Title: Irritable bowel syndrome agents (Xifaxan, Viberzi, Amitiza, Relistor)

Policy #: Rx.01.182

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Intent:
The intent of this policy is to communicate the medical necessity criteria for rifaximin (Xifaxan®), eluxadoline (Viberzi™), lubiprostone (Amitiza®), methylnatrexone (Relistor®) as provided under the member’s pharmacy benefit.

Description:
Irritable bowel syndrome (IBS), a common, functional gastrointestinal disorder, is defined as abdominal discomfort associated with altered bowel habits. Three subtypes of IBS exist: IBS with constipation (IBS-C), IBS with diarrhea (IBS-D), and mixed type (IBS-M). Diagnosis of IBS is based solely on clinical criteria as there are no radiologic or endoscopic abnormalities in IBS and no biomarker has proven reliable for diagnosis. Approximately 10-15% of the general adult population is affected by IBS.

Chronic idiopathic constipation (CIC), a common, functional gastrointestinal disorder, is defined as constipation (a symptom-based disorder defined as unsatisfactory defecation and is characterized by infrequent stools, difficult stool passage, or both) for at least 3 months. The estimate prevalence of CIC is 14% and may be more common in women, elderly, and lower socioeconomic status.

Opioid induced constipation (OIC) is the most common gastrointestinal adverse effect. The prevalence of OIC increases as the duration of opioid analgesia increases.

Hepatic encephalopathy (HE) is defined as 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.
Rifaximin (Xifaxan), a semisynthetic antibiotic, is derived from rifampin. It inhibits bacterial protein synthesis and growth by binding to the beta-subunit of bacterial DNA-dependent RNA polymerase, blocking one of the steps in transcription. Rifaximin 550mg is indicated for reduction in risk of overt HE recurrence in adults and for treatment of IBS-D in adults. When treating IBS-D, the course of therapy is 14 days. The regimen may be repeated up to 2 times.

Lubiprostone (Amitiza) is a locally acting chloride channel activator that enhances chloride rich intestinal fluid secretion without altering sodium and potassium concentrations in serum. The result in increased motility in the intestine, facilitating the passage of stool. Lubiprostone is indicated for CIC in adults, OIC in adults with chronic, non-cancer pain, and IBS-C in adult women.

Eluxadoline (Viberzi) is a mu and kappa opioid receptor agonist and a delta opioid receptor antagonist indicated in adults with IBS-D.

Methylnaltrexone (Relistor) is a selective mu-receptor antagonist that works mainly in the gastrointestinal tract due to its inability to cross the blood brain barrier. It decreases the constipating effects of opioids without affecting analgesia. Methylnaltrexone tablets and injection are indicated for OIC in adults with chronic, non-cancer pain. Methylnaltrexone injection is indicated for OIC in adults with advanced illness who are receiving palliative care, when response to laxative therapy has not been sufficient.

**Policy:**

Rifaximin (Xifaxan) 550 mg is approved when ONE of the following are met:

1. Diagnosis of hepatic disease with risk for hepatic encephalopathy (ie previous episode of hepatic encephalopathy, advanced liver disease, hepatocellular carcinoma) AND inadequate response or inability to tolerate lactulose; or
2. Diagnosis or irritable bowels syndrome- diarrhea AND inadequate response or inability to tolerate BOTH of the following:
   a. Tricyclic antidepressant or selective serotonin reuptake inhibitor; and
   b. Antispasmodic

Duration of approval:

1. Hepatic disease with risk for encephalopathy: indefinite
2. Irritable bowel syndrome- diarrhea: 14 days (42 tablets)

Reauthorization criteria irritable bowels syndrome- diarrhea: Member does not exceed 3 courses (42 days) of therapy in 365 days.

Eluxadoline (Viberzi) is approved when there is a diagnosis or irritable bowels syndrome- diarrhea AND inadequate response or inability to tolerate BOTH of the following:

1. Tricyclic antidepressant or selective serotonin reuptake inhibitor; and
2. Antispasmodic

Lubiprostone (Amitiza) or methylnaltrexone (Relistor) is approved when there is diagnosis of an FDA approved indication and inadequate response or inability to tolerate ONE for the following:

1. Linaclotide (Linzess); or
2. Naloxegol (Movantik)

**Black Box Warning:**

None

**Guidelines:**

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.
BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the pharmacy benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

References:


Applicable Drugs:

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Generic Name</th>
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<tbody>
<tr>
<td>Amitiza®</td>
<td>Lubiprostone</td>
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<tr>
<td>Relistor®</td>
<td>Methylnaltrexone</td>
</tr>
<tr>
<td>Viberzi™</td>
<td>Eluxadoline</td>
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<tr>
<td>Xifaxan®</td>
<td>Rifaximin</td>
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Cross References:
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