

PRIOR AUTHORIZATION POLICY

POLICY: Antibiotics – Xifaxan Prior Authorization Policy

- Xifaxan® (rifaximin tablets – Salix)

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OVERVIEW

Xifaxan, a rifamycin antibiotic, is indicated for the following uses:¹

- **Hepatic encephalopathy (HE)**, to reduce the risk of overt disease in adults.
- **Irritable bowel syndrome with diarrhea (IBS-D)**, in adults.
- **Travelers' diarrhea (TD)**, caused by noninvasive *Escherichia coli* in patients \geq 12 years of age.

Limitations of Use: TD: Xifaxan should not be used in patients with diarrhea complicated by fever or blood in the stool or diarrhea due to pathogens other than *E. coli*.¹

In the trials of Xifaxan for HE, 91% of the patients were using lactulose concomitantly.¹ Due to small sample size, differences in the treatment effect of those patients not using lactulose concomitantly could not be assessed. Data are lacking to support the use of Xifaxan without concomitant use of lactulose.

Guidelines

- **Hepatic Encephalopathy:** The European Association for the Study of the Liver (EASL) guidelines for HE (2022) recommend Xifaxan as an adjunct to lactulose as secondary prophylaxis following \geq 1 additional episode of overt HE within 6 months of the first episode.² Guidelines also state that in patients with cirrhosis and previous episodes of overt HE, Xifaxan can be considered for prophylaxis of HE prior to non-urgent transjugular intrahepatic portosystemic shunt (TIPS) placement.
- **IBS with Diarrhea:** The American College of Gastroenterology (ACG) guidelines for the management of IBS (2021) suggest Xifaxan to reduce the global symptoms of IBS and to reduce bloating in non-constipated IBS patients.³ In addition, the American Gastroenterological Association (AGA) guidelines on the management of IBS-D (2022) suggest Xifaxan over no drug treatment for patients with IBS-D (conditional recommendation, moderate evidence).⁴
- **Small Intestine Bacterial Overgrowth (SIBO):** Clinical guidelines from the ACG (2020) and the AGA (2020) list Xifaxan as an option for the treatment of SIBO.^{9,10} ACG also states that the diagnosis of SIBO can be made with breath testing (glucose hydrogen or lactulose hydrogen), or by small bowel aspiration and culture. Of note, in clinical trials, patients were treated with Xifaxan for a 7-day course for SIBO.⁵⁻⁸
- **Travelers' Diarrhea:** The Centers for Disease Control and Prevention Yellow Book – Health Information for International Travel (2024) states that Xifaxan may be used for the treatment of moderate, noninvasive travelers' diarrhea and may be used for the treatment of severe, non-dysenteric travelers' diarrhea.¹¹ In addition, guidelines developed by an expert panel (2017) state that Xifaxan is appropriate for moderate or severe, non-dysenteric travelers' diarrhea, and when indicated for the prophylaxis of travelers' diarrhea.¹²
- **Pouchitis:** The American Gastroenterological Association (AGA) guidelines on the management of pouchitis and inflammatory pouch disorders (2024) suggest using antibiotic therapy for the treatment of infrequent symptoms of pouchitis and list the preferred antibiotics as ciprofloxacin and/or metronidazole with a treatment duration of 2 to 4 weeks. The AGA suggests against the use

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of antibiotics for primary prevention of pouchitis. Chronic antibiotic-dependent pouchitis (CADP) is defined as recurrent episodes of pouchitis that respond to antibiotic therapy but relapse shortly after stopping antibiotics. The AGA suggests using chronic antibiotic therapy to treat CADP after ruling out alternative etiologies.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Xifaxan. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of chronic antibiotic-dependent pouchitis, approval for this condition requires Xifaxan to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Xifaxan is recommended in those who meet one of the following criteria:

FDA-Approved Indications

- Hepatic Encephalopathy.** Approve Xifaxan 550 mg tablets for 6 months if the patient meets ALL of the following (A, B, and C):
 - Patient is ≥ 18 years of age; AND
 - According to the prescriber, the patient has previously had overt hepatic encephalopathy; AND
 - Patient meets ONE of the following criteria (i or ii):
 - Xifaxan will be used concomitantly with lactulose; OR
 - According to the prescriber, the patient has a contraindication or significant intolerance to treatment with lactulose.
- Irritable Bowel Syndrome with Diarrhea.** Approve Xifaxan 550 mg tablets for 14 days if the patient is ≥ 18 years of age.
- Travelers' Diarrhea.** Approve Xifaxan 200 mg tablets for 3 days if the patient meets ALL of the following (A, B, and C):
 - Patient is ≥ 12 years of age; AND
 - According to the prescriber, the patient is afebrile; AND
 - According to the prescriber, the patient does not have blood in the stool.

Other Uses with Supportive Evidence

- Small Intestine Bacterial Overgrowth.** Approve Xifaxan (either strength) for 14 days if small intestine bacterial overgrowth is diagnosed by ONE of the following (A, B, or C):
 - Glucose hydrogen breath test; OR
 - Lactulose hydrogen breath test; OR
 - Small bowel aspiration and culture.
- Pouchitis, Chronic Antibiotic-Dependent.** Approve Xifaxan (either strength) for 1 year if the patient meets ALL of the following (A, B, C, D, and E):

- A) Patient has recurrent pouchitis; AND
Note: Recurrent pouchitis is typically considered a of ≥ 3 pouchitis episodes within a 12 month period.
- B) According to the prescriber, the episodes of pouchitis respond to antibiotic therapy but relapse shortly after antibiotic discontinuation; AND
- C) According to the prescriber, alternative causes of recurrent pouchitis have been ruled out; AND
Note: Alternative etiologies of recurrent pouchitis include but are not limited to *Clostridioides difficile* infection of the pouch, mechanical obstructions, pelvic floor dysfunction.
- D) Patient has tried long-term antibiotic therapy trials (at least 4 weeks) of BOTH ciprofloxacin and metronidazole for remission maintenance; AND
- E) The medication is prescribed by, or in consultation with, a gastroenterologist.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Xifaxan is not recommended in the following situations:

1. ***Helicobacter pylori* Infection.** The ACG guidelines for the treatment of *H. pylori* do not address the use of Xifaxan.¹³ There are limited trials assessing the efficacy of Xifaxan in the treatment of *H. pylori* infection in adults; the available studies are small, of poor quality, and not conducted in the United States. More data are needed to define the place in therapy of rifaximin in the treatment of *H. pylori*.
2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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