BlueCross BlueShield
Federal Employee Program
Federal Employee Program®
1310 G Street, N.W.
Washington, D.C. 20005
202.942.1000
Fax 202.942.1125

5.01.34

Section:	Prescription Drugs	**Effective Date:**	January 1, 2019
Subsection:	Anti-Infective Agents	**Original Policy Date:**	July 24, 2015
Subject:	Xifaxan	**Page:**	1 of 5

Last Review Date: November 30, 2018

Xifaxan

Description

Xifaxan (rifaximin)

Background
Xifaxan is a semi-synthetic antibacterial derived from rifampin. Xifaxan is used for the treatment of travelers' diarrhea (TD) caused by *Escherichia coli* (E.coli), for the reduction of the risk of recurring overt hepatic encephalopathy (HE), and for the treatment of irritable bowel syndrome with diarrhea (IBS-D) characterized by pain or discomfort in the abdomen and loose or watery stools. While an off-label use, Xifaxan is considered the standard of care in the treatment of small intestinal bacterial overgrowth, as studies have shown its superior efficacy and side effect profile when compared to alternatives. Xifaxan acts by binding to the beta-subunit of bacterial DNA-dependent RNA polymerase blocking one of the steps in transcription. This results in inhibition of bacterial protein synthesis and consequently inhibits the growth of bacteria (1-3).

Regulatory Status
FDA-approved indication: Xifaxan is a rifamycin antibacterial indicated for: (1)

1. Treatment of travelers' diarrhea (TD) caused by noninvasive strains of *Escherichia coli* in adults and pediatric patients 12 years of age and older.
2. Reduction in the risk of overt hepatic encephalopathy recurrence in adults
3. Treatment of irritable bowel syndrome with diarrhea in adults

Limitation 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 *Escherichia coli* (1).

Off-label Use:

1. Small intestinal bacterial overgrowth (SIBO) - Xifaxan has been studied in adults 18 years of age or older for the off-label use for treatment of small intestinal bacterial overgrowth at a dose of one 550 mg tablet taken orally three times per day for 14 days (2-3)

Xifaxan is contraindicated in people with a hypersensitivity to rifaximin, any of the rifamycin antimicrobial agents, or any of the components of Xifaxan (1).

Xifaxan was not found to be effective in patients with diarrhea complicated by fever and/or blood in the stool or diarrhea due to pathogens other than *Escherichia coli*. Discontinue Xifaxan if diarrhea symptoms get worse or persist more than 24 to 48 hours and alternative antibiotic therapy should be considered. Xifaxan has been associated with *Clostridium difficile*-associated diarrhea (CDAD) and may range in severity from mild diarrhea to fatal colitis (1).

Xifaxan dosage for irritable bowel syndrome with diarrhea is one 550 mg tablet taken orally three times a day for 14 days. Patients who experience a recurrence of symptoms can be retreated up to two times with the same dosage regimen (1).

The safety and effectiveness of Xifaxan have not been established in pediatric patients less than 12 years of age with TD or in patients less than 18 years of age for HE and IBS-D (1).

Related policies
Viberzi

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Xifaxan may be considered **medically necessary** for patients 12 years of age or older for the treatment of travelers' diarrhea caused by noninvasive strains of *Escherichia coli,* or patients 18 years of age or older for the reduction in risk of hepatic encephalopathy; for the treatment of irritable bowel syndrome with diarrhea in patients who have had an inadequate treatment response, intolerance, or contraindication two anti-diarrheal medications and dietary modification; for the treatment of small intestinal bacterial overgrowth in patients 18 years of age or older.
Xifaxan is considered **investigational** in patients under 12 years of age and for all other indications.

Prior-Approval Requirements

Diagnoses

Patient must have **ONE** of the following:

1. Travelers' diarrhea caused by noninvasive strains of *Escherichia coli*
    a. 12 years of age or older

2. Hepatic encephalopathy
    a. 18 years of age and older

3. Irritable bowel syndrome with diarrhea (IBS-D)
4. Small intestinal bacterial overgrowth (SIBO)

    AND ALL of the following for **BOTH** IBS-D and SIBO:
    a. 18 years of age or older
    b. Inadequate treatment response, intolerance, or contraindication to **TWO** anti-diarrheal medications
    c. Inadequate treatment response to dietary modification (such as low carbohydrate diet, exclusion of gas producing foods, lactose free diet if intolerant)

Prior – Approval *Renewal* Requirements

Diagnoses

Patient must have the following:

1. Travelers' diarrhea caused by noninvasive strains of *Escherichia coli*
    a. 12 years of age or older

2. Hepatic encephalopathy
    a. 18 years of age and older

3. Irritable bowel syndrome with diarrhea (IBS-D)
4. Small intestinal bacterial overgrowth (SIBO)

AND ALL of the following for **BOTH** IBS-D and SIBO:

a. 18 years of age or older
b. Inadequate treatment response, intolerance, or contraindication to **TWO** anti-diarrheal medications
c. Inadequate treatment response to dietary modification (such as low carbohydrate diet, exclusion of gas producing foods, lactose free diet if intolerant)

Policy Guidelines

Pre - PA Allowance

Age	12 years of age or older
Quantity	200 mg – 9 tablets per 365 days

Prior - Approval Limits

Quantity	**Travelers' Diarrhea** 200 mg – 9 tablets per 90 days
Duration	3 months
Quantity	**Hepatic Encephalopathy** 550 mg – 180 tablets per 90 days
Duration	12 months
Quantity	**Irritable Bowel Syndrome with Diarrhea (IBS-D) OR Small Intestinal Bacterial Overgrowth (SIBO)** 550 mg – 126 tablets per **365 days**

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Xifaxan is a semi-synthetic antibacterial derived from rifampin indicated for use in patients 12 years of age and older with travelers' diarrhea caused by noninvasive strains of *Escherichia coli* and in patients 18 years of age and older for the reduction in risk of overt hepatic

encephalopathy recurrence and the treatment of irritable bowel syndrome with diarrhea or small intestinal bacterial overgrowth (SIBO). There are no adequate and well-controlled studies to document the safety and efficacy of Xifaxan in children (1).

Prior approval is required to ensure the safe, clinically appropriate and cost effective use of Xifaxan while maintaining optimal therapeutic outcomes.

References

1. Xifaxan [package insert]. Bridgewater, NJ: Salix Pharmaceuticals, Inc.; January 2018.
2. Lauritano EC, Gabriello M, Scarpellini E, et al. Antibiotic therapy in small intestinal bacterial overgrowth: rifaximin versus metronidazole. *Eur Rev Med Pharmacol Sci.* 2009 Mar-Apr;13(2):111-6.
3. Scarpellini E, Gabrielli M, Lauritano CE, et al. High dosage rifaximin for the treatment of small intestinal bacterial overgrowth. *Aliment Pharmacol Ther* 2007; 25:781.

Policy History

Date	Action
July 2015	New addition to PA
September 2015	Annual review
December 2015	Annual review
March 2016	Annual review Removal of renewal for irritable bowel syndrome Policy code changed from 5.03.34 to 5.01.34
September 2016	Match initiation to renewal and add renewal limits for IBS-D
December 2016	Annual review
December 2017	Annual editorial review and reference update Change of duration for Hepatic Encephalopathy from 3 months to 12 months Addition of Small intestinal bacterial overgrowth (SIBO)
November 2018	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on November 30, 2018 and is effective on January 1, 2019.