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Note: Information on indications for use or diagnosis is assumed to be unavailable. All criteria may be applied retrospectively; prospective application is indicated with an asterisk [*]. The information contained is for the convenience of the public. HHSC is not responsible for any errors in transmission or any errors or omissions in the document.
Rifaximin (Xifaxan®)

1. Dosage [*]

Rifaximin is not indicated for treatment of systemic infections as less than 0.4% of drug is absorbed after oral administration.¹

1.1. Adults

Rifaximin, a derivative of rifampin, is a nonsystemically absorbed antibiotic with bactericidal activity against aerobic and anaerobic gram-positive and gram-negative microorganisms. Rifaximin is FDA-approved for use in managing travelers’ diarrhea due to noninvasive strains of *Escherichia coli* (*E. coli*) in adults and children 12 years of age and older, and should not be used in diarrhea due to pathogens other than *E. coli* or complicated by fever or blood in the stool.¹-¹¹

Rifaximin is also FDA-approved for reducing risk of overt hepatic encephalopathy (HE) recurrence in patients 18 years of age and older.¹, ⁵-⁷ In a randomized, double-blind, placebo-controlled trial over a six-month time period, Bass and cohorts¹² evaluated rifaximin safety and efficacy to maintain remission from HE episodes in 299 adult outpatients receiving concurrent lactulose therapy with a recent history of recurrent, overt HE. Results showed that the risk of a breakthrough HE episode was significantly lower with rifaximin therapy compared to placebo [hazard ratio (HR), 0.42; 95% confidence interval (CI), 0.28 to 0.64; P< 0.001]. The risk of hospitalization was also significantly lower in rifaximin-treated patients compared to those receiving placebo (HR, 0.50; 95% CI, 0.29 to 0.87; P = 0.01).

In May 2015, rifaximin gained FDA approval for treating irritable bowel syndrome with diarrhea (IBS-D) in adults. Pimentel and cohorts¹³ compared rifaximin efficacy to placebo in two separate trials involving a total of 1260 patients with IBS without constipation. Patients were randomly administered rifaximin 550 mg three times daily or placebo for 14 days, and then followed for 10 weeks. Results showed that rifaximin was significantly better than placebo in relieving IBS symptoms (e.g., bloating; abdominal pain; loose, watery stools). Data have also shown that rifaximin-treated patients respond better than those receiving placebo with a first recurrence of IBS-D.¹ A few small studies have evaluated rifaximin use in irritable bowel syndrome/Crohn’s disease. Gionchetti and cohorts¹⁴ assessed rifaximin efficacy compared to placebo in 26 ulcerative colitis patients unresponsive to steroid therapy and found that while overall clinical response was not significantly better than placebo, rifaximin-treated patients showed a significant reduction in stool frequency and rectal bleeding. Prantera and colleagues¹⁵ evaluated rifaximin dosing and efficacy compared to placebo in 83 Crohn’s disease patients and found no statistical difference in clinical response or clinical remission but observed a significantly reduced number of treatment failures in rifaximin-treated patients.

Although not FDA-approved, rifaximin has shown some efficacy in hepatic encephalopathy treatment and infectious diarrhea due to *Salmonella*, noninvasive *Shigella* and *Campylobacter*.¹⁶-²⁷ One small, open-label, randomized trial in 54 Korean patients with liver cirrhosis evaluated rifaximin therapy in hepatic encephalopathy and found rifaximin comparable to lactulose in improving blood ammonia, flapping tremor and mental status.²³ Similarly, Mas et al²⁴, in a randomized, double-blind, double-dummy trial, compared rifaximin to lactitol in 103 acute hepatic encephalopathy patients and found rifaximin as effective as lactitol in managing hepatic encephalopathy episodes. Investigators found rifaximin significantly better than lactitol in improving ammonia levels and EEG grade, which led to better portal-systemic encephalopathy scores in rifaximin-treated patients. Miglo and cohorts²⁵ assessed rifaximin benefit and tolerability when compared to neomycin in 49 cirrhosis patients with hepatic encephalopathy and found rifaximin as effective as neomycin in improving neuropsychiatric signs and blood ammonia levels.
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Table 1 summarizes adult oral recommended maximum rifaximin dosages. Dosages exceeding these recommendations will be reviewed.

Table 1 - Adult Maximum Recommended Oral Rifaximin Dosages

<table>
<thead>
<tr>
<th>Indication</th>
<th>Maximum Recommended Dosage</th>
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<tbody>
<tr>
<td>Travelers’ diarrhea (due to noninvasive E. coli strains)</td>
<td>200 mg three times daily (600 mg/day) x 3 days¹-⁸</td>
</tr>
<tr>
<td>HE recurrence</td>
<td>550 mg twice daily (1100 mg/day) ¹, ⁵-⁷, ¹⁰</td>
</tr>
<tr>
<td>IBS-D</td>
<td>550 mg 3 times daily for 14 days; retreatment for patients with symptom recurrence may occur up to 2 times with same dosage regimen</td>
</tr>
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Table notes:
- HE = hepatic encephalopathy
- IBS-D = irritable bowel syndrome with diarrhea

1.2. Pediatrics

Rifaximin is FDA-approved in children 12 years of age and older for use in managing travelers’ diarrhea due to noninvasive strains of *E. coli*. The recommended oral rifaximin dose for pediatric patients is 200 mg three times daily for three days. Rifaximin should not be prescribed for use in diarrhea caused by pathogens other than *E. coli* or complicated by fever or blood in the stool.¹, ⁵-⁷

The safety and efficacy of rifaximin 200 mg for travelers’ diarrhea in pediatric patients younger than 12 years of age or rifaxamin 550 mg for HE or IBS-D in pediatric patients younger than 18 years of age have not been established.¹, ⁵-⁷

2. Duration of Therapy

The recommended treatment duration for rifaximin use in *E. coli*-mediated travelers’ diarrhea is a maximum of three days.¹, ⁸-¹⁰ Treatment regimens lasting greater than three days will be reviewed.

Rifaximin 550 mg tablets may be prescribed on a chronic basis (i.e., for at least 6 months) to reduce the risk of HE recurrence, based on results from the study by Bass and colleagues¹².

Rifaximin 500 mg tablets may be administered for 14 days to treat acute IBS-D episodes, and may be repeated for up to two IBS-D recurrences per treatment course. IBS-D is a chronic condition, however, and rifaximin may be prescribed on a chronic basis to manage this disease state.

3. Duplicative Therapy [*]

Concurrent administration of rifaximin with other approved antibiotic therapies for travelers’ diarrhea (i.e., azithromycin, fluoroquinolones, trimethoprim-sulfamethoxazole) is not recommended as these combinations do not provide additional therapeutic benefit and may result in enhanced adverse events. Patient profiles containing concurrent prescriptions for rifaximin and additional travelers’ diarrhea antibiotic therapy will be reviewed.
4. References