Description
Rifaximin (Xifaxan®) is an oral rifamycin antibiotic.

FDA approved indication
Xifaxan is indicated:
- For the treatment of travelers’ diarrhea (TD) caused by noninvasive strains of *Escherichia coli* in adult and pediatric patients 12 years of age and older
- For the reduction in risk of overt hepatic encephalopathy (HE) recurrence in adults
- For the treatment of irritable bowel syndrome with diarrhea (IBS-D) in adults

Limitation of use:
- TD: Do not use in patients with diarrhea complicated by fever or blood in the stool or diarrhea due to pathogens other than *Escherichia coli*.

Policy/Criteria
*Provider must submit documentation (including office chart notes and lab results) supporting that member has met all approval criteria*

I. Initial Approval Criteria
A. Travelers' Diarrhea (must meet all):
   1. Diagnosis of traveler’s diarrhea;
   2. Failure of one of the following regimens, unless contraindicated or clinically significant adverse effects are experienced (a or b):
      a. Ciprofloxacin 500 mg twice daily for 1-3 days;
      b. Levofloxacin 500 mg once daily for 1-3 days;
   3. Failure of azithromycin 1000 mg single dose unless contraindicated or clinically significant adverse effects are experienced;
   4. Dose does not exceed 600 mg/day (3 tablets/day).
   **Approval duration:** 200 mg 3 times daily for 3 days

B. Hepatic Encephalopathy (must meet all):
   1. Diagnosis of hepatic encephalopathy;
   2. Failure of lactulose in the past 30 days at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
   3. Dose does not exceed 1100 mg/day (2 tablets/day).
   **Approval duration:** 550 mg 2 times daily for 6 months

C. Irritable Bowel Syndrome with Diarrhea (must meet all):
1. Diagnosis of irritable bowel syndrome with diarrhea;
2. Failure of an antispasmodic agent (e.g., dicyclomine) at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
3. Failure of ≥ 10 day trial of loperamide at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
4. Dose does not exceed 1650 mg/day (3 tablets/day).

**Approval duration: 550 mg 3 times daily for 14 days**

**D. Other diagnoses/indications**
1. Refer to HIM.PHAR.21 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized);

**II. Continued Therapy**

**A. Travelers’ Diarrhea** (must meet all):
1. May not be renewed as maximum allowed treatment duration is 3 days. Review initial approval criteria for new cases of travelers’ diarrhea unrelated to original medication request.

**B. Hepatic Encephalopathy** (must meet all):
1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Documentation of positive response to therapy;
3. Xifaxan is being used concurrently with lactulose, unless contraindicated or clinically significant adverse effects are experienced;
4. Dose does not exceed 1100 mg/day (2 tablets/day).

**Approval duration: 12 months**

**C. Irritable Bowel Syndrome with Diarrhea** (must meet all):
1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Documentation of positive response to therapy;
3. Member has not had ≥ two 14-day treatment course in the last 6 months;
4. Dose does not exceed 1650 mg/day (3 tablets/day).

**Approval duration: 14 days**

**D. Other diagnoses/indications** (must meet 1 or 2):
1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy.

**Approval duration: Duration of request or 12 months (whichever is less); or**
2. Refer to HIM.PA.21 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

**III. Diagnoses/Indications for which coverage is NOT authorized:**

**A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – HIM.PA.21 or evidence of coverage documents**
Appendices/General Information

Appendix A: Abbreviation Key
FDA: Food and Drug Administration
HE: hepatic encephalopathy
IBS-D: irritable bowel syndrome with diarrhea
TD: travelers’ diarrhea

References

Reviews, Revisions, and Approvals

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<thead>
<tr>
<th>Description</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
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<tbody>
<tr>
<td>Changed guideline to new format.</td>
<td>08/16</td>
<td>08/16</td>
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<tr>
<td>Removed age requirement as age is not an absolute contraindication for all diagnoses. For travelers’ diarrhea: added levofloxacin as a trial option and removed BID dosing for azithromycin per IDSA For traveler’s diarrhea: removed Patient does not exhibit symptoms of severe or systemic bacterial infection, including fever and bloody stools (i.e. invasive infection); For hepatic encephalopathy: Removed “Documented adherent use of lactulose at dosing of 30-45 ml 3 to 4 times daily. Dosage should be titrated to produce 2 to 3 soft formed stools daily, unless contraindicated or not tolerated.” Replaced with general statement of use at the max indicated dose.</td>
<td>04/17</td>
<td>08/17</td>
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**Important Reminder**
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

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**Note:** For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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