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Medication Policy Manual

Policy No: dru410

Topic: Xifaxan, rifaximin

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Next Review Date: 2026

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IMPORTANT REMINDER

This Medication Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medication policy is to provide a guide to coverage. Medication Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

Xifaxan (rifaximin) is an oral antibiotic used to treat various gastrointestinal issues.

Policy/Criteria

Most contracts require pre-authorization approval of Xifaxan (rifaximin) prior to coverage.

I. Continuation of therapy (COT): Xifaxan (rifaximin) may be considered medically necessary for COT when criterion A or B below is met.

A. For diagnoses of **irritable bowel syndrome with diarrhea** (IBS-D), **small intestinal bacterial overgrowth** (SIBO), or any diagnosis NOT listed in the coverage criteria below, full policy criteria must be met for coverage.

OR

B. For a diagnosis of **overt hepatic encephalopathy**, criteria 1 and 2 must be met:

1. The patient was established on therapy prior to current health plan membership AND attestation that the medication was covered by another health plan.

AND

2. There is documentation of clinical benefit, such as disease stability as detailed in the reauthorization criteria.

Please note*: Medications obtained as samples, coupons, or promotions, paying cash for a prescription ("out-of-pocket") as an eligible patient, or any other method of obtaining medications outside of an established health plan benefit (from your insurance) does NOT necessarily establish medical necessity. Medication policy criteria apply for coverage, per the terms of the member contract with the health plan.*

II. New starts: Xifaxan (rifaximin) may be considered medically necessary when there is clinical documentation (including but not limited to chart notes) that criterion A, B, or C below is met:

A. A diagnosis of **overt hepatic encephalopathy** when criteria (1 and 2) below are met:

1. Treatment with lactulose has been ineffective, not tolerated, or is contraindicated.

AND

2. Xifaxan (rifaximin) will be used in combination with lactulose therapy, unless not tolerated or contraindicated.

OR

B. A diagnosis of **irritable bowel syndrome with diarrhea** (IBS-D) when treatment with a tricyclic antidepressant (such as amitriptyline, nortriptyline, imipramine, or clomipramine) has been ineffective, not tolerated, or is contraindicated.

OR

C. A diagnosis of **small intestinal bacterial overgrowth** (SIBO) when criteria (1 through 4) below are met:

1. Diagnosis has been confirmed by, or in consultation with, a gastroenterologist.

AND

2. Treatment with metronidazole has been ineffective, not tolerated, or is contraindicated.

AND

3. Treatment with ciprofloxacin has been ineffective, not tolerated, or is contraindicated.

AND

4. There have been no prior treatment courses with Xifaxan (rifaximin).

III. Administration, Quantity Limitations, and Authorization Period

A. Regence Pharmacy Services considers Xifaxan (rifaximin) coverable only under the pharmacy benefit (as a self-administered medication).

B. When pre-authorization is approved, Xifaxan (rifaximin) will be authorized in quantities as follows:

1. **Initial Authorization**:

   a. For **overt hepatic encephalopathy**, a maximum of 60 of the 550 mg tablets per 30 days for one year (based on 2 rifaximin 550 mg tablets per day).

   b. For **IBS-D**, a maximum of 42 of the 550 mg tablets total (based on 3 rifaximin 550 mg tablets per day for 14 days). Subsequent courses require additional prior authorization; see "Continued Authorization" criteria below.

   c. For **SIBO,** a maximum of 30 of the 550mg tablets total (based on 3 rifaximin 550 mg tablets per day for 10 days).

2. **Continued Authorization**:

   a. For **overt hepatic encephalopathy**, authorization **may** be reviewed at least annually to confirm that current medical necessity criteria are met and that there is clinical documentation (including but not limited to chart notes) that the medication is effective.

   b. For **IBS-D**, patients who meet medical necessity criteria above, with a previous response (based on clinical documentation, including but not limited to chart notes) to Xifaxan (rifaximin) therapy who subsequently relapsed **may** be reauthorized for up to two additional treatments per lifetime (three treatments total).

   c. For **SIBO**, patients **may** be authorized for a single course per lifetime.

IV. Xifaxan (rifaximin) is considered not medically necessary when policy criteria are not met and/or used for travelers' diarrhea.

