Pugh C) f. Pancreatitis g. Sphincter of Oddi disease or dysfunction 4. History of failure, contraindication or intolerance to ≥ 2 week trial of **TWO** of the following conventional therapies: a. Antidiarrheal (e.g. loperamide) at up to maximally indicated doses; b. Antispasmodics (e.g. dicyclomine, hyoscyamine) at up to maximally indicated doses; c. Antibiotics (e.g. rifaximin); d. Antidepressants (e.g. amitriptyline, nortriptyline); e. Bile acid sequestrants (e.g. cholestyramine, colestipol); **AND** 5. Patient is greater than or equal to (≥) 18 years of age If ALL criteria are met, the request may be approved for **12 months** If all criteria are not met, but there are documented medically necessary or situational circumstances, based on the professional judgement of the clinical reviewer, requests may be approved on a case-by-case basis up to the initial authorization duration.
Severe diarrhea-predominant irritable bowel syndrome (IBS)	1. Diagnosis of severe diarrhea-predominant IBS; **AND** 2. Patient does not have a history of known or suspected GI obstruction; **AND** 3. Patient has a history of at least one of the following symptoms: a. Frequent and severe abdominal pain/discomfort; **OR** b. Frequent bowel urgency or fecal incontinence; **OR** c. Disability or restriction of daily activities due to IBS-D; **AND** 4. No history of the following: a. Crohn's disease or ulcerative colitis b. Diverticulitis c. Toxic megacolon d. Gastrointestinal perforation or adhesions

	e. Ischemic colitis f. Impaired intestinal circulation g. Thrombophlebitis or hypercoagulable state h. Severe hepatic impairment 5. History of failure, contraindication or intolerance to ≥ 2 week trial of **TWO** of the following conventional therapies: a. Antidiarrheal (e.g. loperamide) at up to maximally indicated doses; b. Antispasmodics (e.g. dicyclomine, hyoscyamine) at up to maximally indicated doses; c. Antibiotics (e.g. rifaximin); d. Antidepressants (e.g. amitriptyline, nortriptyline); e. Bile acid sequestrants (e.g. cholestyramine, colestipol); **AND** 6. Patient is greater than or equal to (≥) 18 years of age; **AND** 7. Patient must be biologically female. If ALL criteria are met, the request may be approved for **12 months** If all criteria are not met, but there are documented medically necessary or situational circumstances, based on the professional judgement of the clinical reviewer, requests may be approved on a case-by-case basis up to the initial authorization duration.
Opioid-induced constipation (OIC) in patients with advanced illness or pain caused by active cancer requiring opioid dosage escalation for palliative care	1. Diagnosis of OIC with advanced illness or pain caused by active cancer requiring opioid dose escalation for palliative care; **AND** 2. History of failure, contraindication or intolerance to ≥ 2 week trial of **TWO** of the following conventional therapies: a. Bulk-forming laxative (e.g. psyllium) b. Stool softener (e.g. docusate sodium) c. Osmotic agents (e.g. lactulose, polyethylene glycol) d. Stimulant laxative (e.g. sennoside); **AND** 3. Known or suspected GI obstruction has been ruled out; **AND** 4. Greater than or equal to (≥) 18 years of age If ALL criteria are met, the request may be approved for **12 months** If all criteria are not met, but there are documented medically necessary or situational circumstances, based on the professional judgement of the clinical reviewer, requests may be approved on a case-by-case basis up to the initial authorization duration.
Criteria (Reauthorization)	

Diagnosis of irritable bowel syndrome with constipation (IBS-C)	Documentation of response defined as all of the following: 1. ≥30% reduction in average daily abdominal pain score compared to baseline; **AND** 2. Documentation of ≥3 or more spontaneous bowel movements per week; **AND** 3. An increase of ≥1 spontaneous bowel movement per week compared to baseline If ALL criteria are met, the request may be reauthorized for **12 months** If all criteria are not met, but there are documented medically necessary or situational circumstances, based on the professional judgement of the clinical reviewer, requests may be approved on a case-by-case basis up to the reauthorization duration.
Diagnosis of chronic idiopathic constipation (CIC), or opioid-induced constipation (OIC)	Documentation of response defined as all of the following: 1. Documentation of ≥3 or more spontaneous bowel movements per week; **AND** 2. Documentation of an increase of ≥1 spontaneous bowel movement per week compared to baseline If ALL criteria are met, the request may be reauthorized for **12 months** If all criteria are not met, but there are documented medically necessary or situational circumstances, based on the professional judgement of the clinical reviewer, requests may be approved on a case-by-case basis up to the reauthorization duration.
Diagnosis of irritable bowel syndrome with diarrhea (IBS-D) or severe diarrhea predominant irritable bowel syndrome (IBS)	Documentation of response defined as all of the following: 1. ≥30% reduction in average daily abdominal pain score compared to baseline, and 2. ≥50% reduction in number of days per week with at least 1 stool that has a type 6 or 7 consistency according the Bristol Stool Form Scale (BSFS) compared to baseline. If ALL criteria are met, the request may be reauthorized for **12 months** If all criteria are not met, but there are documented medically necessary or situational circumstances, based on the professional judgement of the clinical reviewer, requests may be approved on a case-by-case basis up to the reauthorization duration.

