BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

IBSRELA® (tenapanor hydrochloride)
MOTEGRITY™ (prucalopride)
Prucalopride
RELISTOR® (methylnaltrexone bromide)
SYMPROIC® (naldemedine tosylate)
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):`

- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope

- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance

- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Medical Necessity Requirements for IBSRELA (tenapanor hydrochloride)

Criteria for Initial Therapy:

Prescriber Qualifications

- Prescribed by a Gastroenterologist or in consultation with a Gastroenterologist

PHARMACY COVERAGE GUIDELINE

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Indication
- Irritable bowel syndrome with constipation (IBS-C)

Age Requirement
- 18 years or older

Baseline Clinical Evaluation
- Diagnosis of constipation confirmed by **ALL** of the following Rome III/IV criteria:
  - Less than 3 complete spontaneous bowel movements per week occurring in the absence of laxative use
  - 5 or fewer spontaneous bowel movements per week in the absence of laxative use
  - Has abdominal pain
- Constipation is not due to any secondary cause or suspected to be drug induced
- Drugs known to cause constipation have been discontinued

Alternative Therapies
- Failure, contraindication, intolerance to **ALL** the following:
  - ONE oral senna with a stool softener used on schedule (not on an as needed basis)
  - ONE oral osmotic agent OR saline agent (scheduled or as needed)
  - ONE oral OR rectal stimulant used on an as needed basis
  - Linaclotide
  - Lubiprostone

Brand Specific Criteria
- Have failure, contraindication, or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety
- Does not have any FDA-labeled contraindications including:
  - Age less than 6 years due to risk of serious dehydration
  - Known or suspected mechanical gastrointestinal obstruction

Documentation Requirements
- A completed request form must be submitted, including:
  - Chart notes
  - Lab results
  - Supporting clinical documentation

PHARMACY COVERAGE GUIDELINE

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Initial Therapy Criteria Approval Duration
- 6 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy)
Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy

Prescriber Qualifications
- Continues to be seen by a Gastroenterologist or in consultation

Clinical Response
- Increase in stool frequency of at least 1 complete spontaneous bowel movement in the weekly average compared to baseline
- Thirty percent reduction in abdominal pain in the weekly average compared to baseline

Adherence
- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria
- Have failure, contraindication, or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety
- No new contraindications or significant adverse effects including:
  - Severe diarrhea
  - Severe dehydration
  - Age less than 6 years due to risk of serious dehydration
  - Known or suspected mechanical gastrointestinal obstruction

Documentation Requirements
- Chart notes
- Supporting clinical documentation with evidence of improvement in irritable bowel syndrome with constipation
- Lab values that confirm safe use

Continuation Therapy Criteria Approval Duration
- 12 months OR end of plan year

PHARMACY COVERAGE GUIDELINE

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Generic Equivalent (if available)

Medical Necessity Requirements for MOTEGRITY (prucalopride) and Prucalopride generic

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by a Gastroenterologist or in consultation with a Gastroenterologist

Indication
- Chronic idiopathic constipation (CIC)

Age Requirement
- 18 years or older

Baseline Clinical Evaluation
- Diagnosis confirmed by ALL of the following Rome III/IV criteria:
  - Less than 3 spontaneous bowel movements per week
  - Bristol Stool Form Scale of Type 1 or 2 for at least 25% of bowel movements
  - Straining during at least 25% of bowel movements
  - Sensation of incomplete evacuation for at least 25% of bowel movements
  - Sensation of anorectal obstruction/blockage for at least 25% of bowel movements
- Constipation is not due to secondary cause or drug-induced
- Drugs known to cause constipation have been discontinued

Alternative Therapies
- Failure, contraindication, intolerance to **ALL** the following:
  - **ONE** Oral senna with stool softener used on schedule
  - **ONE** Oral osmotic agent or saline agent used (scheduled or as needed)
  - **ONE** Oral or rectal stimulant used as needed
  - Lubiprostone
  - Linaclotide

