

Applicable Drugs: Xifaxan (rifaximin)

Preferred: N/A

Non-preferred: N/A

Date of Origin: 2/1/2013

Date Last Reviewed / Revised: 5/21/2025

PRIOR AUTHORIZATION CRITERIA

(May be considered medically necessary when criteria I and III are met)

- I. Documented diagnosis of one of the following conditions A through C AND must meet criteria listed under applicable diagnosis:
 - A. Treatment of traveler's diarrhea caused by noninvasive strains of *Escherichia coli* and criteria 1 and 2 are met:
 1. Documented treatment failure or contraindication to azithromycin or a fluoroquinolone (ie, ciprofloxacin, levofloxacin).
 2. Minimum age requirement: 12 years old.
 - B. Irritable bowel syndrome with diarrhea (IBS-D) and criteria 1 and 2 are met:
 1. Documented treatment failure or contraindication a tricyclic antidepressant (eg, amitriptyline, nortriptyline) and an antispasmodic agent (eg, diphenoxylate-atropine, dicyclomine, hyoscyamine)
 2. Minimum age requirement: 18 years old.
 - C. Hepatic encephalopathy and criteria below are met:
 1. Documented recurrence of hepatic encephalopathy despite adherence with optimally dosed lactulose (titrated to maintain 2-3 bowel movements daily).
 2. Patient will continue to take and is adherent with optimally dosed lactulose therapy
 3. At least two episodes of overt hepatic encephalopathy (Conn score, ≥ 2) during the past six months
 4. Minimum age requirement: 18 years old.
 - D. Small intestinal bacterial overgrowth (SIBO) and criteria 1 and 2 are met:
 1. Documentation of one of the following:
 - a. Endoscopic culture with $>10^3$ bacteria colony forming units/mL.
 - b. Positive lactulose or glucose breath test with hydrogen increase of ≥ 20 ppm above baseline within 90 minutes.
 - c. Positive lactulose or glucose breath test for methane (≥ 10 ppm at any point during testing).

2. Documented treatment failure to at least two or contraindication to all systemic antibiotics (eg, ciprofloxacin, metronidazole, amoxicillin/clavulanate, doxycycline, neomycin, norfloxacin, trimethoprim-sulfamethoxazole).
 3. For methane-predominant bacterial overgrowth, Xifaxan will be used in combination with neomycin.
 4. Minimum age requirement: 12 years old.
- II. Request is supported with the appropriate FDA labeling, or its use is supported by current clinical practice guidelines.
 - III. Refer to plan document for the list of preferred products. If requested agent is not listed as a preferred product, must have a documented failure, intolerance, or contraindication to a preferred product(s).

EXCLUSION CRITERIA

- Treatment of diarrhea caused by pathogens other than *Escherichia coli*.
- Treatment of diarrhea complicated by fever or blood in stool
- Prevention of traveler's diarrhea.

OTHER CRITERIA

- N/A

QUANTITY / DAYS SUPPLY RESTRICTIONS

- Traveler's diarrhea: Nine 200 mg tablets for one 3-day course of therapy per 30 days.
- IBS-D: Forty-two 550 mg tablets for one 14-day course of therapy per 90 days.
- Hepatic encephalopathy: Sixty 550 mg tablets per 30 days.
- SIBO:
 - Adults: Forty-two 550 mg tablets for one 14-day course of therapy.
 - Pediatrics 12 to 17 years old: twenty-one 200 mg tablets for one 7-day course of therapy.

APPROVAL LENGTH

1. **Authorization:**
 - Traveler's Diarrhea: 1 time only per 30 days.
 - IBS-D: 1 time only per 90 days.
 - Hepatic Encephalopathy: 12 months.

- SIBO: 1 time per treatment course.

2. Re-Authorization:

- Traveler's Diarrhea: N/A
- IBS-D: patients who have a documented prior response to Xifaxan® but have relapsed may be authorized to receive a maximum of two additional courses of therapy (for a total of three courses of therapy).
- Hepatic Encephalopathy: 12 months: An updated letter of medical necessity or progress notes showing current medical necessity criteria are met and that the medication is effective, ie positive clinical response in mental status.

APPENDIX

- N/A

REFERENCES

1. Riddle MS, DuPont HL, Connor BA. ACG clinical guideline: Diagnosis, treatment, and prevention of acute diarrheal infections in adults. *Am J Gastroenterol*. 2016;111(5):602-622. doi: 10.1038/ajg.2016.126.
2. Lembo A, Sultan S, Chang L, Heidelbaugh JJ, Smalley W, Verne GN. AGA clinical practice guideline on the pharmacological management of irritable bowel syndrome with diarrhea. *Gastroenterology*. 2022;163(1):137-151. doi: 10.1053/j.gastro.2022.04.017.
3. Vilstrup H, Amodio P, et al. Hepatic encephalopathy in chronic liver disease: 2014 Practice Guideline by the American Association for the Study Of Liver Diseases and the European Association for the Study of the Liver. *Hepatology*. 2014;60(2):715-735. doi: 10.1002/hep.27210.
4. Pimentel M, Saad RJ, Long MD, Rao SSC. ACG clinical guideline: Small intestinal bacterial overgrowth. *Am J Gastroenterol*. 2020;115(2):165-178. doi: 10.14309/ajg.0000000000000501.
5. Xifaxan. Prescribing information. Salix Pharmaceuticals Inc; 2023. Accessed May 21, 2025. <https://www.xifaxan.com/globalassets/pi/xifaxan550-pi.pdf>
6. Kimberlin DW, Brady MT, Jackson MA, Long SS. Section 4: antimicrobial agents and related therapy. In: Red Book, 32nd ed, Committee on Infectious Diseases (Ed); American Academy of Pediatrics, Itasca 2021.
7. Bass NM, Mullen KD, Sanyal A, et al. Rifaximin treatment in hepatic encephalopathy. *N Engl J Med*. 2010;362(12):1071-81. doi: 10.1056/NEJMoa0907893.

DISCLAIMER: Medication Policies are developed to help ensure safe, effective and appropriate use of selected medications. They offer a guide to coverage and are not intended to dictate to providers how to practice medicine. Refer to Plan for individual adoption of specific Medication Policies. Providers are expected to exercise their medical judgement in providing the most appropriate care for their patients.