PRIOR AUTHORIZATION POLICY

POLICY: Antibiotics – Xifaxan Prior Authorization Policy
- Xifaxan® (rifaximin tablets – Salix Pharmaceuticals)

REVIEW DATE: 11/18/2020

OVERVIEW

Xifaxan, a rifamycin antibiotic, is indicated for the following uses:[1]
- **Hepatic encephalopathy**, to reduce the risk of overt disease in adults.
- **Irritable bowel syndrome (IBS) with diarrhea**, in adults.
- **Traveler's diarrhea**, caused by noninvasive *Escherichia coli* in patients ≥ 12 years of age.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Xifaxan and other antibacterial drugs, Xifaxan when used to treat infection should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria.[1] When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Limitations 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 *E. coli*.[1]

Clinical Efficacy

The efficacy of Xifaxan for the treatment of small intestinal bacterial overgrowth (SIBO) was established in four clinical trials.[2-4] In two prospective, parallel-group trials, the efficacy of Xifaxan was assessed in 170 patients with a diagnosis of SIBO established with a glucose breath test (GBT).[2,3] Patients were randomized to rifaximin 600 mg/day, 800 mg/day, 1,200 mg/day, or 1,600 mg/day for 7 days. One month after treatment, the GBT normalization rate was 58% to 60% with 1,200 mg/day and 80% with 1,600 mg/day. In a clinical trial, 142 patients with SIBO were randomized to Xifaxan 1,200 mg/day or metronidazole 750 mg/day, both given for 7 days.[4] The GBT normalization rate, 1 month after treatment, was significantly higher with Xifaxan compared with metronidazole (63.4% vs. 43.7% odds ratio: 1.50; 95% confidence interval: 1.14, 4.38; $P < 0.05$). In a prospective trial, 50 consecutive children (mean age: 9.9 years; range: 3.2 to 15 years) with IBS were screened for SIBO.[5] There were 33 patients with SIBO and all patients were treated with rifaximin 600 mg/day for 7 days. Normalization of the lactulose breath test occurred in 64% of the patients with SIBO.

Guidelines

- **Hepatic Encephalopathy**: The American Association for the Study of Liver Diseases and the European Association for the Study of the Liver (AASLD/EASL) developed practice guidelines for the management of hepatic encephalopathy (2014).[6] The AASLD/ESLD guidelines state that Xifaxan add-on to lactulose is effective for the prevention of overt hepatic encephalopathy and for the prevention of recurrent episodes of hepatic encephalopathy after the second episode.
- **Irritable Bowel Syndrome with Diarrhea (IBS-D)**: The American College of Gastroenterology (ACG) guidelines for the management of IBS (2018) suggest Xifaxan to reduce the global symptoms of IBS and to reduce bloating in non-constipated IBS patients.[7] In addition, the American Gastroenterological Association (AGA) guidelines on the management of IBS (2014) suggest Xifaxan over no drug treatment for patients with IBS-D.[8]

- **Small Intestine Bacterial Overgrowth:** Clinical guidelines from the ACG (2020) list Xifaxan 550 mg three times daily as a suggested antibiotic for the treatment of SIBO.[9] 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. In addition, practice guidelines from the AGA (2020) list Xifaxan 800 – 1,200 mg/day as an option for the treatment of SIBO.[10]
- **Travelers' Diarrhea**: The Centers for Disease Control and Prevention (CDC) Yellow Book – Health Information for International Travel (2020) state that Xifaxan may be used for the treatment of moderate, noninvasive travelers' diarrhea and may be used for the treatment of severe, nondysenteric travelers' diarrhea.[11] In addition, guidelines developed by an expert panel (2017) state that Xifaxan is appropriate for moderate or severe, nondysenteric travelers' diarrhea, and when indicated for the prophylaxis of travelers' diarrhea.[12]

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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

FDA-Approved Indications

1. **Hepatic Encephalopathy.** Approve Xifaxan 550 mg tablets for 6 months if the patient meets the following criteria (A, B, and C):
   A) Patient is ≥ 18 years of age; AND
   B) According to the prescriber, the patient has previously had overt hepatic encephalopathy; AND
   C) Xifaxan will be used concomitantly with lactulose.

2. **Irritable Bowel Syndrome with Diarrhea.** Approve Xifaxan 550 mg tablets for 14 days if the patient is ≥ 18 years of age.

3. **Traveler's Diarrhea**. Approve Xifaxan 200 mg tablets for 3 days if the patient meets the following criteria (A, B, and C):
   A) Patient is ≥ 12 years of age; AND
   B) According to the prescriber, the patient is afebrile; AND
   C) According to the prescriber, the patient does not have blood in the stool.

Other Uses with Supportive Evidence

4. **Small Intestine Bacterial Overgrowth:** Approve Xifaxan (either strength) for 14 days if small intestine bacterial overgrowth is diagnosed by ONE of the following criteria (A, B or C):
   A) Glucose hydrogen breath test; OR
   B) Lactulose hydrogen breath test; OR
   C) Small bowel aspiration and culture.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Xifaxan is not recommended in the following situations:

1. ***Helicobacter pylori* Infection**. There are limited data assessing the efficacy of Xifaxan in the treatment of *H. pylori* infection in adults.[7-9] The available studies are small, of poor quality, and none of the studies were conducted in the United States. In addition, treatment guidelines from the American College of Gastroenterology do not address the use of Xifaxan for 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.

REFERENCES

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