Dosage and quantity limits

Drug Name	Dose and Quantity Limits
Alosetron (LOTRONEX®)	2 mg per day; #60 tablets per 30-day supply
Eluxadoline (VIBERZI™)	200mg per day; #60 tablets per 30-day supply Moderate or severe renal impairment (eGFR < 60 mL/min): 150 mg per day; #60 tablets per 30-day supply ESRD not yet on dialysis (eGFR < 15 mL/min): 150 mg per day; #60 tablets per 30-day supply Mild or moderate hepatic impairment (Child-Pugh A or B): 150 mg per day; #60 tablets per 30-day supply
Linaclotide (LINZESS®)	CIC: 145mcg per day; #30 capsules per 30-day supply IBS-C: 290mcg per day; #30 capsules per 30-day supply
Lubiprostone (AMITIZA®)	CIC/OIC: 48 mcg per day; #60 capsules per 30-day supply Moderate hepatic impairment (Child-Pugh B) for CIC/OIC: 32 mcg per day, may increase to 48 mcg per day; #60 capsules per 30-day supply Severe hepatic impairment (Child-Pugh C) for CIC/OIC: 16 mcg per day, may increase to 48 mcg per day; #60 capsules per 30-day supply IBS-C: 16mcg per day; #60 capsules per 30-day supply Severe hepatic impairment (Child-Pugh C) for IBS-C: 8 mcg per der day; #30 capsules per 30-day supply
Methylnaltrexone (RELISTOR®)	**Oral** 150mg tablet; #90 tablets per 30-day supply Moderate to severe renal or hepatic impairment (CrCl < 60 mL/min or Child-Pugh B or C): 150 mg per day; #30 tablets per 30-day supply **Injection:** 12mg vial/syringe; #30 vials/syringe per 30-day supply 8mg syringe; #30 syringes per 30-day supply *For dose adjustments, see Appendix
Naldemadine (SYMPROIC®)	0.2mg per day; #30 for 30-day supply
Naloxegol (MOVANTIK®)	25mg per day; #30 tablets per 30-day supply Use with moderate CYP3A4 inhibitor or patients with renal impairment: 12.5mg per day but can increase to 25 mg if tolerate. #30 tablets per 30-day supply
Plecanatide (TRULANCE™)	CIC: 3mg per day; #30 tablets per 30-day supply

	IBS-C: 3mg per day; #30 tablets per 30-day supply
Prucalopride (MOTEGRITY™)	2mg per day; #60 tablets per 30-day supply Renal impairment CrCl) < 30mL/min: 1mg per day; #30 tablets per 30 day supply

Coding:

HCPCS Code	Description
J2212	Injection, methylnaltrexone, 0.1 mg

Appendix:

Weight-Based Dosing in Moderate and Severe Hepatic or Renal Impairment for Adult Patients with OIC and Advanced Illness		
Weight of Adult Patient	**Subcutaneous Dose**	**Injection Volume**
Less than 38 kg	0.075 mg/kg	See below*
38 kg to less than 62 kg	4 mg	0.2 mL
62 kg to 114 kg	6 mg	0.3 mL
More than 114 kg	0.075 mg/kg	See below*

*Calculate the injection volume by multiplying [patient weight (kg)] x (0.00375). Round up the volume to the nearest 0.1 mL.

References

1. Ford A, Moayyedi P, Lacy B, et al. Task Force on the Management of Functional Bowel Disorders. American College of Gastroenterology monograph on the management of irritable bowel syndrome and chronic idiopathic constipation. Am J Gastroenterol 2014; 109:S2-S26.
2. Product Information: VIBERZI™ oral tablets, eluxadoline oral tablets. Allergan USA, Inc (per FDA), Irvine, CA, 2017.
3. Product Information: MOVANTIK® oral tablets, naloxegol oral tablets. AstraZeneca Pharmaceuticals LP (per FDA), Wilmington, DE, 2016
4. Product Information: RELISTOR® oral tablets, subcutaneous injection, methylnaltrexone bromide oral tablets, subcutaneous injection. Salix Pharmaceuticals (per FDA), Bridgewater , NJ, 2016
5. Product Information: AMITIZA® oral capsules, lubiprostone oral capsules. Sucampo Pharma Americas, LLC and Takeda Pharmaceuticals America, Inc. (per Manufacturer), Rockville, MD, 2016.
6. Product Information: LOTRONEX® oral tablets, alosetron HCl oral tablets. Prometheus Laboratories Inc. (per FDA), San Diego, CA, 2016.
7. Product Information: LINZESS® oral capsules, linaclotide oral capsules. Allergan USA Inc (per manufacturer), Irvine, CA, 2017
8. Product Information: TRULANCE™ oral tablets, plecanatide oral tablets. Synergy Pharmaceuticals Inc (per manufacturer), New York, NY, 2017
9. Micromedex® 2.0, (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: http://www.micromedexsolutions.com/ (cited: 01/31/2018).

10. Product Information: SYMPROIC® oral tablets, naldemedine oral tablets. Shionogi Inc (per manufacturer), Florham Park, NJ, 2017.
11. Product information: MOTEGRITY™ oral tablets, prucalopride oral tablets. Shire US Inc (per FDA), Lexington, MA, 12/2018

History

Date	Action and Summary of Changes
10/21/2020	Approved by DUR Board
07/23/2020	Annual policy update and add Zelnorm and Motegrity.
10/03/2019	Updated formatting. Edited Note. Changed Policy name
07/31/2019	Addition of prucalopride to policy
04/12/2019	Limit use of alosetron to biological females only
02/21/2018	New Policy