Rifaximin (XIFAXAN) in Symptomatic Small Intestinal Bacterial Overgrowth (SIBO) and Irritable Bowel Syndrome with Diarrhea (IBS-D) Criteria for Use

November 2021

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. THE CLINICIAN SHOULD USE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.

The Product Information should be consulted for detailed prescribing information.

See the VA National PBM-MAP-VPE Monograph on this drug at the *PBM INTRAnet* site for further information.

Exclusion Criteria

If ANY of the following are true, the patient will not meet criteria for rifaximin.

- ☐ Known hypersensitivity to rifaximin, rifamycin antimicrobial agents, or any other component of rifaximin.
- ☐ No documented benefit from prior rifaximin therapy for SIBO or IBS-D.
- ☐ **For SIBO**: Reoccurrences of SIBO after durable response (e.g., ≥ 3 months) to one of the antibiotic regimens listed under **Additional Inclusion Criteria**. These reoccurrences should be retreated rather than proceed to rifaximin.[1]

Inclusion Criteria for Rifaximin Treatment of SIBO without IBS-D

ALL of the following must be met:

- ☐ Patient is under the care of a VA or VA Community Care gastroenterologist or locally designated provider qualified to diagnose and treat both symptomatic SIBO and irritable bowel syndrome with diarrhea (IBS-D)
- ☐ Documented diagnosis or working diagnosis of SIBO (without IBS-D) based on typical clinical presentation and, if testing is feasible, positive carbohydrate breath test or jejunal aspirate culture

Additional Inclusion Criteria for Rifaximin Treatment of SIBO without IBS-D

Symptoms that do not respond to a 7- to 10-day therapeutic trial of ONE of the following, unless the treatment is medically inadvisable or the patient has a history of intolerance to the treatment:

- ☐ **Metronidazole** alone (250–500 mg 2–3 times a day; maximum two courses in a 6-month period)
- ☐ **Metronidazole in combination** with either **cephalexin** (500 mg 3–4 times a day) or **sulfamethoxazole / trimethoprim** double-strength (1 tab 2 times a day)
- ☐ **Amoxicillin-clavulanate** 500 mg 3 times a day or 875 mg 2 times a day
- ☐ **Neomycin** 500 mg 2 times a day

☐ **Previous ciprofloxacin** (250–500 mg twice a day) for SIBO. May count as the required prior antibiotic if already tried. It is not recommended because of its adverse effect profile.[1]

Inclusion Criteria for Rifaximin Prophylaxis of Recurrent SIBO

ALL of the following must be met:

☐ Patient is under the care of a VA or VA Community Care gastroenterologist or locally designated provider qualified to diagnose and treat both symptomatic SIBO and irritable bowel syndrome with diarrhea (IBS-D)

☐ Documented diagnosis or working diagnosis of SIBO (without IBS-D) based on typical clinical presentation and, if testing is feasible, positive carbohydrate breath test or jejunal aspirate culture

☐ Documented lack of benefit from prior metronidazole or other antibiotic therapy for SIBO

☐ Documented benefit from prior rifaximin for SIBO

☐ ≥ 4 distinct and well-documented SIBO episodes in one year

☐ Risk factor for recurrent SIBO (e.g., small intestinal strictures [Crohn's disease, radiation, surgery]; surgically created blind loops [end-to-side anastomosis]; etc.[2])

☐ Prescription is written for periodic administration of rifaximin (e.g., for 5–10 days out of every month or every other week).

Inclusion Criteria for IBS-D (with or without SIBO)

ALL of the following must be met:

☐ Patient is under the care of a VA or VA Community Care gastroenterologist or locally designated provider qualified to diagnose and treat both symptomatic SIBO and IBS-D.

☐ Moderate to severe IBS-D (with or without SIBO).

☐ Moderate to severe symptoms (e.g., pain, bloating) continue or recur despite treatment.

☐ Trial of **soluble fiber** (e.g., psyllium) for 4 weeks unless it is medically inadvisable or was not tolerated.