Brand Specific Criteria
- **For Motegrity:** Have failure, contraindication, or intolerance with **THREE** generic equivalents of **prucalopride** (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

PHARMACY COVERAGE GUIDELINE

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Generic Equivalent (if available)

Safety
- No FDA-labeled contraindications including:
  - Intestinal perforation or obstruction
  - Severe inflammatory conditions (e.g., Crohn's disease, ulcerative colitis)
  - Toxic megacolon/megarectum
- No end-stage renal disease requiring dialysis

Documentation Requirements
- A completed request form must be submitted, including:
  - Chart notes
  - Lab results
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration
- 6 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy)
Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy

Prescriber Qualifications
- Continues to be seen by a Gastroenterologist or in consultation

Clinical Response
- Achieves and maintains **BOTH** of the following:
  - Bristol Stool Form Type 3 or 4
  - 3 or more spontaneous bowel movements per week without laxative use

Adherence
- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria
- **For Motegrity:** Have failure, contraindication, or intolerance with **THREE** generic equivalents of **prucalopride** (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety
- No new contraindications or significant adverse effects including:
  - Intestinal perforation or obstruction

  - Severe inflammatory conditions (e.g., Crohn's disease, ulcerative colitis)
  - Toxic megacolon/megarectum
  - Worsening depression or suicidal thoughts
  - Unusual changes in mood or behavior
  - Severe or persistent diarrhea
  - Severe, persistent, or worsening abdominal pain
- No end-stage renal disease requiring dialysis

Additional Requirements
- Constipation is not due to secondary cause or drug-induced
- Drugs known to cause constipation have been discontinued

Documentation Requirements
- Chart notes
- Supporting clinical documentation with evidence of improvement
- Lab values confirming safe use

Continuation Therapy Criteria Approval Duration
- 12 months OR end of plan year

Medical Necessity Requirements for RELISTOR (methylnaltrexone bromide)

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by a Gastroenterologist, Oncologist, or Pain Management Specialist or in consultation with a Gastroenterologist, Oncologist, or Pain Management Specialist

Indication
- Opioid-induced constipation (OIC)

Age Requirement
- 18 years or older

Baseline Clinical Evaluation
- Diagnosis of opioid-induced constipation confirmed by **ALL** of the following:

  - Less than 3 spontaneous bowel movements per week
  - Bristol Stool Form Scale of Type 1 or 2 for at least 25 percent of bowel movements
  - Straining during at least 25 percent of bowel movements
  - Sensation of incomplete evacuation for at least 25 percent of bowel movements
  - Sensation of anorectal obstruction/blockage for at least 25 percent of bowel movements
- Taking opioid medication for at least 4 weeks
- **ONE** of the following:
  - **For Relistor oral & SQ**: For chronic non-cancer pain and does not require frequent (e.g., weekly) opioid dosage escalation and is to continue with same opioid regimen (same drug, same dose, and same frequency) for pain control **and** there is medical record documentation of a trial and failure of **opioid dose reduction** of ≥ 15%
  - **For Relistor SQ only:** Receiving palliative care for an advanced illness or pain caused by active cancer **AND** requires opioid dosage escalation
- Constipation is not due to any secondary cause or suspected to be drug induced other than from use of opioids
- Drugs known to cause constipation have been discontinued

Alternative Therapies

- Failure, contraindication, intolerance to **ALL** the following:
  - **ONE** Oral senna with stool softener used on schedule
  - **ONE** Oral osmotic agent or saline agent used (scheduled or as needed)
  - **ONE** Oral or rectal stimulant used as needed
  - Lubiprostone
  - Movantik (naloxegol)
  - **For Relistor SQ:** oral Relistor

Brand Specific Criteria

- Have failure, contraindication, or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety

