Meet Paul

58 years old

Xifaxan® rifaximin 550 mg tablets

PATIENT PROFILE SERIES

A Clinical Look at XIFAXAN to Reduce the Risk of Overt Hepatic Encephalopathy (HE) Recurrence and HE-Related Hospitalization[1]

AASLD GUIDELINES GRADE I,A,1

XIFAXAN earned AASLD/EASL's highest possible recommendation (GRADE I, A, 1) as an add-on therapy to lactulose to reduce the risk of overt HE recurrence after a patient has a recurrence while on lactulose alone.[2,*]

AASLD, American Association for the Study of Liver Diseases; EASL, European Association for the Study of the Liver.

*Per the GRADE System for Evidence: Grade I=randomized, controlled trials; A=evidence is "high quality" and further research is very unlikely to change our confidence in the estimated effect; and 1=recommendation is "strong" with factors influencing strength of recommendation including the quality of evidence, presumed patient-important outcomes, and costs.[2]

Reason for Visit

- Routine visit with his gastroenterologist (occurs every 3-6 months) to monitor for progression of cirrhosis and potential related complications.

Presentation

- During routine screening for overt HE, cognitive dysfunction and disorientation to time, abnormal gait, and slow/monotonous speech were noted.
- Paul's wife expressed concern about changes in his personality, including forgetfulness, disorientation, and irritability over the past few weeks.

Medical History

- Obesity (current BMI 32)
- Dyslipidemia
- Type 2 diabetes mellitus
- Hypertension (currently controlled 130/85 mm Hg)
- Cirrhosis caused by nonalcoholic steatohepatitis
- Hospitalized for overt HE precipitated by GI bleed

Current Medications

- Propranolol 80 mg twice daily
- Amlodipine 5 mg once daily
- Atorvastatin 40 mg once daily
- Metformin ER 2000 mg once daily
- Liraglutide 1.8 mg SQ once daily
- Degludec 10 units SQ once daily
- Lactulose 25 mL three times daily

Diagnosis

Stage II Overt HE[2]

- Along with cognitive dysfunction, disorientation, and slowness of speech, asterixis was present during examination.[2]
- Blood glucose level (98 mg/dL) and blood pressure (130/85 mm Hg) were normal.[2]
- Signs and symptoms were all suggestive of overt HE, despite compliance with lactulose therapy, as other causative factors of cognitive dysfunction and disorientation were ruled out.[2]

Treatment

- Lactulose 25 mL every 1-2 hours until at least 2 soft bowel movements per day are produced. Then, titrate dose to maintain 2 or 3 bowel movements per day to reduce the risk of recurrence.[2]

XIFAXAN 550 mg twice daily was added to reduce the risk of overt HE recurrence and HE-related hospitalizations.[1,2]

INDICATION

- XIFAXAN® (rifaximin) 550 mg tablets are indicated for the reduction in risk of overt hepatic encephalopathy (HE) recurrence in adults.

IMPORTANT SAFETY INFORMATION

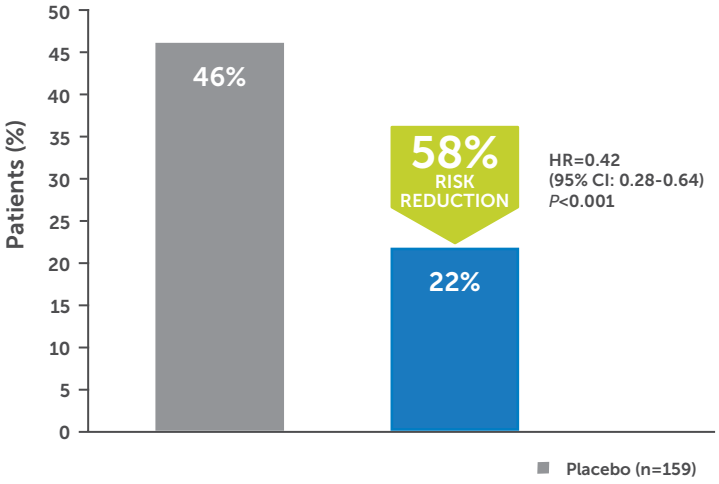
- XIFAXAN is contraindicated in patients with a hypersensitivity to rifaximin, rifamycin antimicrobial agents, or any of the components in XIFAXAN. Hypersensitivity reactions have included exfoliative dermatitis, angioneurotic edema, and anaphylaxis.

