

Rifaximin (Xifaxan) for Irritable Bowel Syndrome

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STEPS new drug reviews cover Safety, Tolerability, Effectiveness, Price, and Simplicity. Each independent review is provided by authors who have no financial association with the drug manufacturer.

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Rifaximin (Xifaxan) is an oral antibiotic previously marketed for the treatment of traveler's diarrhea and hepatic encephalopathy. It is now also labeled for the treatment of irritable bowel syndrome (IBS) with diarrhea.¹ Rifaximin has activity against anaerobic, gram-positive, and gram-negative bacteria, including *Clostridium difficile*. It is not systemically absorbed and is active only in the gastrointestinal tract. It may work by reducing bacterial byproducts and altering intestinal microbiota.²

Drug	Dosage	Dose form	Cost*
Rifaximin (Xifaxan)	500 mg orally three times per day for 14 days	500 mg tablets	\$1,400

*—Estimated retail price of 14 days of treatment based on information obtained at <http://www.goodrx.com> (accessed December 6, 2016).

SAFETY

Serious adverse effects from rifaximin are rare (less than 1%).³ It should not be used in patients with severe hepatic impairment and rarely causes *C. difficile*-associated colitis. Rifaximin does not alter the pharmacokinetics of a single dose of oral contraceptives, but its effect on daily oral contraceptive use is uncertain. Taking rifaximin with cyclosporine (Sandimmune) dramatically increases systemic availability of rifaximin (124-fold),¹ although the clinical significance of this is unknown.

Rifaximin is a U.S. Food and Drug Administration pregnancy risk category C drug, and its safety for use in breastfeeding women is unknown.

TOLERABILITY

Rifaximin is well tolerated, which is partially because of no systemic absorption. In controlled trials, the discontinuation rates because of adverse reactions were similar between rifaximin and placebo (0.4%).¹ Rare adverse effects include diarrhea, loss of taste, anorexia, nausea, and irritation of nasal passages.¹

EFFECTIVENESS

In those who have IBS with diarrhea that consists of abdominal symptoms and more than three bowel movements per day, rifaximin improves the patient's global impression of IBS symptoms compared with placebo. In two randomized trials with a total of 1,258 patients who had IBS with diarrhea, those taking rifaximin were more likely than those taking placebo to report adequate symptom relief after one month (41% vs. 31%; $P < .001$).⁴ For every 10 patients treated, one additional patient reported relief (number needed to treat [NNT] = 10; 95% confidence interval [CI], 5.8 to 48). Regarding specific symptoms, the NNT was 11 for a 30% decrease in abdominal pain (95% CI, 5.9 to 56) and 9 for decrease in diarrhea frequency (95% CI, 5.5 to 43).

The long-term effect of rifaximin has not been studied. Relief of IBS symptoms is sustained for at least 10 weeks following treatment in about 80% of patients who initially responded.² If symptoms recur after an initial response, retreatment is no more effective than placebo.² No studies have evaluated retreatment in patients who do

not respond to the initial treatment. No studies have directly compared rifaximin with other IBS treatments.

PRICE

A course of rifaximin costs approximately \$1,400 (available only as a generic), compared with \$20 (\$68) for dicyclomine (Bentyl), which is also used to relieve abdominal pain and discomfort from IBS.

SIMPLICITY

Rifaximin is given as one tablet every eight hours for 14 days.¹ There is currently no indication for a repeated course of therapy.

Bottom Line

Rifaximin has good overall tolerability. A relatively short course of treatment results in sustained clinical benefit for at least 10 weeks, eliminating the need for continued therapy, with an NNT of 10. However, it is

expensive and should be reserved for patients who cannot tolerate or did not respond to more affordable therapies.

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