- Does not have any FDA-labeled contraindications including:
  - Known or suspected mechanical gastrointestinal obstruction
  - Increased risk of recurrent obstruction
- No concomitant use with another opioid antagonist (e.g., Movantik [naloxegol], Symproic [naldemedine])

PHARMACY COVERAGE GUIDELINE

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Generic Equivalent (if available)

Documentation Requirements
- A completed request form must be submitted, including:
  - Chart notes
  - Lab results
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration
- For opioid-induced constipation with chronic non-cancer pain: 6 months OR end of plan year
- For opioid-induced constipation in palliative care for advanced illness: 4 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy)
Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy

Prescriber Qualifications
- Continues to be seen by a Gastroenterologist, Oncologist, or Pain Management Specialist or in consultation

Clinical Response
- Achieved and maintained **BOTH** of the following:
  - Bristol Stool Form Type 3 or 4
  - 3 or more spontaneous bowel movements per week without laxative use
- Continues to meet **ONE** of the following:
  - Chronic non-cancer pain who does not require frequent opioid dosage escalation and is to continue with same opioid regimen (same drug, same dose, and same frequency) for pain control
  - Receiving palliative care for an advanced illness or pain caused by active cancer AND requires stable opioid dosage

Adherence
- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria
- Have failure, contraindication, or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety
- No new contraindications or significant adverse effects including:

- Known or suspected mechanical gastrointestinal obstruction
- Increased risk of recurrent obstruction
- Gastrointestinal perforation
- Severe or persistent diarrhea
- Severe, persistent, or worsening abdominal pain

- No concomitant use with another opioid antagonist (e.g., Movantik [naloxegol], Symproic [naldemedine])

Documentation Requirements

- Chart notes
- Supporting clinical documentation with evidence of improvement in opioid-induced constipation
- Lab values that confirm safe use

Continuation Therapy Criteria Approval Duration

- For opioid-induced constipation with chronic non-cancer pain: 6 months OR end of plan year
- For opioid-induced constipation in palliative care for advanced illness: 6 months OR end of plan year

Medical Necessity Requirements for SYMPROIC (naldemedine tosylate)

Criteria for Initial Therapy:

Prescriber Qualifications

- Prescribed by a Gastroenterologist, Oncologist, or Pain Management Specialist or in consultation with a Gastroenterologist, Oncologist, or Pain Management Specialist

Indication

- Opioid-induced constipation (OIC)

Age Requirement

- 18 years or older

Baseline Clinical Evaluation

- Diagnosis of opioid-induced constipation confirmed by **ALL** of the following:
  - Less than 3 spontaneous bowel movements per week
  - Bristol Stool Form Scale of Type 1 or 2 for at least 25 percent of bowel movements
  - Straining during at least 25 percent of bowel movements
  - Sensation of incomplete evacuation for at least 25 percent of bowel movements

  - Sensation of anorectal obstruction/blockage for at least 25 percent of bowel movements
- Taking opioid medication for at least 4 weeks
- Constipation is not due to any secondary cause or suspected to be drug induced other than from use of opioids
- Drugs known to cause constipation have been discontinued

Alternative Therapies

- Failure, contraindication, intolerance to **ALL** the following:
  - **ONE** Oral senna with stool softener used on schedule
  - **ONE** Oral osmotic agent or saline agent used (scheduled or as needed)
  - **ONE** Oral or rectal stimulant used as needed
  - Lubiprostone
  - Movantik (naloxegol)

Brand Specific Criteria

- Have failure, contraindication, or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety

- Does not have any FDA-labeled contraindications including:
  - Known or suspected mechanical gastrointestinal obstruction
  - Increased risk of recurrent obstruction
- Severe hepatic impairment (Child-Pugh Class C)
- No concomitant use with another opioid antagonist (e.g., Movantik [naloxegol], Relistor [methylnaltrexone])
- No concomitant use with strong CYP3A inducers (e.g., rifampin, carbamazepine, phenytoin, St. John's Wort)

