Xifaxan

Description

Xifaxan (rifaximin)

Background
Xifaxan is a semi-synthetic antibacterial derived from rifampin. Xifaxan is used for the treatment of travelers’ diarrhea (TD) caused by *Escherichia coli* (E.coli), for the reduction of the risk of recurring overt hepatic encephalopathy (HE), and for the treatment of irritable bowel syndrome with diarrhea (IBS-D) characterized by pain or discomfort in the abdomen and loose or watery stools. The exact mechanism of action of Xifaxan for the treatment of IBS-D is not known, but is thought to be related to changes in the bacterial content in the gastrointestinal tract (1).

Regulatory Status
FDA-approved indication: Xifaxan is a rifamycin antibacterial indicated for: (2)

1. Treatment of travelers’ diarrhea caused by noninvasive strains of *Escherichia coli* in adults and pediatric patients 12 years of age and older.
2. Reduction in the risk of overt hepatic encephalopathy recurrence in adults
3. Treatment of irritable bowel syndrome with diarrhea in adults

Limitation of Use:
Xifaxan should not be used in patients with diarrhea complicated by fever or blood in the stool or diarrhea due to pathogens other than *Escherichia coli* (2).

Xifaxan is contraindicated in people with a hypersensitivity to rifaximin, any of the rifamycin antimicrobial agents, or any of the components of Xifaxan (2).
Xifaxan was not found to be effective in patients with diarrhea complicated by fever and/or blood in the stool or diarrhea due to pathogens other than *Escherichia coli*. Discontinue Xifaxan if diarrhea symptoms get worse or persist more than 24 to 48 hours and alternative antibiotic therapy should be considered. Xifaxan has been associated with *Clostridium difficile*-associated diarrhea (CDAD) and may range in severity from mild diarrhea to fatal colitis (2).

Xifaxan dosage for irritable bowel syndrome with diarrhea is one 550 mg tablet taken orally three times a day for 14 days. Patients who experience a recurrence of symptoms can be retreated up to two times with the same dosage regimen (2).

The safety and effectiveness of Xifaxan has not been established in pediatric patients less than 12 years of age with TD or in patients less than 18 years of age for HE and IBS-D (2).

**Related policies**
Viberzi

**Policy**
This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Xifaxan may be considered medically necessary for patients 12 years of age or older for the treatment of travelers’ diarrhea caused by noninvasive strains of *Escherichia coli*, or patients 18 years of age or older for the reduction in risk of hepatic encephalopathy; for the treatment of irritable bowel syndrome with diarrhea in patients who have had an inadequate treatment response, intolerance, or contraindication two anti-diarrheal medications and dietary modification.

Xifaxan is considered investigational in patients who are less than 12 years of age without an indication for travelers’ diarrhea and in patients who are less than 18 years of age without hepatic encephalopathy or irritable bowel syndrome with diarrhea.

**Prior-Approval Requirements**

**Diagnoses**

Patient must have ONE of the following:
1. Travelers’ diarrhea caused by noninvasive strains of *Escherichia coli*
   a. 12 years of age or older

2. Hepatic encephalopathy
   a. 18 years of age and older

3. Irritable bowel syndrome with diarrhea (IBS-D)
   a. 18 years of age or older
   b. Inadequate treatment response, intolerance, or contraindication to
      **TWO** anti-diarrheal medications
   c. Inadequate treatment response to dietary modification (such as low
      carbohydrate diet, exclusion of gas producing foods, lactose free diet
      if intolerant)

**Prior – Approval Renewal Requirements**

**Diagnoses**

Patient must have the following:

1. Travelers’ diarrhea caused by noninvasive strains of *Escherichia coli*
   a. 12 years of age or older

2. Hepatic encephalopathy
   a. 18 years of age and older

3. Irritable bowel syndrome with diarrhea (IBS-D)
   a. 18 years of age or older
   b. Inadequate treatment response, intolerance, or contraindication to
      **TWO** anti-diarrheal medications
   c. Inadequate treatment response to dietary modification (such as low
      carbohydrate diet, exclusion of gas producing foods, lactose free diet
      if intolerant)

**Policy Guidelines**

**Pre - PA Allowance**

<table>
<thead>
<tr>
<th>Age</th>
<th>12 years of age or older</th>
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<tbody>
<tr>
<td>Quantity</td>
<td>200 mg – 9 tablets per 365 days</td>
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</table>
Prior - Approval Limits

Quantity Travelers' Diarrhea
200 mg – 9 tablets per 90 days

Quantity Hepatic Encephalopathy
550 mg – 180 tablets per 90 days

Duration
3 months

Quantity Irritable Bowel Syndrome with Diarrhea
550 mg – 126 tablets per 365 days

Prior – Approval Renewal Limits

Quantity Travelers' Diarrhea
200 mg – 9 tablets per 90 days

Quantity Hepatic Encephalopathy
550 mg – 180 tablets per 90 days

Duration
3 months

Quantity Irritable Bowel Syndrome with Diarrhea
550 mg – 126 tablets per 365 days

Rationale

Summary
Xifaxan is a semi-synthetic antibacterial derived from rifampin indicated for use in patients 12 years of age and older with travelers' diarrhea caused by noninvasive strains of *Escherichia coli* and in patients 18 years of age and older for the reduction in risk of overt hepatic encephalopathy recurrence and the treatment of irritable bowel syndrome with diarrhea. There are no adequate and well-controlled studies to document the safety and efficacy of Xifaxan in children (2).
Prior approval is required to ensure the safe, clinically appropriate and cost effective use of Xifaxan while maintaining optimal therapeutic outcomes.

References
1. FDA News Release. Press announcements. FDA approves two therapies to treat IBS-D.

Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
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<tbody>
<tr>
<td>July 2015</td>
<td>New addition to PA</td>
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<tr>
<td>September 2015</td>
<td>Annual review</td>
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<tr>
<td>December 2015</td>
<td>Annual review</td>
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<tr>
<td>March 2016</td>
<td>Annual review</td>
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<tr>
<td></td>
<td>Removal of renewal for irritable bowel syndrome</td>
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<tr>
<td></td>
<td>Policy code changed from 5.03.34 to 5.01.34</td>
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<tr>
<td>September 2016</td>
<td>Match initiation to renewal and add renewal limits for IBS-D</td>
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Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 2, 2016 and is effective on January 1, 2017.

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