PHARMACY COVERAGE GUIDELINE

VIBERZI™ (eluxadoline)
XIFAXAN® (rifaximin)
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 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.

Criteria:

Section A. Irritable Bowel Syndrome with Diarrhea:
VIBERZI (eluxadoline)
XIFAXAN (rifaximin)

- **Criteria for initial therapy:** Viberzi (eluxadoline), Xifaxan (rifaximin) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Gastroenterologist

2. Individual is 18 years of age or older

3. Individual has a confirmed diagnosis of moderate to severe **Irritable Bowel Syndrome with Diarrhea (IBS-D)** with symptoms of moderate abdominal pain, discomfort and bloating

4. The recurrent symptoms are present, on average, at least 1 day per week during the preceding 3 months associated with **TWO or more** of the following:
    a. Related to defecation
    b. Associated with a change in stool frequency
    c. Associated with a change in stool form/appearance

5. The abnormal diarrheal bowel movements are Bristol Stool Form Scale (BSFS) type 6 or 7

6. Individual has failed dietary modification that includes lactose restricted diet, if lactose-intolerant; exclusion of gas-producing foods; low carbohydrate diet and elimination of fermentable oligo-, di-, and monosaccharides and polyols (FODMAPs)

7. **For EITHER Viberzi or Xifaxan:** Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for **ALL** of the following:
    a. Loperamide
        AND
    b. One bile acid sequestrant (e.g., cholestyramine, colestipol, colesevelam)
        AND
    c. Dicyclomine
        AND
    d. Either amitriptyline **OR** nortriptyline

8. **Additional criteria for Xifaxan**: Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for Viberzi

9. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

10. There are **NO** FDA-label contraindications such as:
    a. **For Viberzi** (eluxadoline):
        i. Individual without a gallbladder
        ii. Known or suspected biliary duct obstruction or sphincter of Oddi disease or dysfunction
        iii. Alcoholism, alcohol abuse or alcohol addiction, or in patients who drink > 3 alcoholic beverages per day
        iv. A history of pancreatitis; structural diseases of the pancreas, including known or suspected pancreatic duct obstruction
        v. Severe hepatic impairment (Child-Pugh Class C)
        vi. A history of chronic or severe constipation or sequelae from constipation, or known or suspected mechanical gastrointestinal obstruction

b. **For Xifaxan**: Individual does not have a history of hypersensitivity to rifaximin, rifamycin antimicrobial agents, or any of the components of Xifaxan

11. **For Viberzi**: Individual is not using drugs that cause constipation such as alosetron, opioids (e.g., morphine, codeine, hydrocodone, etc.), or drugs with significant anticholinergic effects (e.g., hydroxyzine, meclizine, dimenhydrinate, diphenhydramine, benztropine, trihexyphenidyl, etc.)

Initial approval duration:
Viberzi: 3 months
Xifaxan: 550 mg three times a day for 14-day course with two refills
No other dose, frequency, or duration will be approved

- **Criteria for continuation of coverage (renewal request):** Viberzi (eluxadoline) **only** and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Gastroenterologist

2. Individual's condition has responded while on therapy with response defined as **BOTH** of the following:
   a. Achieved and maintains BSFS type of 3 or 4 on at least 3 or 4 days
   b. At least a 50% reduction in symptoms of abdominal pain, discomfort, and bloating

3. Individual has been adherent with the medication

4. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use as follows:
   a. Contraindications as listed in the criteria for initial therapy section
   b. Significant adverse effect such as:
      i. Liver toxicity
      ii. Pancreatitis
      iii. Sphincter of Oddi spasm
      iv. Severe constipation
      v. Hypersensitivity

6. **For Viberzi**: Individual is not using drugs that cause constipation such as alosetron, opioids (e.g., morphine, codeine, hydrocodone, etc.), or drugs with significant anticholinergic effects (e.g., hydroxyzine, meclizine, dimenhydrinate, diphenhydramine, benztropine, trihexyphenidyl, etc.)

Renewal duration: 12 months

- 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**

Section B. Travelers' Diarrhea: XIFAXAN (rifaximin)

- **Criteria for therapy:** Xifaxan (rifaximin) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual is 12 years of age or older

  2. Individual has a confirmed diagnosis of **Travelers' diarrhea** caused by noninvasive strains of *Escherichia coli*

  3. Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for azithromycin

  4. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

  5. Individual does not have a history of hypersensitivity to rifaximin, rifamycin antimicrobial agents, or any of the components of Xifaxan

  6. Will not be used for diarrhea complicated by fever or blood in stool

  7. Will not be used for diarrhea caused by bacteria other than *Escherichia coli* such as *Campylobacter jejuni*, *Shigella* spp., or *Salmonella* spp.