V. Xifaxan (rifaximin) is considered investigational when used for all other conditions, including but not limited to Crohn's disease**.**

Position Statement

Summary

- Xifaxan (rifaximin) is an orally administered antibiotic which inhibits bacterial protein synthesis and thereby inhibits the growth of susceptible bacteria. [1]
- The intent of this policy is to cover Xifaxan (rifaximin) for the indications for which it has been shown to be safe and effective, as detailed in the coverage criteria, with consideration for other available treatment options.
    * Effective is defined by having a known health benefit and/or an additional health benefit relative to available treatment alternatives.
    * Where there is lack of proven additional benefit for Xifaxan (rifaximin) relative to alternatives, use of Xifaxan (rifaximin) is not coverable ("not medically necessary" or "investigational").
    * It is important to note that the fact that a medication is FDA approved for a specific indication does not make the treatment medically reasonable and necessary.
- In hepatic encephalopathy, Xifaxan (rifaximin) has been shown to be effective when used concomitantly with lactulose. Evidence-based guidelines recommend use of Xifaxan (rifaximin) as adjunctive treatment to patients who are not adequately treated by lactulose. [1 2]
- In IBS-D, Xifaxan (rifaximin) has been shown to decrease abdominal bloating and improve stool consistency in IBS-D. Evidence-based guidelines recommend treatment with Xifaxan (rifaximin) over no treatment, however they do note the very small effect size. Standard of care for the treatment of IBS-D includes tricyclic antidepressants (TCAs). There is no evidence that Xifaxan is safer or more effective than these treatments, but it is more costly. [1 3 4]
- Xifaxan (rifaximin) is not recommended for use in patients with diarrhea complicated by fever or blood in the stool or diarrhea due to pathogens other than *Escherichia coli*. Because of no added benefit compared to lower-cost generic alternatives, the use of Xifaxan (rifaximin) for travelers' diarrhea is considered not medically necessary.
- In small intestinal bacterial overgrowth (SIBO), several small clinical trials have demonstrated efficacy after a course of rifaximin. Standard of care for the treatment of SIBO includes metronidazole and ciprofloxacin. There is no evidence that Xifaxan is safer or more effective than these treatments, but is more costly. [5] In addition, there is insufficient data to support repeated courses of Xifaxan (rifaximin) for SIBO. Data is limited to a small subset of patients in clinical trials without a comparator arm.

Clinical Efficacy

HEPATIC ENCEPHALOPATHY

- Use of Xifaxan (rifaximin) to maintain remission in hepatic encephalopathy is recommended by evidence-based guidelines on the basis of a randomized, double-blinded trial in patients with recurrent hepatic encephalopathy. [2 6]
- Addition of Xifaxan (rifaximin) reduced the risk of a recurrent by 68% over the six-month trial.
- There is inadequate data to support the use of Xifaxan (rifaximin) as monotherapy to maintain remission in hepatic encephalopathy. [2]

IRRITABLE BOWEL SYNDROME WITH DIARRHEA

- Evidence for initial treatment of IBS-D with Xifaxan (rifaximin) comes from two identically designed randomized, double-blinded, placebo-controlled clinical trials. [1]
- Xifaxan (rifaximin) treatment was associated with a significant improvement in abdominal pain and stool consistency.
- The primary endpoint was adequate relief by Subject Global Assessment (SGA), as defined by an answer of "yes" to the question "In regard to your IBS symptoms, compared to the way you felt before you started study medication, have you, in the past 7 days, had adequate relief of your IBS symptoms?"
- The placebo-subtracted responder rates in the two trials varied from 8-11%.
- A third trial studied retreatment with Xifaxan (rifaximin) in patients who initially responded to treatment but subsequently relapsed.
- Placebo-subtracted responder rates with retreatment were 2-9%.
- Xifaxan (rifaximin) has not been studied for repeat treatment in IBS-D beyond two additional 14-day courses (a total of three treatment courses).[1]
- Evidence-based guidelines recommend treatment with Xifaxan (rifaximin) over no treatment. [3 4]
- There is no data comparing Xifaxan (rifaximin) to other treatments, including best-value generic medications.

