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## PRESCRIBING ALERT<sup>®</sup>

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 about **XIFAXAN (rifaximin) 550 mg tablets** from **Salix Pharmaceuticals, Inc.**

XIFAXAN 550 mg is FDA approved for the reduction in risk of overt hepatic encephalopathy (HE) recurrence in patients 18 years and older.<sup>1</sup> Recurrent episodes of HE may lead to long-term cognitive dysfunction, which may be irreversible in patients with a history of overt HE.<sup>2</sup> In a pivotal clinical trial, XIFAXAN 550 mg demonstrated its ability to reduce the risk of overt HE recurrence over a 6-month period and reduce HE-related hospitalization.<sup>1</sup>

More information regarding the use of XIFAXAN 550 mg is available in the current edition of *MPR*.

For your reference, please see the complete [Prescribing Information](#) for XIFAXAN 550 mg.

Sincerely,

Grace L. McBride  
Editorial Director  
*MPR* Custom Programs

### REFERENCES

1. XIFAXAN [prescribing information]. Morrisville, NC: Salix Pharmaceuticals, Inc.; 2010.
2. Bajaj JS, Schubert CM, Heuman DM, et al. Persistence of cognitive impairment after resolution of overt hepatic encephalopathy. *Gastroenterology*. 2010;138(7):2332-2340.

### IMPORTANT SAFETY INFORMATION

XIFAXAN 550 mg is indicated for reduction in risk of overt hepatic encephalopathy (HE) recurrence in patients  $\geq$ 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%).

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# MPR PRESCRIBING ALERT

## XIFAXAN550

(rifaximin) 550 mg tablets



Shown to reduce risk of overt hepatic encephalopathy recurrence

Rx

**Company:** Salix Pharmaceuticals, Inc.  
**Pharmacologic Class:** Rifamycin derivative

**Active Ingredients:** Rifaximin 550 mg tablets.

**Indications:** Reduce the risk of overt hepatic encephalopathy (OHE) recurrence in patients 18 years and older.

**Adults:** 550 mg 2 times daily.

**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). *Clostridium difficile*-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including XIFAXAN; may range in

severity from mild diarrhea to fatal colitis. If CDAD is suspected/confirmed, ongoing antibiotic use not directed against *C. difficile* may need to be discontinued.

**Interactions:** See full Prescribing Information.

**Adverse Reactions:** (≥10%): Peripheral edema, nausea, dizziness, fatigue, ascites.

**How Supplied:** Tablets: 550 mg—60 count bottle

✓ **Overt hepatic encephalopathy (OHE) is a chronic condition<sup>1</sup>**

- OHE is a chronically debilitating complication of cirrhosis<sup>1</sup>
- Prevention of OHE episodes is an important goal in the treatment of patients with liver disease<sup>1</sup>

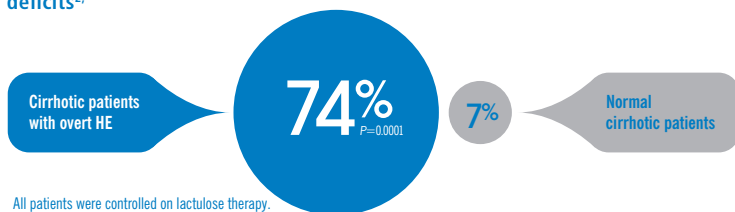
✓ **Long-term cognitive impairment may occur due to recurrent overt HE**

- A clinical study showed that cirrhotic patients with OHE (n=54) had more cognitive dysfunction than normal cirrhotic patients (n=52) despite treatment with lactulose<sup>2</sup> (**Figure 1**)
  - Patients with OHE performed significantly worse on a battery of psychometric tests ( $P<0.001$ ) and were unable to demonstrate a capacity for learning<sup>2</sup>

Figure 1

### DIFFERENCE IN THE INCIDENCE OF LEARNING DEFICITS

#### Comparison of cirrhotic patients with and without overt hepatic encephalopathy experiencing learning deficits<sup>2,7</sup>



\*This study evaluated the cognitive function of cirrhotic patients using psychometric tests and the inhibitory control test (ICT). Outcomes were used to determine learning of response inhibition. Two cross-sectional studies (A and B) compared data from stable cirrhotic patients with or without prior OHE. Study A included 226 cirrhotic patients, and study B included 50 additional patients who developed ≥1 documented OHE episodes during follow-up. A prospective analysis assessed the cognitive performance of 79 patients in a psychometric evaluation. Of the 59 patients who returned for a retest, 15 had developed OHE and were treated with lactulose for 36 ± 25 days before another test.<sup>2</sup>

OHE = overt hepatic encephalopathy.