☐ Trial of a **tricyclic antidepressant** (e.g., desipramine, nortriptyline) for 4 weeks unless it is medically inadvisable (e.g., elderly, suicidal ideation, QT prolongation, etc.) or was not tolerated.

☐ **Only if female with severe, chronic IBS-D (generally ≥ 6 months), and requirements of the Alosetron REMS Program are met**: Trial of **alosetron** for 4 weeks unless it is medically inadvisable or was not tolerated.

☐ **Only if SIBO is diagnosed**: A 7- to 10-day therapeutic trial of one of the antibiotics listed for SIBO without IBS-D (in addition to meeting all the other criteria for IBS-D).

Footnotes

[1] Ciprofloxacin-naïve patients with SIBO should first be tried on one of the other antibiotics listed under **Additional Inclusion Criteria**.

[2] Other example risk factors for recurrent SIBO: Gastrocolic or jejunocolic fistula, ileocecal valve resection, or other abnormal communication between the proximal and distal gastrointestinal tract.

Supplemental Information

This supplemental information is provided to assist in adjudication of requests for rifaximin for SIBO and IBS-D.

Section	Issues for Consideration

Use of Rifaximin for SIBO and IBS-D	• Some patients with SIBO may have IBS, and vice versa.
	• **Rifaximin is not FDA-approved for the treatment of SIBO.**
	• Rifaximin is FDA-approved for the treatment of IBS-D in adults.
	  ○ Rifaximin for IBS should be restricted to patients who have the IBS-D subtype and have not responded to effective and less costly symptom-based alternative therapies.
	  ○ For more information, refer to the monograph on rifaximin for IBS-D available at *PBM INTRAnet* .

Dosage and Administration	• **For SIBO without IBS-D**: 200 mg 3 times a day for 7 days to 550 mg 3 times a day for 10 days.
	  ○ Clinical study doses for SIBO have ranged from 200 to 550 mg 3 times a day, and duration has often been 7 to 10 days (range, 5 to 28 days).
	  ○ The optimal dosage regimen of rifaximin in SIBO has not been determined.
	  ○ In case there is reoccurrence of SIBO signs and symptoms after a documented benefit from rifaximin, retreatment with rifaximin may be given up to two times for a maximum of 3 courses of treatment.
	• **For IBS-D:** The approved dose for IBS-D is 550 mg 3 times a day for 14 days.
	  ○ Patients who experience reoccurrence can be retreated up to two times with the same regimen for a total of up to 3 courses of treatment.

Dispensing Limit	• Authorize one course of rifaximin with a maximum dispensing limit of three 200-mg or 550-mg tablets per day for up to 14 days.
Retreatment for SIBO	• Additional retreatments (renewals or refills) do not require re-evaluation of the patient if an initial course of rifaximin had been previously approved.
Prophylaxis for Recurrent SIBO	• If the patient benefited from metronidazole or other prior antibiotic therapy, has 4 or more distinct and well-documented SIBO episodes in one year, and has risk factors for recurrent SIBO, then that antibiotic may be used for prophylaxis.
Alosetron REMS Program	• See Alosetron Risk Evaluation and Mitigation Strategy (REMS) at https://www.alosetronrems.com/ • The purpose of the Alosetron REMS program is to reduce the risk of serious gastrointestinal adverse reactions including ischemic colitis and serious complications of constipation.

Revised: November 2021 (For SIBO, added two Exclusion Criteria previously noted under old Renewal Criteria; removed statements referring to renewals and refills, removed requirement for re-evaluation of patients prior to renewals or refills; retitled Inclusion Criteria for SIBO to "Treatment" of SIBO; changed previous ciprofloxacin from a note to an Inclusion Criterion for rifaximin treatment; added new Inclusion Criteria for rifaximin prophylaxis previously noted under old Renewal Criteria. For IBS-D, updated prior drugs to be consistent with the 2021 American College of Gastroenterology guideline on management of IBS by removing bile acid sequestrants, antispasmodics, antidiarrheals / loperamide, and low FODMAP diet, and adding soluble fiber and alosetron. Reformatted criteria for Cerner.)

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