rifaximin (Xifaxan®)

EOCCO POLICY

Policy Type: PA Pharmacy Coverage Policy: EOCCO056

Description

Rifaximin (Xifaxan) is an orally administered rifamycin antibacterial agent that inhibits bacterial RNA synthesis by binding to bacterial DNA-dependent RNA polymerase.

Length of Authorization

- Initial:
  - i. Irritable Bowel Syndrome with Diarrhea (IBS-D): one time approval
  - ii. Hepatic encephalopathy: six months
  - iii. Traveler's diarrhea: one time approval
- Renewal:
  - i. IBS-D: one-time approval, maximum of three fills per lifetime
  - ii. Hepatic encephalopathy: 12 months
  - iii. Traveler's diarrhea: N/A

Quantity limits

Product Name	Dosage Form	Indication	Quantity Limit	DDID
rifaximin (Xifaxan)	550 mg tablets	Treatment of irritable bowel syndrome with diarrhea (IBS-D).	42 tablets/ 14 days	150969, 152498
		Hepatic encephalopathy recurrence.	60 tablets/30 days	
	200 mg tablets	Travelers' diarrhea caused by noninvasive strains of Escherichia coli	9 tablets/3 days	088395, 088393

Initial Evaluation

I. Rifaximin (Xifaxan) may be considered medically necessary when the following criteria below are met:
  A. A diagnosis of one of the following:
    i. **Irritable Bowel Syndrome with Diarrhea (IBS-D)**; **AND**
      a. Member is 18 year of age or older; **AND**
      b. Rifaxamin (Xifaxan) is prescribed by or in consultation with a gastroenterologist; **AND**
      c. Treatment with at least <u>three therapies from different groups</u> have been tried and failed, not tolerated or all are contraindicated (please note, if one or more groups is contraindicated, a trial of three agents from the remaining classes will be required):

a. Group 1: antidiarrheal (e.g., loperamide, bismuth subsalicylate, diphenoxylate/atropine, paregoric)
b. Group 2: bile acid sequestrant (e.g., cholestyramine, colestipol)
c. Group 3: antispasmodic (e.g., dicyclomine, hyoscyamine)
d. Group 4: Tricyclic serotonergic agent: (e.g., amitriptyline, nortriptyline, imipramine, desipramine)

OR

ii. **Traveler's diarrhea**; **AND**
   a. Member is 12 years of age or older; **AND**
   b. Treatment with azithromycin (Zithromax) or a fluoroquinolone (e.g., ciprofloxacin) have been ineffective, not tolerated, or BOTH are contraindicated; **OR**

iii. **Hepatic encephalopathy**; **AND**
   a. Member is 18 year of age or older; **AND (a or b)**
      a. Treatment with lactulose has been ineffective, contraindicated, or not tolerated; **OR**
      b. Rifaxamin (Xifaxan) will be used as add-on treatment

II. Rifaximin (Xifaxan) is considered investigational when used for all other conditions, including but not limited to:
   A. Small Intestinal Bacterial Overgrowth (SIBO)

Renewal Evaluation

I. **Irritable Bowel Syndrome with Diarrhea (IBS-D); AND**
   A. There has been a 10 week treatment-free period since prior approval of rifaximin (Xifaxan); **AND**
   B. The member has not had more than two prior treatments with rifaximin (Xifaxan). A maximum of three approvals is allowed per lifetime for the treatment of IBS-D; **OR**

II. **Hepatic encephalopathy; AND**
   A. Clinical documentation indicating disease stability or improvement.

Supporting Evidence

I. Rifaximin (Xifaxan) is indicated for adults and pediatric patients 12 years of age and older with travelers' diarrhea, and adults older than 18 years of age with hepatic encephalopathy or IBS-D. Infectious Diseases Society of America clinical practice guidelines recommend treatment with fluoroquinolones or azithromycin as first line treatment of travelers' diarrhea.

II. The FDA approved dose is 200 mg three times daily for three days for traveler's diarrhea.

III. The American Association for the Study of Liver Diseases and European Association for the Study of the Liver clinical practice guidelines suggest initial therapy with lactulose for the

treatment of hepatic encephalopathy. Rifaximin (Xifaxan) is an effective add-on therapy to lactulose for prevention of recurrence.

IV. Treatment options for IBS-D include antidiarrheals, antibiotics, antispasmodics, antidepressants, and bile acid sequestrants. The American College of Gastroenterology gave moderate or weak recommendations for all IBS-D therapies due to poor quality of evidence and applicability to patient groups. Due to insufficient comparative evidence for efficacy, other treatment options provide a better value over rifaximin (Xifaxan). Of the antidepressants, tricyclic agents have shown to slow intestinal transit; however, SSRI/SNRI agents have less published data and the data available is inconsistent in showing benefit in IBS.

V. Rifaximin (Xifaxan) will be authorized for a total of three courses per lifetime for IBS-D per FDA label. In clinical studies, 14-day repeat treatment courses were separated by 10 weeks.

Investigational or Not Medically Necessary Uses

I. Small Intestinal Bacterial Overgrowth (SIBO)
   A. Although likely an association exists between IBS-D and SIBO, the evidence linking a causal relationship between the two diagnoses is conflicting.
   B. Intestinal motility disorders and chronic pancreatitis are estimated to account for approximately 90 percent of cases of SIBO. Underlying etiology of SIBO should be addressed prior to pharmacologic therapy. Common causes of SIBO include: anatomic abnormalities; strictures, motility Issues, hypochlorhydria, immunodeficiency, chronic pancreatitis, cirrhosis, end stage renal disease, or medications (e.g., proton pump inhibitors, tricyclic antidepressants, opioids).
   C. Rifaximin (Xifaxan) use in adults with SIBO has not been evaluated in multicenter, prospective, randomized, placebo-controlled trials. Although five single-site, open-label, randomized controlled trials demonstrated a potential modest benefit of rifaximin (Xifaxan) use in adults with a SIBO, the studies were poorly designed, had a small sample size, and had minimal follow up.
   D. Gastroenterological Association Institute clinical guidelines for treatment of SIBO have not been established.

References

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Policy Implementation/Update:

Date Created	August 2015
Date Effective	August 2015
Last Updated	July 2019
Last Reviewed	08/2015; 04/2019, 07/2019

Action and Summary of Changes	Date
Criteria for the IBS-d indicated updated to require three prior therapies prior to payment consideration. Additionally, agents with low quality or conflicting data were removed from the list of conventional agents allowed for previous trial and failure. Rearrangement of criteria to include the most requested indication first.	07/2019
Updated to policy format, evidence for the investigational use of rifaximin (Xifaxan) in SIBO updated, addition of specialist involvement in prescribing for IBS-D, age criteria edited.	04/2019