TRAVELERS' DIARRHEA

- The efficacy of Xifaxan (rifaximin) in travelers' diarrhea was established in two randomized, double-blind, placebo-controlled trials. [1]
    * Xifaxan (rifaximin) significantly shortened the duration of symptoms as well as the rate of clinical cure.
- Although Xifaxan (rifaximin) is safe and effective for travelers' diarrhea, it has not been shown to be as effective as other less costly alternatives (including generic ciprofloxacin, generic levofloxacin, and generic azithromycin).
- The American College of Gastroenterology (ACG) 2016 guidelines recommend empiric treatment with antibiotics in moderate-to-severe travelers' diarrhea without bloody stool and does not give preference for one treatment over another. Antibiotic treatments include generic fluoroquinolones, generic azithromycin, or rifaximin. [7]

- Due to poor drug absorption, Xifaxan (rifaximin) is not recommended for use in patients with diarrhea complicated by fever or blood in the stool or diarrhea due to pathogens other than *Escherichia coli*.[1] Azithromycin and fluoroquinolones are the preferred treatment options for travelers' diarrhea with fever and bloody stools (invasive, systemic infections). [8]
- Given the no added benefit in invasive systemic infections and the availability of significantly less costly generic alternatives, the use of Xifaxan (rifaximin) is considered not medically necessary.

SMALL INTESTINAL BACTERIAL OVERGROWTH

- One meta-analysis of antibiotics in SIBO found that studies were small, of low quality, and heterogenous. [5] However, overall, treatment with antibiotics was more effective than placebo at achieving breath test normalization.
- There was no statistically significant difference in breath test normalization between treatment with Xifaxan (rifaximin) and placebo. There was a numerical trend towards efficacy, but the small number of studies and subjects may have limited power.
- There is no established guideline for the diagnosis of SIBO. Reported specificity and sensitivity of breath tests is low. The American College of Gastroenterology (ACG) recognizes the lack of a gold standard for diagnosis of SIBO and the wide variation in the administration and interpretation of breath test results. In addition, SIBO is linked to a variety of other conditions such as irritable bowel syndrome (IBS), which may complicate the clinical diagnosis. [9] Therefore, Xifaxan (rifaximin) is coverable only when the diagnosis of SIBO is established by a specialist (gastroenterologist).
- The data is insufficient to support the superiority of any studied antibiotic to any other.
- There is no published clinical trial evidence for the use of repeated courses of antibiotics, such as rifaximin, for recurrent SIBO. The practice of antibiotic retreatment in SIBO is solely based on anecdotal evidence and expert opinion. [9]
- Data to support the use of Xifaxan (rifaximin) in children is limited to one low-quality, small, single-center, open-label study. [10] There is no data comparing Xifaxan (rifaximin) to any other treatment in this population.

Cross References
Viberzi, eluxadoline, Medication Policy Manual, Policy No. dru458

References

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Revision History

Revision Date	Revision Summary
7/10/2025	No criteria change with this annual review.
6/20/2024	No criteria changes with this annual review.
6/15/2023	No changes to criteria with this annual update.
12/9/2022	• For COT: Removed IBS-D and SIBO from COT eligibility as indications are for acute management; full policy criteria must be met. • For SIBO: Added "no prior treatment with Xifaxan" to ensure consistent application for new and existing members.
6/17/2022	No criteria changes with this annual update.
7/16/2021	Removed antispasmodic step criteria when Xifaxan (rifaximin) is used for IBS-D.
4/21/2021	Modified COT language to allow correct coverage criteria for covered diagnoses. No change to intent of policy.
7/22/2020	• For SIBO: Added requirement for diagnosis by a specialist (gastroenterologist). • For hepatic encephalopathy: Authorization duration changed to "may." • Added continuation of therapy language.
7/24/2019	Removed coverage criteria for use in travelers' diarrhea (moved to "not medically necessary").
9/21/2018	No criteria changes with this annual update.
9/8/2017	Criteria for IBS-D updated to include hyoscyamine step therapy; added requirement for diagnosis by a gastroenterologist for SIBO.
6/10/2016	Criteria for hepatic encephalopathy updated, step therapy added for IBS-D, criteria for SIBO added.

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