Documentation Requirements

- A completed request form must be submitted, including:
  - Chart notes
  - Lab results
  - Supporting clinical documentation

Initial approval duration:

- For opioid-induced constipation with chronic non-cancer pain: 6 months OR end of plan year
- For opioid-induced constipation in palliative care for advanced illness: 4 months OR end of plan year

PHARMACY COVERAGE GUIDELINE

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Criteria for Continuation of Therapy (renewal therapy)

Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy

Prescriber Qualifications

- Continues to be seen by a Gastroenterologist, Oncologist, or Pain Management Specialist or in consultation

Clinical Response

- Achieved and maintained **BOTH** of the following:
  - Bristol Stool Form Type 3 or 4
  - 3 or more spontaneous bowel movements per week without laxative use
- Continues to meet **ONE** of the following:
  - Chronic non-cancer pain who does not require frequent opioid dosage escalation and is to continue with same opioid regimen (same drug, same dose, and same frequency) for pain control
  - Receiving palliative care for an advanced illness or pain caused by active cancer AND requires stable opioid dosage

Adherence

- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria

- Have failure, contraindication, or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety

- No new contraindications or significant adverse effects including:
  - Known or suspected mechanical gastrointestinal obstruction
  - Increased risk of recurrent obstruction
  - Gastrointestinal perforation
  - Severe or persistent diarrhea
  - Severe, persistent, or worsening abdominal pain
- Does not have any FDA-labeled contraindications including:
- Severe hepatic impairment (Child-Pugh Class C)
- No concomitant use with another opioid antagonist (e.g., Movantik [naloxegol], Relistor [methylnaltrexone])
- No concomitant use with strong CYP3A inducers (e.g., rifampin, carbamazepine, phenytoin, St. John's Wort)

PHARMACY COVERAGE GUIDELINE

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Generic Equivalent (if available)

Documentation Requirements

- Chart notes
- Supporting clinical documentation with evidence of improvement in opioid-induced constipation
- Lab values that confirm safe use

Continuation Therapy Criteria Approval Duration

- For opioid-induced constipation with chronic non-cancer pain: 6 months OR end of plan year
- For opioid-induced constipation in palliative care for advanced illness: 6 months OR end of plan year

Criteria for Off-Label Use Requests:

Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. Off-Label Use of Non-Cancer Medications

2. Off-Label Use of Cancer Medications

Description:

Ibsrela (tenapanor) is a sodium/hydrogen exchanger 3 (NHE3) inhibitor indicated for the treatment of irritable bowel syndrome with constipation (IBS-C).

Tenapanor is a locally acting inhibitor of NHE3, an antiporter expressed on the apical surface of the small intestine and colon primarily responsible for the absorption of dietary sodium. By inhibiting NHE3 on the apical surface of the enterocytes, tenapanor reduces absorption of sodium from the small intestine and colon, resulting in an increase in water secretion into the intestinal lumen, which accelerates intestinal transit time and results in a softer stool consistency.

Tenapanor has also been shown to reduce abdominal pain by decreasing visceral hypersensitivity and by decreasing intestinal permeability in animal models. In rat model of colonic hypersensitivity, tenapanor reduced visceral hyperalgesia and normalized colonic sensory neuronal excitability.

Prucalopride (e.g., brand Motegrity) is a serotonin type-4 (5-HT4) receptor agonist indicated for the treatment of chronic idiopathic constipation (CIC) in adults. Prucalopride is a gastrointestinal (GI) prokinetic agent that stimulates colonic peristalsis (high amplitude propagating contractions [HAPCs]), which increases bowel motility. In animal studies, prucalopride facilitates acetylcholine release to enhance the amplitude of contractions and stimulate peristalsis and stimulates gastrointestinal motility with contractions starting from the proximal colon to the anal sphincter.

