I. Medication Description

Rifaximin is a non-systemically absorbed antibiotic that acts by inhibiting bacterial RNA synthesis. It is not suitable for treating systemic infections because the drug remains in the gastrointestinal tract. While the mechanism of action of rifaximin in the treatment of travelers’ diarrhea and bacterial overgrowth is local antibiotic activity, use in hepatic encephalopathy is to decrease bacterial production of ammonia in the gut. Ammonia is primarily produced in the gastrointestinal tract by enterocyte metabolism of glutamine and by colonic bacterial catabolism of nitrogenous sources such as protein digestion and urea secretion. When excess ammonia accumulates, it crosses into the brain via the blood stream and causes neurotoxicity. The use of non-absorbable, broad spectrum antibiotics (like rifaximin) has shown benefit by decreasing bacterial digestive activity that otherwise produces ammonia.

II. Position Statement

Coverage is provided immediately for a three-day course of treatment for Traveler’s diarrhea (200mg tablets, #9, limit 1 course every 30 days).

Coverage is determined through a prior authorization process with supporting clinical documentation for all other requests.

III. Policy

Coverage of Xifaxan is provided for the following indications:

- Traveler’s diarrhea (200mg tablets only)
- Hepatic encephalopathy (550mg tablets only) when documentation (chart notes) are submitted verifying the diagnosis of hepatic encephalopathy
- Irritable Bowel Syndrome with diarrhea (IBS-D) when chart notes are submitted verifying the diagnosis
- Small intestinal bacterial overgrowth (SIBO):
  - When chart notes are submitted verifying the diagnosis AND
  - Clinical documentation is provided showing positive results on a carbohydrate breath test
IV. Quantity Limitations

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dosage Form</th>
<th>Quantity/Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Travelers' diarrhea</strong></td>
<td>200 mg tablets</td>
<td>9 tablets/30 days</td>
</tr>
<tr>
<td><strong>Hepatic Encephalopathy</strong></td>
<td>550 mg tablets</td>
<td>60 tablets/30 days</td>
</tr>
<tr>
<td><strong>IBS-D</strong></td>
<td>550 mg tablets</td>
<td>42 tablets/14 days</td>
</tr>
<tr>
<td><strong>SIBO</strong></td>
<td>550 mg tablets</td>
<td>42 tablets/14 days</td>
</tr>
<tr>
<td></td>
<td>200 mg tablets</td>
<td>As supported by available literature</td>
</tr>
</tbody>
</table>

V. Coverage Duration

- Traveler’s diarrhea: 1 month and may be renewed
- Hepatic encephalopathy: 12 months and may be renewed
- SIBO: Covered for up to 14 days and may be renewed after 3 months if needed
- IBS-D: Covered for up to 14 days and may be renewed after 3 months if needed, up to a lifetime maximum of three treatment courses

VI. Coverage Renewal Criteria

- Traveler’s diarrhea and hepatic encephalopathy: Coverage may be renewed based on original prior authorization criteria and member has received clinical benefit from the drug as shown in decreasing disease signs and symptoms.
- IBS-D: Coverage may be renewed if the following criteria have been met:
  - At least 10 weeks have passed since the completion of the previous treatment course AND
  - Member is experiencing symptoms associated with IBS-D AND
  - Member has not yet received a lifetime maximum of three treatment courses with Xifaxan
- SIBO: Coverage may be renewed if the following criteria have been met:
  - At least 10 weeks have passed since the completion of the previous treatment course AND
  - Clinical documentation showing positive results on a repeat carbohydrate breath test may be required.

VII. Billing/Coding Information

Xifaxan is available as 200 mg and 550 mg tablets.
VIII. Summary of Policy Changes

- 6/1/11: Addition of criteria for use in Irritable Bowel Syndrome, without constipation; Addition of prior authorization review for up to 60 of the 550 mg tablets per 30 days in order to verify use is for hepatic encephalopathy.
- 9/1/11: Addition of PA criteria and quantity limits for each covered diagnosis
- 9/15/12: Addition of coverage criteria for SIBO without constipation, change in approval duration to allow for once course of therapy at a time for IBS/SIBO.
- 9/15/13: Clarification of coverage in SIBO and IBS
- 9/15/14: no policy changes
- 6/3/15: updated policy to cover IBS with diarrhea specifically per FDA approval language
- 7/1/15: formulary distinctions made
- 12/15/15: no policy changes
- 9/15/16: no policy changes
- 10/16/17: no policy changes
- 11/1/18: no policy changes
- 8/15/19: updated coverage criteria, quantity limits, coverage duration, and renewal criteria for SIBO and IBS-D
- 11/15/19: no policy changes
- 1/30/20: clarified renewal criteria
- 5/1/20: clarified SIBO coverage

IX. References


The Plan fully expects that only appropriate and medically necessary services will be rendered. The Plan reserves the right to conduct pre-payment and post-payment reviews to assess the medical appropriateness of the above-referenced therapies.

The preceding policy applies only to members for whom the above named pharmacy benefit medications are included on their covered formulary. Members with closed formulary benefits are subject to trying all appropriate formulary alternatives before a coverage exception for a non-formulary medication will be considered.

The preceding policy is a guideline to allow for coverage of the pertinent medication/product, and is not meant to serve as a clinical practice guideline.