Please see additional Important Safety Information on back and accompanying full Prescribing Information.

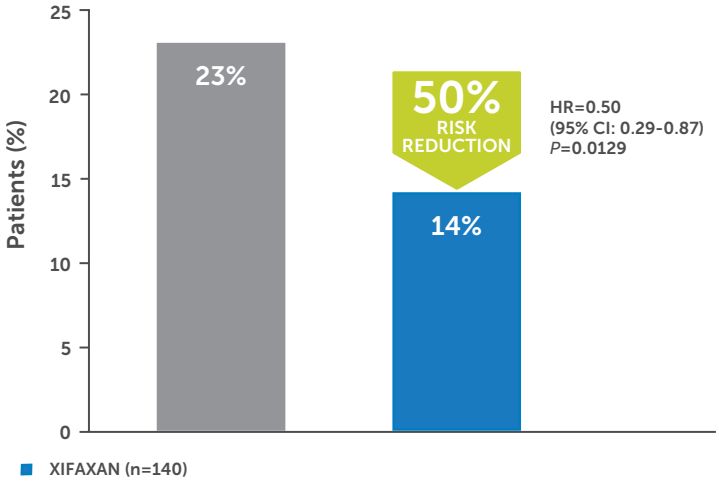
Xifaxan® rifaximin 550 mg tablets

In a clinical trial, XIFAXAN Reduced the Risk of Overt HE Recurrence and HE-Related Hospitalization[1,*]

Overt HE Recurrences During 6 Months of Therapy



HE-Related Hospitalizations During 6 Months of Therapy



*Study Design: In a randomized, placebo-controlled, double-blind, multicenter, multinational, 6-month study, the efficacy of XIFAXAN 550 mg twice a day was evaluated in 299 adult patients. 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. The primary endpoint was the time to first breakthrough overt 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). HE-related hospitalization was a key secondary endpoint and was defined as hospitalization directly resulting from HE or hospitalization complicated by HE. Lactulose was used concomitantly by 91% of patients in both arms of the study.[1,3]

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- XIFAXAN® (rifaximin) 550 mg tablets are indicated for the reduction in risk of overt hepatic encephalopathy (HE) recurrence in adults.

IMPORTANT SAFETY INFORMATION (continued)

- *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. If CDAD is suspected or confirmed, ongoing antibiotic use not directed against *C. difficile* may need to be discontinued.
- There is an increased systemic exposure in patients with severe (Child-Pugh Class C) hepatic impairment. Caution should be exercised when administering XIFAXAN to these patients.
- Caution should be exercised when concomitant use of XIFAXAN and P-glycoprotein (P-gp) and/or OATPs inhibitors is needed. Concomitant administration of cyclosporine, an inhibitor of P-gp and OATPs, significantly increased the systemic exposure of rifaximin. In patients with hepatic impairment, a potential additive effect of reduced metabolism and concomitant P-gp inhibitors may further increase the systemic exposure to rifaximin.
- In a clinical study, the most common adverse reactions for XIFAXAN in HE (≥10%) were peripheral edema (15%), nausea (14%), dizziness (13%), fatigue (12%), and ascites (11%).
- INR changes have been reported in patients receiving rifaximin and warfarin concomitantly. Monitor INR and prothrombin time. Dose adjustment of warfarin may be required.
- XIFAXAN may cause fetal harm. Advise pregnant women of the potential risk to a fetus.

To report SUSPECTED ADVERSE REACTIONS, contact Salix Pharmaceuticals at 1-800-321-4576 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see additional Important Safety Information on front and accompanying full Prescribing Information.

References: 1. XIFAXAN (rifaximin) tablets [package insert]. Bridgewater, NJ: Salix Pharmaceuticals. **2.** Vilstrup H et al. *Hepatology.* 2014;60(2):715-735. **3.** Bass NM et al. *N Engl J Med.* 2010;362(12):1071-1081.

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