Source: Bajaj 2010.<sup>2</sup>

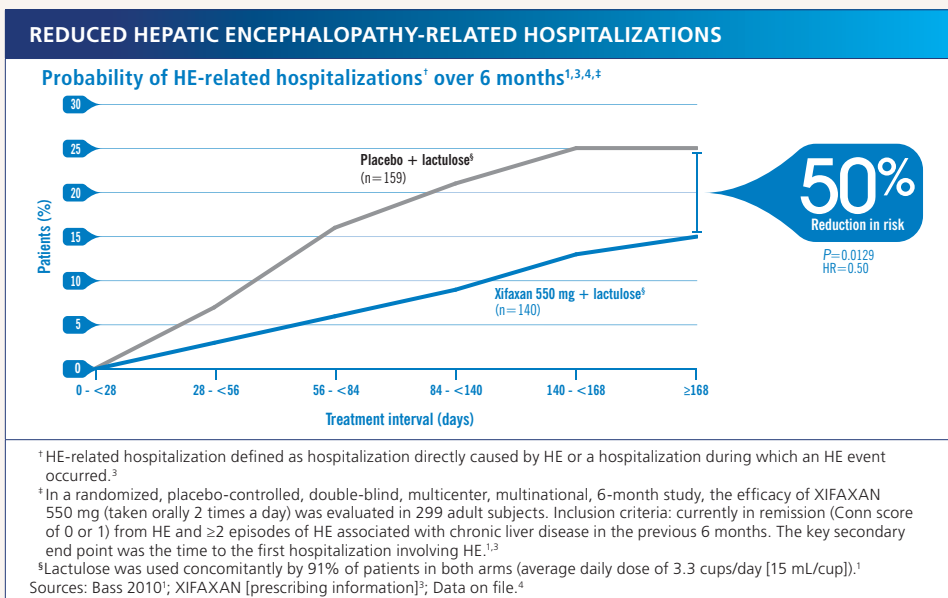
**Please see Important Safety Information and complete Prescribing Information.**

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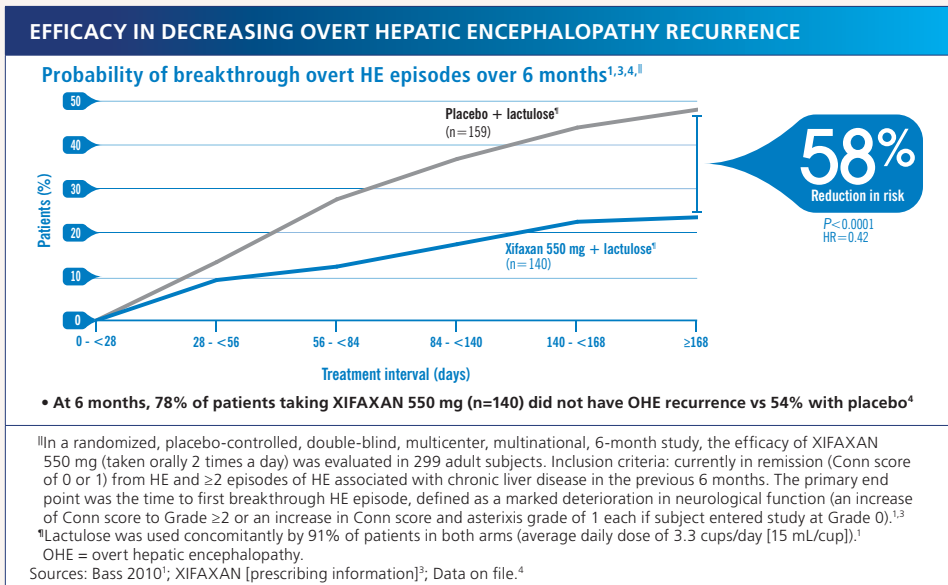
✓ XIFAXAN 550 mg reduced HE-related hospitalizations over 6 months<sup>1,3</sup> (Figure 2)

Figure 2



✓ XIFAXAN 550 mg reduced the risk of overt HE recurrence over a 6-month period<sup>3</sup> (Figure 3)

Figure 3



Please see Important Safety Information and complete Prescribing Information.

