



RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Xifaxan is a semi-synthetic antibacterial derived from rifampin. Xifaxan is used for the treatment of traveler's 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 traveler's 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 (IBS-D) 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)
2. Prevention of Traveler's Diarrhea (TD) – Xifaxan has been studied in adults 18 years of age or older for the off-label use for treatment of prevention of traveler's diarrhea at a dose of one 200 mg tablet taken up to three times per day for 14 days (4)

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).

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.; October 2020.
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.
4. DuPont, H.L., Z.D. Jiang, et al. 2005. A randomized, double-blind, placebo-controlled trial of rifaximin to prevent travelers' diarrhea. *Ann. Intern. Med.* 142: 805-812.