MPR
GASTROENTEROLOGY & HEPATOLOGY EDITION®
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# PRESCRIBING ALERT®

Dear Healthcare Professional,

At *MPR* we strive to bring you important drug information in a concise and timely fashion. In keeping with this goal, we are pleased to bring you this PRESCRIBING ALERT featuring a new brand–Xifaxan550 (rifaximin) 550 mg tablets–from Salix Pharmaceuticals, Inc.

Xifaxan550 has gained FDA approval for the reduction in risk of overt hepatic encephalopathy (HE) recurrence in patients 18 years and older.[1] HE, a condition characterized by periods of relapse and remission, is observed in approximately 50% to 70% of all patients with cirrhosis.[2,3] A therapeutic goal in managing HE is reducing the risk of HE recurrence. Xifaxan550 demonstrated its ability to reduce the risk of HE recurrence over a 6-month period and reduce HE-related hospitalization in a pivotal clinical trial.[1]

More information regarding the use of Xifaxan550 is available in the current edition of *MPR*.

For your reference, please see the accompanying complete Prescribing Information for Xifaxan550.

Sincerely,

Grace L. McBride
Editorial Director
*MPR* Custom Programs

**REFERENCES**

**1.** Xifaxan [prescribing information]. Morrisville, NC: Salix Pharmaceuticals, Inc.; 2010.
**2.** Tavares de Melo R, Charneski L, Hilas O. Rifaximin for the treatment of hepatic encephalopathy. *Am J Health-Syst Pharm*. 2008;65(9):818-822.
**3.** Merck Manual Home Edition. http://www.merck.com/mmhe/index.html. Accessed April 6, 2010.

## IMPORTANT SAFETY INFORMATION

Xifaxan 550 mg is indicated for reduction in risk of overt hepatic encephalopathy (HE) recurrence in patients ≥18 years of age. In the trials of Xifaxan for HE, 91% of the patients were using lactulose concomitantly. Xifaxan has not been studied in patients with MELD scores >25, and only 8.6% of patients in the controlled trial had MELD scores over 19. There is increased systemic exposure in patients with more severe hepatic dysfunction. Therefore, caution should be exercised when administering Xifaxan to patients with severe hepatic impairment (Child-Pugh C).

Xifaxan is contraindicated in patients with a hypersensitivity to rifaximin, any of the rifamycin antimicrobial agents, or any of the components in Xifaxan. Hypersensitivity reactions have included exfoliative dermatitis, angioneurotic edema, and anaphylaxis.

*Clostridium difficile*-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including Xifaxan, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon which may lead to overgrowth of *C. difficile*. If CDAD is suspected or confirmed, ongoing antibiotic use not directed against *C. difficile* may need to be discontinued.

The most common adverse reactions occurring in >8% of patients in the clinical study were edema peripheral (15%), nausea (14%), dizziness (13%), fatigue (12%), ascites (11%), muscle spasms (9%), pruritus (9%), and abdominal pain (9%).

## PRESCRIBING ALERT

# Xifaxan550

## (rifaximin) 550 mg Tablets

**Company:** Salix Pharmaceuticals, Inc. ℞
**Pharmacological Class:** Rifamycin
**Active Ingredient:** Rifaximin 550 mg tablets.
**Indications:** Reduce the risk of overt hepatic encephalopathy (HE) recurrence in patients 18 years and older.
**Adults:** 550 mg 2 times daily.
**Children: <18 years: Not recommended.**
**Precautions:** Not studied in patients with MELD scores >25; only 8.6% of patients in the controlled trial had MELD >19. Increased systemic exposure in patients with more severe hepatic dysfunction; caution should be exercised in patients with severe hepatic impairment (Child-Pugh C). Elderly. Pregnancy (Cat.C). Nursing mothers.
**Interactions:** Clinically irrelevant.
**Adverse Reactions:** (≥10%): Peripheral edema, nausea, dizziness, fatigue, ascites.
**How Supplied:** Tablets: 550 mg—60

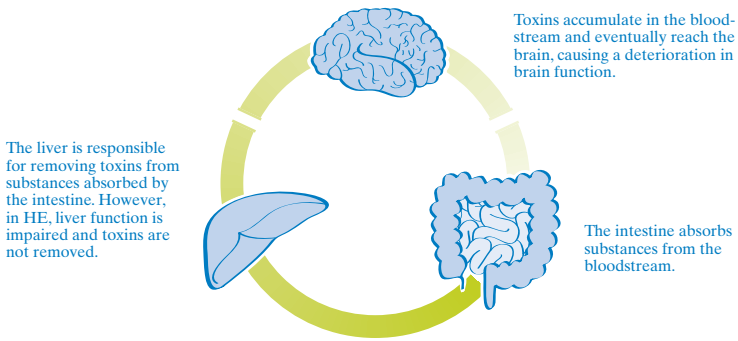

*Approved for use in hepatic encephalopathy*

### Hepatic encephalopathy (HE) is difficult to treat

- Constitutes a wide spectrum of potentially reversible neuropsychiatric abnormalities[1]
- Characterized by symptoms ranging from altered mental status to deep coma[1]
- Results when toxins originating in the gut are not cleared out by a diseased or damaged liver[1] (**Figure 1**)

**Figure 1**

**HEPATIC ENCEPHALOPATHY DEVELOPMENT**




Source: Merck Manual Home Edition.[1]

***Please see accompanying complete Prescribing Information.***

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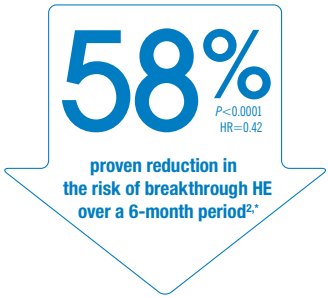
### Xifaxan550 has demonstrated efficacy over a 6-month period