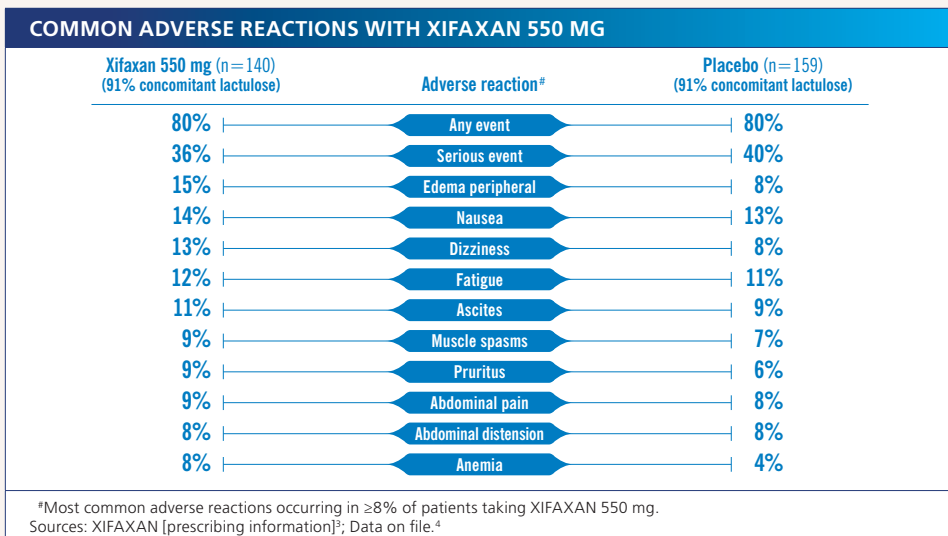
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## ✓ Offers favorable safety and tolerability profile when used as directed

- Incidence of adverse reactions with nonsystemic XIFAXAN 550 mg was comparable to placebo<sup>3,4</sup> (Figure 4)

Figure 4



## ✓ XIFAXAN 550 mg has not been shown to cause clinically relevant resistance when used as directed<sup>5,6</sup>

## ✓ The HE Living Program offers patients, caregivers, and healthcare professionals (HCPs) ongoing treatment support for overt HE management

- Adults ≥18 years of age with OHE are eligible to participate in the HE Living Program
- Reimbursement support is part of the HE Living Program
  - You or your staff can call the XIFAXAN Reimbursement Helpline at 1-866-XIFAXAN (1-866-943-2926) to get answers to third-party coverage questions and for timely solutions to issues you encounter before or after submitting a patient's claim
  - The XIFAXAN Reimbursement Helpline can negotiate appeals on behalf of patients, should their claims be denied
- Financial support is part of the HE Living Program
  - \$100 co-pay card is available for eligible patients to use each month
  - Patients on Medicare will also receive financial support from drug manufacturers under the Part D plan
  - According to the plan, Salix will pay 50% of the cost of XIFAXAN 550 mg while a patient is in the "donut hole" (gap in coverage)

*Please see Important Safety Information and complete Prescribing Information.*

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- Ongoing treatment is part of the HE Living Program
  - The 24-hour call center (1-866-XIFAXAN [1-866-943-2926]) is available to answer patients' or caregivers' questions
  - Compliance calls with associated prescription and appointment reminders help patients stay on therapy
  - Patient education brochures contain information about disease education, the importance of staying on therapy to avoid an overt HE episode, and what to expect from treatment with XIFAXAN 550 mg

## Enrolling patients in the HE Living Program is easy

- HCPs, patients, or caregivers can enroll in the HE Living Program by visiting [www.helpenroll.com](http://www.helpenroll.com) or by calling 1-866-XIFAXAN (1-866-943-2926)

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***Please see full Prescribing Information.***

## REFERENCES

1. Bass NM, Mullen KD, Sanyal A, et al. Rifaximin treatment in hepatic encephalopathy. *N Engl J Med*. 2010;363(12):1071-1081.
2. Bajaj JS, Schubert CM, Heuman DM, et al. Persistence of cognitive impairment after resolution of overt hepatic encephalopathy. *Gastroenterology*. 2010;138 (7):2332-2340.
3. XIFAXAN [prescribing information]. Morrisville, NC: Salix Pharmaceuticals, Inc.;2010.
4. Data on file. Salix Pharmaceuticals, Inc.
5. De Leo C, Eftimiadi C, Schito GC. Rapid disappearance from the intestinal tract of bacteria resistant to rifaximin. *Drugs Exp Clin Res*. 1986;12(12):979-981.
6. Koo HL, DuPont HL. Current and future developments in travelers' diarrhea therapy. *Expert Rev Infect Ther*. 2006;4(3):417-427.