  8. Will not be used for diarrhea associated with use of antibiotics

  Approval duration:
  200 mg three times a day for 3 days, **one-time approval**, no refills
  No other dose, frequency, or duration will be approved

- 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**

Section C. Hepatic Encephalopathy: XIFAXAN (rifaximin)

- **Criteria for initial therapy:** Xifaxan (rifaximin) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Gastroenterologist or Hepatologist

  2. Individual is 18 years of age or older

  3. Individual has a confirmed diagnosis of **hepatic encephalopathy** that is in remission defined as having a West Haven Criteria (also known as Conn Score) of 0 or 1 and an asterixis grade of 0 (see Definitions section)

  4. In the previous 6-months, the individual has had at least 2 episodes of hepatic encephalopathy associated with chronic liver disease

  5. Individual has documented failure, contraindication per FDA-label, intolerance, or is not a candidate for lactulose

  6. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a generic equivalent [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

  7. Individual does not have a history of hypersensitivity to rifaximin, rifamycin antimicrobial agents, or any of the components of Xifaxan

  Initial approval duration:
  6 months
  550 mg two times a day
  No other dose or frequency will be approved

- **Continuation of coverage (renewal request):** Xifaxan (rifaximin) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met **(samples are not considered for continuation of therapy)**:

  1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Gastroenterologist or Hepatologist

  2. Individual's condition has responded while on therapy with response for reduction in risk of overt hepatic encephalopathy defined as **TWO** of the following:

a. Achieved and maintains no asterixis tremors or only few asterixis flaps
b. Achieved and maintains at least a 50% reduction in neurologic dysfunction, seen as a reduction in lethargy or apathy, disorientation for time or place, inappropriate behavior, euphoria or anxiety, somnolence, or coma
c. Achieved and maintains at least a 50% reduction in overt hepatic encephalopathy hospitalizations

3. Individual has been adherent with the medication

4. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use

Renewal duration:
550 mg two times a day for 1 year
No other dose or frequency will be approved

- 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**

Section D. Small Intestinal Bacterial Overgrowth: XIFAXAN (rifaximin)

- **Criteria for therapy:** Xifaxan (rifaximin) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Gastroenterologist or Hepatologist

2. Individual is 18 years of age or older

3. Individual has a confirmed diagnosis of **small intestinal bacterial overgrowth**

4. Individual has documentation of **ONE** of the following:
   a. Positive lactulose/glucose breath test showing **either** of the following:
      i. An absolute increase in hydrogen by greater than or equal to 20 ppm above baseline within 90 minutes

ii. A methane level greater than or equal to 10 ppm regardless of the time during the breath test

b. A bacterial concentration of greater than 10^3 colony forming units/mL of jejunal aspirate

5. Individual has documented failure, contraindication per FDA-label, intolerance, or is not a candidate for **TWO** of the following:
   a. Amoxicillin/clavulanic acid
   b. Ciprofloxacin or norfloxacin
   c. Doxycycline or tetracycline
   d. Metronidazole
   e. Trimethoprim-sulfamethoxazole

6. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

7. Individual does not have a history of hypersensitivity to rifaximin, rifamycin antimicrobial agents, or any of the components of Xifaxan

Approval duration:
550 mg three times a day for 14-days course with one refill
No other dose, frequency, or duration will be approved

- 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:

Viberzi (eluxadoline) is indicated in adults for the treatment of irritable bowel syndrome with diarrhea (IBS-D). Eluxadoline is a mu-opioid receptor agonist. It is also a delta opioid receptor antagonist and a kappa opioid receptor agonist. In animals, eluxadoline interacts with opioid receptors in the gut. Stimulation of the opioid receptors within the gut causes inhibition of gastric emptying, inhibition of peristalsis, increased muscle tone, induction of non-propulsive motility, and a delay in gastrointestinal transit.