- Xifaxan 550 mg can help patients reduce the risk of overt HE recurrence over a 6-month period[2] (**Figure 2**)
- At 6 months, 78% of patients taking Xifaxan 550 mg (n=140) did not have overt HE recurrence vs 54% with placebo[2]

**Figure 2**

**EFFICACY IN HEPATIC ENCEPHALOPATHY**




*In a randomized, placebo-controlled, double-blind, multicenter, multinational, 6-month study, the efficacy of Xifaxan 550 mg (taken orally 2 times a day) was evaluated in 299 adult subjects. Inclusion criteria: currently in remission (Conn score of 0 or 1) from HE and ≥2 episodes of HE associated with chronic liver disease in the previous 6 months. Lactulose was used concomitantly by 91% of patients (average daily dose of 3.3 cups/day [15 mL/cup]). The primary end point was the time to first breakthrough HE episode, defined as a marked deterioration in neurological function (an increase of Conn score to Grade ≥2 or an increase in Conn score and asterixis grade of 1 each if subject entered study at Grade 0).

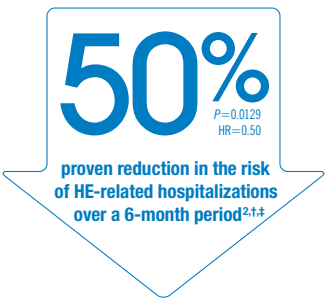
Source: Xifaxan [prescribing information].[2]

### Xifaxan550 reduced HE-related hospitalizations over 6 months

- Risk of HE-related hospitalizations was reduced by 50% vs. placebo in the pivotal clinical trial[2] (**Figure 3**)
- Over the 6-month treatment period, only 14% of patients taking Xifaxan 550 mg (n=140), vs. 23% taking placebo (n=159), required HE-related hospitalization[2]

**Figure 3**

**REDUCED HEPATIC ENCEPHALOPATHY-RELATED HOSPITALIZATIONS**




†In a randomized, placebo-controlled, double-blind, multicenter, multinational, 6-month study, the efficacy of Xifaxan 550 mg (taken orally 2 times a day) was evaluated in 299 adult subjects. Inclusion criteria: currently in remission (Conn score of 0 or 1) from HE and ≥2 episodes of HE associated with chronic liver disease in the previous 6 months. Lactulose was used concomitantly by 91% of patients (average daily dose of 3.3 cups/day [15 mL/cup]).

‡HE-related hospitalization defined as hospitalization directly caused by HE or a hospitalization during which an HE event occurred.

Source: Xifaxan [prescribing information].[2]

The most common adverse reactions occurring in >8% of patients in the clinical study were edema peripheral (15%), nausea (14%), dizziness (13%), fatigue (12%), ascites (11%), muscle spasms (9%), pruritus (9%), and abdominal pain (9%).

***Please see accompanying complete Prescribing Information.***

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### Reduces burden of HE

- For every 4 patients treated with Xifaxan 550 mg for 6 months, 1 case of breakthrough HE can be prevented[3]
- For every 9 patients treated with Xifaxan 550 mg for 6 months, 1 case of hospitalization can be prevented[3]

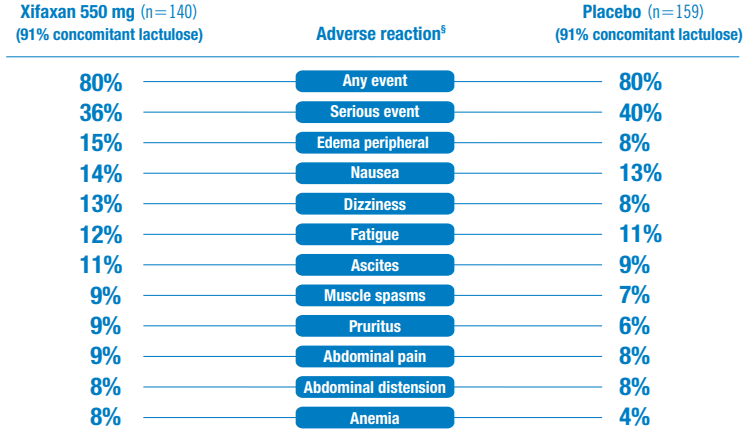
### Evaluated exposure over a long-term period

- In the pivotal clinical trial, 202 patients were exposed to Xifaxan 550 mg for more than 1 year (mean exposure 364 days)[2]
- Includes 264 patients exposed for 6 months[2]

### Offers safety and tolerability when used as directed

**COMMON ADVERSE EVENTS WITH XIFAXAN550 AND PLACEBO**

The incidence of adverse reactions with Xifaxan 550 mg was comparable to placebo[2,4]




§Most common adverse reactions occurring in ≥8% of patients taking Xifaxan 550 mg.

Source: Xifaxan [prescribing information][2]; Data on file.[4]

### Xifaxan550 has no clinically relevant drug-drug interactions[2,‖]

‖The effect of rifaximin on CYP3A4 in patients with impaired liver function who have elevated systemic exposure is not known.

***Please see accompanying complete Prescribing Information.***

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**Xifaxan550 is taken twice daily[2]**

- Can be taken with or without food[2]

**Ongoing provider and patient support is available through H.E.L.P., the HE Living Program**

- A 24-hour toll-free support hotline
- Provides educational resources, treatment adherence support, and copay assistance for eligible patients
- Available at *www.HELPenroll.com* or by calling 1-866-XIFAXAN (943-2926)

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**3.** Bass NM, Mullen KD, Sanyal A, et al. Rifaximin treatment in hepatic encephalopathy. *N Engl J Med*. 2010;362(12):1071-1081.
**4.** Data on file. Salix Pharmaceuticals, Inc.


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