PHARMACY COVERAGE GUIDELINE

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Relistor (methylnaltrexone) oral tablet is indicated for the treatment of opioid-induced constipation (OIC) in adult patients with chronic non-cancer pain. **Relistor (methylnaltrexone)** injection is indicated for the treatment of OIC in adults with chronic non-cancer pain and the treatment of OIC in adults with advanced illness who are receiving palliative care and response to laxative therapy has not been sufficient. Methylnaltrexone is an antagonist of opioid binding at the mu-opioid receptor. It does not cross the blood brain barrier; it is a peripherally acting mu-opioid receptor antagonist in tissues, including the gastrointestinal tract, thereby decreasing the constipating effects of opioids without impacting with the centrally opioid-mediated effects of opioid analgesia.

Symproic (naldemedine) tablets are indicated for the treatment of 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. Naldemedine is a derivative of naltrexone; where a modification in the chemical structure of naltrexone side chain reduced its ability to cross the blood-brain barrier. As a result, the penetration of naldemedine into central nervous system is expected to be negligible at the recommended dose levels, limiting the potential for interference with centrally mediated opioid analgesia. Opioid receptors are widely distributed in the central and peripheral nervous system, intestines, and other tissues. There are three types of receptors involved in mediating the effects of opioids. These include delta, kappa, and mu receptors. They belong to the family of G-protein coupled receptors that regulate adenylate cyclase. Stimulation of the receptor results in inhibition of adenyate cyclase with a reduction of neuron excitability and neurotransmitter release. The end result is inhibition of the affected neuron.

Constipation is a syndrome that may be defined by symptoms of difficult or infrequent passage of stool, hardness of stool, or a feeling of incomplete evacuation that may occur either alone or due to another medical disorder. The definition of constipation will differ from individual to individual, culture to culture, and even region to region. Patients may define constipation as straining during defecation or change in stool consistency or frequency.

Functional constipation may be defined by the Rome IV criteria as the presence of at least two of the following: straining during at least 25% of bowel movements; passage of lumpy or hard stools at least 25% of bowel movements; sensation of incomplete evacuation at least 25% of bowel movements; anorectal obstruction or blockage at least 25% of bowel movements; the need to use manual maneuvers to facilitate defecation at least 25% of bowel movements; and passing fewer than three stools per week. The criteria also include that loose stools may only rarely be present without the use of laxatives, and that there are insufficient criteria for a diagnosis of irritable bowel syndrome (IBS).

Chronic constipation can result in hemorrhoid formation, rectal pain and burning, bowel obstruction, bowel rupture, as well as upper gut dysfunctions, including gastroesophageal reflux disease, nausea, and abdominal distention.

OIC is a result of use of opioid medications with ensuing loss of gastrointestinal tone, contractility, and mobility. OIC is defined as: new or worsening symptoms of constipation when initiating, changing, or increasing opioid therapy and must include two or more of the symptoms defining functional constipation (see above) with the same frequency cutoff (25%). The cause of OIC is multifactorial and includes inhibition of gastric emptying; reduction of mucosal secretions; reduced bowel tone and contractility; decreased peristalsis with delayed transit; and

increased fluid and electrolyte absorption from increased contact time. Tolerance to opioid induced gastrointestinal adverse effects does not occur.

Opioid medications are increasingly used not only for the management of acute pain but also for the long-term management of cancer related and non-cancer related chronic pain syndromes. With increased use of opioids for pain there is also an increase in adverse effects from their use which includes OIC and opioid bowel dysfunction.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

The Bristol Stool Form Scale (BSFS) – seven types:

- Type 1: separate hard lumps, like nuts (hard to pass), also known as *goat feces*
- Type 2: sausage-shaped, but lumpy
- Type 3: like a sausage but with cracks on its surface
- Type 4: like a sausage or snake, smooth and soft
- Type 5: soft blobs with clear-cut edges (passed easily)
- Type 6: fluffy pieces with ragged edges, a mushy stool
- Type 7: watery, no solid pieces, entirely liquid