Xifaxan (rifaximin) is indicated for the treatment of: i) Travelers' diarrhea (TD) caused by noninvasive strains of *Escherichia coli (E. coli)* in adults and pediatric patients 12 years of age and older; ii) reduction in risk of overt hepatic encephalopathy (HE) recurrence in adults; and iii) irritable bowel syndrome with diarrhea (IBS-D) in adults. It should not be used in patients with diarrhea complicated by fever or blood in the stool or diarrhea due to pathogens other than *E. coli*. Xifaxan (rifaximin) is a semi-synthetic, non-aminoglycoside, non-systemic antibiotic and is structural analog of rifampin. Rifaximin acts by binding to the beta-subunit of the bacterial DNA-dependent

RNA polymerase blocking one of the steps in transcription to inhibit bacterial RNA synthesis. The result is inhibition of bacterial protein synthesis and consequently it inhibits the growth of bacteria. It has been shown to be active against *E. coli.*

According to the Centers for Disease Control (CDC), bacteria are the most common cause of TD. TD is rarely life threatening, but it can be severely debilitating in children and the elderly, as severe dehydration can occur. The most common pathogen is enterotoxigenic *E. coli*, followed by *Campylobacter jejuni*, *Shigella* species and *Salmonella* species. Antibiotics are used in the treatment of TD and are effective in cases caused by bacterial pathogens as long as they are susceptible to the particular antibiotic prescribed. Microbial resistance to antibiotics is on the rise and is dependent on many factors one of which is area traveled.

HE is a syndrome characterized by personality changes, intellectual impairment, and a depressed level of consciousness. In HE there is the occurrence of confusion, altered level of consciousness, and coma as a result of liver failure. The 2014 American Association for the Study of Liver Disease (AASLD) and the European Association for the Study of the Liver (EASL) practice guideline define HE as a brain dysfunction caused by liver insufficiency and manifests as a wide spectrum of neurological or psychiatric abnormalities ranging from subclinical alterations to coma. The guideline states that lactulose has been shown to reduce recurrence of HE after an episode of overt HE and it can prevent the development of the first episode. It is considered the agent of first choice for episodic overt HE. Rifaximin is considered add-on therapy to lactulose for prevention of overt HE. AASLD & EASL state that neomycin and metronidazole are alternatives choices for the treatment of over HE.

Irritable bowel syndrome (IBS) is a chronic, relapsing and often life-long functional bowel disorder in which abdominal pain or discomfort is associated with defecation and/or a change in bowel habits. IBS is characterized by symptoms of abdominal pain or discomfort associated with abnormal stool frequency, abnormal stool form, abnormal stool passage, and/or bloating or abdominal distension, which may or may not be relieved by defecation. Symptoms vary and are often associated with food intake and, characteristically, with defecation. Symptoms interfere with daily life and social functioning in many patients.

IBS may be subtyped on the basis of the patient's stool characteristics: IBS with diarrhea (IBS-D), IBS with constipation (IBS-C), IBS with mixed bowel habits or cyclic pattern (IBS-M), and un-subtyped IBS (IBS-U). Treatment is determined by the predominant symptom. Milder, less frequent episodes may be managed with dietary modifications such as eliminating or minimizing foods that worsen symptoms (such as those that contain caffeine, lactose, or artificial sweeteners for IBS-D) or eating a high-fiber diet (for IBS-C or IBS-D) and increasing fluid intake (for IBS-C).

Other lifestyle measures IBS include stress management and dietary interventions such as a diet low in fermentable oligo-, di-, and monosaccharides and polyols (FODMAP). FODMAPs are incompletely absorbed in the small intestine and ferment in the colon. They include foods with fructose (such as apples, pears, honey, high-fructose corn syrup), lactose (milk), fructans or galactans (wheat, onions), and polyols (some fruits and vegetables, artificial sweeteners such as sorbitol). Individuals with IBS may see symptom improvement with gluten restriction. This may be due to the fact that gluten is found in wheat, a high FODMAP food. Recent data confirms a role for probiotics in IBS, but also makes it clear that the effects of probiotics in IBS are highly strain specific.

Small intestinal bacterial overgrowth (SIBO) is a condition where the small bowel is over colonized by aerobic and anaerobic microbes that are normally present in the colon. The diagnosis of SIBO should be suspected in patients

with bloating, flatulence, abdominal discomfort, or diarrhea, and is established with a positive carbohydrate breath test or jejunal aspirate culture. A bacterial concentration of $>10^3$ colony forming units/mL of jejunal aspirate is diagnostic of SIBO. However, the test requires an upper endoscopy to obtain an aspirate and the results are poorly reproducible. The carbohydrate breath test is easy to perform, noninvasive, inexpensive, and widely available.

The carbohydrate breath test is diagnostic of SIBO with one of the following: an absolute increase in hydrogen by ≥ 20 ppm above baseline within 90 minutes is diagnostic for SIBO or a methane level ≥ 10 ppm regardless of the time during the breath test is diagnostic for intestinal methanogen overgrowth (IMO).

A positive methane test was previously considered to be diagnostic of SIBO, however, the term IMO has been introduced to describe this condition as methanogens are not bacteria and may also overgrow in the colon and not just the small intestine. *Methanobrevibacter smithii* appears to be the key methanogen responsible for breath methane production.

Approximately 40% of patients with SIBO have persistent symptoms after initial antibiotic treatment and 40% have recurrent SIBO within nine months of antibiotic treatment. Patients may be treated with a second course of antibiotics if they have a partial improvement in symptoms or early recurrence (< 3 months). Individuals with recurrent symptoms ≥ 3 months after initial antibiotic treatment, a repeat breath test confirms the recurrence of SIBO. Patients with no improvement in symptoms after two courses of antibiotic therapy or progressive symptoms should be evaluated for alternative diagnoses.

SIBO occurs with greater frequency in patients who have been diagnosed with IBS compared to healthy controls. The classical features of SIBO are those of digestive problems and malabsorption. SIBO is most common in IBS-D but also occurs in IBS-C. Symptoms of SIBO include bloating, abdominal pain, diarrhea or constipation among others and the symptoms of SIBO overlap with those of IBS, which suggests that SIBO is related to IBS. Some researchers believe that SIBO may lead to IBS. Statistically significant reduction in IBS symptoms occurs following antibiotic therapy for SIBO. However, more research is needed to show a link between SIBO and IBS. SIBO is rare unless the patient has a primary or secondary motility disorder, has had surgery, such as ileocecal resection or bariatric surgery, or has impaired immunity (such as immunoglobulin A deficiency).

Guidelines recommend non-pharmacologic and over-the-counter therapy as first line therapy for IBS-D. Antispasmodics such as dicyclomine decreases abdominal spasms and cramps through reduced smooth muscle contractions. They may improve pain and global symptoms. Their efficacy is based on continuous use and the effect is rated as modest. Tricyclic antidepressants (amitriptyline, nortriptyline) improve abdominal pain and GI symptoms. Modest improvements may not be seen for several weeks. Loperamide may improve abdominal pain, stool consistency & frequency, but may require continuous use. Ondansetron blocks vagal stimulation of the gut, reducing motility & secretions, may reduce loose stools, frequency, and urgency. Lotronex (alosetron) also blocks vagal stimulation of the gut, reducing motility & secretions, it improves pain & stool consistency. Use is associated with a high risk for constipation and rarely, idiopathic ischemic colitis. It is FDA-approved for use in women with IBS-D who have failed conventional treatment. Xifaxan (rifaximin), a semi-synthetic, non-aminoglycoside, non-systemic antibiotic and is structural analog of rifampin, modestly improves abdominal pain and stool consistency. It is limited to a maximum of three 14-day courses of therapy using 550 mg three times a day. Viberzi (eluxadoline) may also modestly improves abdominal pain & loose stool.

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There are few randomized trials of antibiotics to treat bacterial overgrowth and the evidence for use of specific antibiotics is largely from observational studies. Adequate antimicrobial coverage for SIBO can be achieved with either amoxicillin-clavulanic acid, ciprofloxacin, doxycycline, metronidazole, norfloxacin, rifaximin, tetracycline, or trimethoprim-sulfamethoxazole. In patients with IMO a combination of neomycin and rifaximin is recommended.

Definitions:

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

Traveler's Diarrhea:

J Travel Med 2017: Guidelines for the prevention and treatment of travelers' diarrhea: a graded expert panel report		
Azithromycin	1000 mg once OR 500 mg once daily for 3 days	Preferred for dysentery (diarrhea with the presence of blood and mucus), travelers from Southeast Asia, and febrile diarrhea & pregnant women
Levofloxacin	500 mg once OR 500 mg once daily for 3 days	Fluoroquinolones are associated with multiple adverse effects
Ciprofloxacin	750 mg once OR 500 mg twice daily for 3 days	
Ofloxacin	400 mg once OR 400 mg once daily for 3 days	
Rifaximin	200 mg three times daily for 3 days	Not for use with dysentery or febrile diarrhea
Rifamycin	388 mg twice daily for 3 days	

Hepatic encephalopathy:

Hepatic encephalopathy is a brain dysfunction caused by liver insufficiency and/or portosystemic shunting; it manifests as a wide spectrum of neurological or psychiatric abnormalities ranging from subclinical alterations to coma. Overt hepatic encephalopathy is diagnosed clinically based on two types of symptoms: impaired mental status, as defined by the West Haven Criteria (WHC), and impaired neuromotor function.