Types 1 and 2 indicate constipation, with types 3 and 4 indicating the ideal stools (especially the latter), as they are easy to defecate while not containing excess liquid, and types 5, 6 and 7 specify diarrheal stools

Rome III/IV Diagnostic criteria for functional gastrointestinal disorders:

Functional Constipation - adult

ALL of the following diagnostic criteria - Criteria must be fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis:

- Must include ***two or more*** of the following:
  - Straining during at least 25% of bowel movements
  - Lumpy or hard stools in at least 25% of bowel movements
  - Sensation of incomplete evacuation for at least 25% of bowel movements
  - Sensation of anorectal obstruction/blockage for at least 25% of bowel movements
  - Manual maneuvers to facilitate at least 25% of bowel movements (e.g., digital evacuation, support of the pelvic floor)
  - Fewer than three bowel movements per week
  - Loose stools are rarely present without the use of laxatives
  - Insufficient criteria for irritable bowel syndrome

Laxatives:

Bulk forming – calcium polycarbophil, cellulose, fiber, malt soup, methylcellulose, psyllium

Osmotic – glycerin, lactulose, polyethylene glycol, sodium phosphate, sorbitol, magnesium salts
Lubricating – mineral oil
Softener – dioctyl calcium sulfosuccinate, dioctyl sodium sulfosuccinate
Stimulant/Irritant – bisacodyl, cascara, senna
Other – castor oil, ceo-two

Partial mu-opioid receptor antagonist (PAMORA):
Relistor (methylnaltrexone) – quaternary derivative of naltrexone
Symproic (naldemedine)
Movantik (naloxegol) – naloxone conjugated with a polyethylene glycol polymer

Type 2 chloride channel activator – Secretagogue:
Lubiprostone (brand Amitiza)

Guanylate cyclase-C receptor agonist – Secretagogue:
Linzess (linaclotide)
Trulance (plecanatide)

5HT4 receptor agonist – Prokinetic agent:
Prucalopride (brand Motegrity)

Sodium/Hydrogen Exchanger 3 (NHE3) inhibitor:
Ibsrela (tenapanor)

FDA-approved indications for some GI drugs:

Drug	Functional bowel	CIC	OIC	IBS-C	IBS	IBS-D
Bentyl (dicyclomine)	✓					
Lotronex (alosetron)						✓
Viberzi (eluxadoline)						✓
Xifaxan (rifaximin)					✓	
Lubiprostone (brand Amitiza)		✓	✓	✓		
Ibsrela (tenapanor)				✓		
Linzess (linaclotide)	✓	✓		✓		
Prucalopride (brand Motegrity)		✓				
Movantik (naloxegol)			✓			
Relistor (methylnaltrexone)			✓			

Symproic (naldemedine)			✓			
Trulance (plecanatide)		✓		✓		
Zelnorm (tegaserod)				✓		

CIC = chronic idiopathic constipation
OIC = opioid induced constipation
IBS-C = irritable bowel syndrome with constipation
IBS = irritable bowel syndrome without constipation
IBD-D = irritable bowel syndrome with diarrhea

Resources:

Ibsrela (tenapanor) product information, revised by Ardelyx, Inc. 04-2022. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 18, 2025.

Motegrity (prucalopride) product information, revised by Takeda Pharmaceuticals America, Inc. 11-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 18, 2025.

Prucalopride product information, revised by, ANI Pharmaceuticals, Inc. 09-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 18, 2025.

Relistor (methylnaltrexone) tab & SQ injection product information, revised by Salix Pharmaceuticals, Inc. 05-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 18, 2025.

Symproic (naldemedine) product information, revised by BioDelivery Sciences International, Inc. 07-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 18, 2025.

Wald A. Management of chronic constipation in adults. In: UpToDate, Talley NJ, Hussain Z (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through January 2025. Topic last updated May 33, 2024. Accessed February 21, 2025.

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