West Haven Criteria (also known as Conn Score)		
Minimal (Grade 0)	• No asterixis • No detectable change in behavior • No detectable change in mental status • Minimal encephalopathy	Minimal encephalopathy may not be obvious on clinical examination but can be detected by abnormal results of established psychometric or neuropsychological tests
Grade 1	• Trivial lack of awareness or attention • Euphoria or anxiety • Shortened attention span • Impairment of addition or subtraction • Altered sleep rhythm	Despite oriented in time and space (see below), the patient appears to have some cognitive/behavioral decay with respect to his or her standard on clinical examination or to the caregivers

Grade 2	• Lethargy or apathy • Disorientation for time • Subtle obvious personality change • Amnesia of recent events • Inappropriate behavior • Dyspraxia • Slurred speech • Asterixis	Disoriented for time (at least three of the followings are wrong: day of the month, day of the week, month, season, or year) + the other mentioned symptoms
Grade 3	• Somnolence to semi-stupor • Responsive to verbal stimuli • Confused • Gross disorientation • Bizarre behavior • Clonus • Nystagmus • Positive Babinski sign	Disoriented also for space (at least three of the following wrongly reported: country, state [or region], city, or place) + the other mentioned symptoms
Grade 4	Coma	Does not respond even to painful stimuli

Asterixis grade:
0 = no tremor
1 = few flaps
2 = occasional flaps
3 = frequent flats
4 = continuous flaps

Irritable Bowel Syndrome (Rome IV criteria):
Recurrent bothersome symptoms of abdominal pain, AND altered bowel habits on average, at least one day per week in the last three months with symptoms onset at 6 months before the diagnosis

Recurrent abdominal pain with two or more of the following:
Related to defecation
Associated with a change in frequency of stool
Associated with a change in form (appearance) of stool

Bristol Stool Form Scale (BSFS):
Seven types of stool are:
- 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 & 2 indicate constipation
Types 3 & 4 indicate the ideal stools (especially the latter)
Types 5, 6 & 7 specify diarrheal stools

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Irritable bowel syndrome with predominant diarrhea (IBS-D):

Abnormal bowel movements are usually diarrhea (BSFS type 6 and 7)
More than 25% of BM with BSFS types 6 or 7 and less than 25% of BM with BSFS types 1 or 2
Based on the patient's reported predominant bowel habit on days with abnormal bowel movements
Off laxatives and off antidiarrheal agents

IBS with predominant constipation (IBS-C):

More than one fourth (25%) of bowel movements with Bristol stool form types 1 or 2
Less than one-fourth (25%) of bowel movements with Bristol stool form types 6 or 7
Based on the patient's reported predominant bowel habit on days with abnormal bowel movements
Off laxatives and off antidiarrheal agents

IBS with mixed bowel habits (IBS-M):

More than one fourth (25%) of bowel movements with Bristol stool form types 1 or 2 and
More than one-fourth (25%) of bowel movements with Bristol stool form types 6 or 7
Based on the patient's reported predominant bowel habit on days with abnormal bowel movements
Off laxatives and off antidiarrheal agents

IBS unclassified (IBS-U):

Patients who meet diagnostic criteria for IBS but whose bowel habits cannot be accurately categorized into 1 of the 3 groups above should be categorized as having IBS unclassified
Based on the patient's reported predominant bowel habit on days with abnormal bowel movements
Off laxatives and off antidiarrheal agents

Small Intestinal Bacterial Overgrowth (SIBO):

Suggested antibiotics for treatment of small intestinal bacterial overgrowth		
Non-absorbable antibiotics	Recommended Dose	Efficacy
Rifaximin¶	550 mg TID for 14-days	51-78%
Systemic antibiotics		
Amoxicillin-clavulanic acid	875 mg BID for 10-days	50%
Ciprofloxacin	500 mg BID for 10-days	43-100%
Doxycycline	100 mg QD to BID for 10-days	No measurements done, but objectively improved
Metronidazole	250 mg TID for 10-days	43-87%
Neomycin¶	500 mg BID for 10-days	33-55%
Norfloxacin	400 mg QD for 10-days	30-100%
Tetracycline	250 mg QID for 10-days	87.5%
Trimethoprim-sulfamethoxazole	160 mg/800 mg BID for 10-days	95%
¶ In patients with intestinal methane overgrowth (IMO) use a combination regimen of oral rifaximin 550 mg three times daily with oral neomycin 500 mg twice daily for 14-days.		

Resources:

Viberzi (eluxadoline) product information, revised by Allergan, Inc. 07-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed August 23, 2024.

Xifaxan (rifaximin) product information, revised by Salix Pharmaceutical, Inc. 10-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed August 23, 2024.

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