

From: {{sender name and email}}

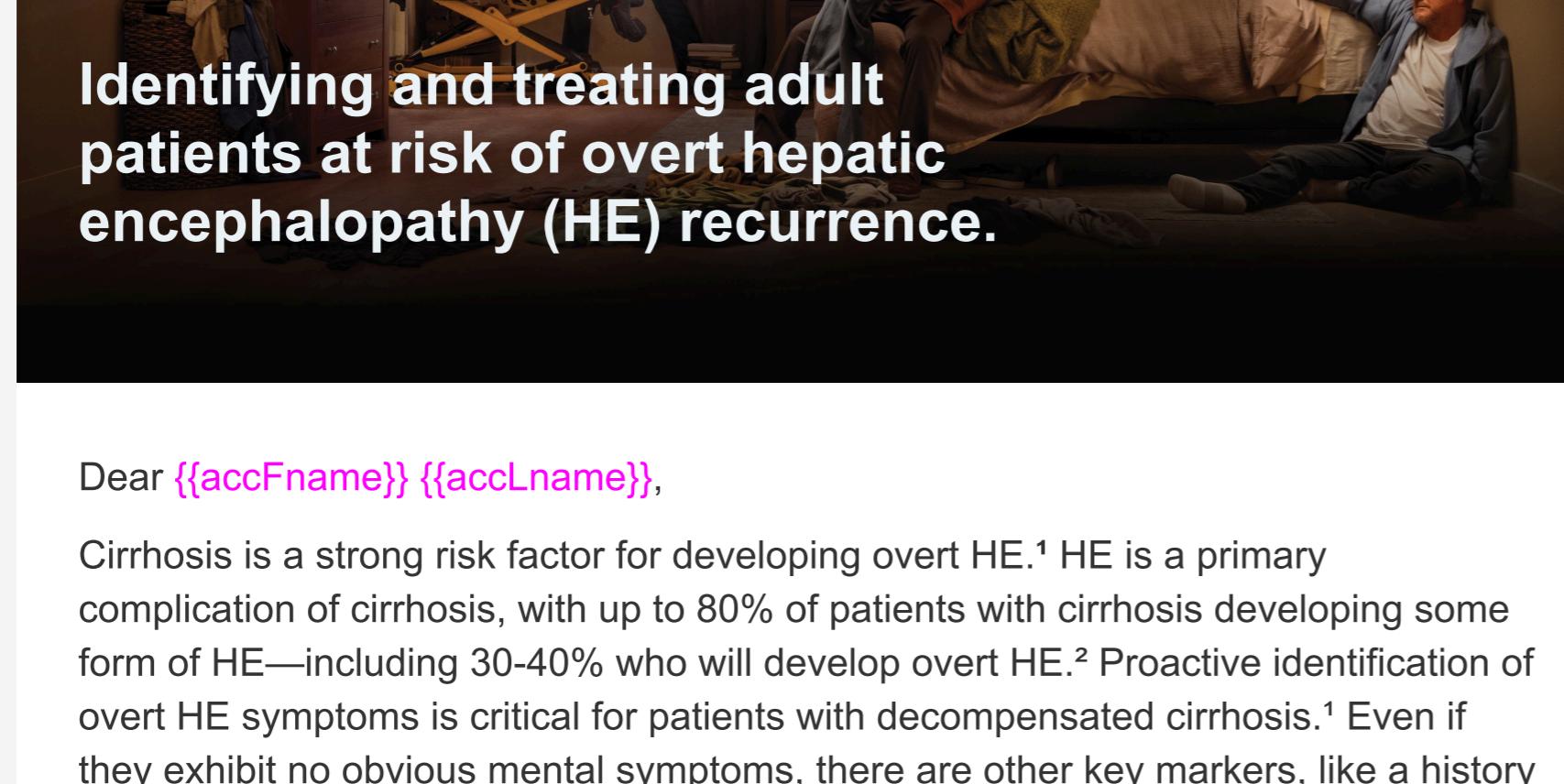
To: {{recipient name and email}}

Subject:

1. How to identify patients at risk for OHE recurrence
2. How to identify a significant complication of cirrhosis
3. Can you recognize this common complication of cirrhosis?
4. Why it's critical to identify patients at risk of OHE recurrence

Preheader:

1. See why screening early is critical
2. Learn about a primary concern
3. Recognize overt HE sooner
4. Understand the symptoms and guideline-based care



links to: <https://www.xifaxan.com/hcp/ISI>

links to: <https://shared.salix.com/globalassets/pi/xifaxan550-pi.pdf>

links to: <https://www.xifaxan.com/hcp/ISI>

Identifying and treating adult patients at risk of overt hepatic encephalopathy (HE) recurrence.

Dear {{accFname}} {{accLname}},

Cirrhosis is a strong risk factor for developing overt HE.¹ HE is a primary complication of cirrhosis, with up to 80% of patients with cirrhosis developing some form of HE—including 30-40% who will develop overt HE.² Proactive identification of overt HE symptoms is critical for patients with decompensated cirrhosis.¹ Even if they exhibit no obvious mental symptoms, there are other key markers, like a history of ascites or variceal bleeds, that can add up to overt HE.²

Once such patients have been identified, remember that XIFAXAN can help reduce the risk of overt HE recurrence in adults.

SELECT 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 below.

The West Haven criteria are the gold standard for grading overt HE symptoms²

HE classification using the West Haven criteria (including minimal HE) ²					
Covert HE		Overt HE			
MINIMAL	GRADE 1	GRADE 2	GRADE 3	GRADE 4	
• No outward signs; deficits in psychometric or neuropsychological tests	• Lack of awareness • Euphoria or anxiety • Short attention span • Inability to add or subtract • Altered sleep	• Lethargy/apathy • No sense of time • Personality change • Inappropriate behavior • Dysgraphia • Asterixis	• Somnolence to semistupor • Responsiveness to stimuli • Confusion • Disorientation • Bizarre behavior	• Coma	
					30% to 40% of patients with cirrhosis will develop OHE ²

Disrupt the pattern of overt HE episodes with XIFAXAN³

Explore how

links to: <https://www.xifaxan.com/hcp/ohe/diagnosis/>

IMPORTANT SAFETY INFORMATION (cont'd)

- *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 clinical studies, the most common adverse reactions for XIFAXAN (alone or in combination with lactulose) were:
 - HE (≥10%): Peripheral edema (17%), constipation (16%), nausea (15%), fatigue (14%), insomnia (14%), ascites (13%), dizziness (13%), urinary tract infection (12%), anemia (10%), and pruritus (10%)
- 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.

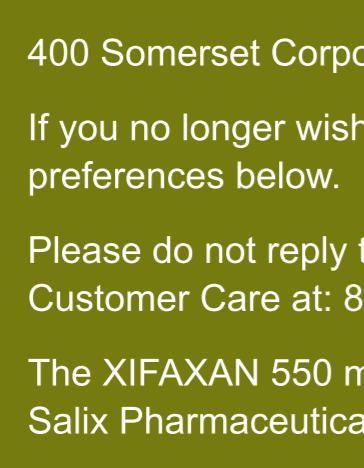
To report SUSPECTED ADVERSE REACTIONS, contact Salix Pharmaceuticals at 1-800-321-4576 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

links to: <https://www.fda.gov/medwatch>

INDICATION

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

Please click [here](#) for full Prescribing Information.



Follow the guidelines

links to: <https://shared.salix.com/globalassets/pi/xifaxan550-pi.pdf>

XIFAXAN earned the highest possible recommendation (GRADE I,A,1) by the AASLD as an add-on therapy to lactulose to reduce the risk of OHE recurrence after a patient has a recurrence while on lactulose alone.^{2*}

Review the AASLD Guidelines

Download now

links to: <https://www.xifaxan.com/siteassets/hehcp/pdf/xifaxan-he-aasld-guidelines-update.pdf>

*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

AASLD, American Association for the Study of Liver Diseases; GI, gastrointestinal; HE, hepatic encephalopathy; OHE, overt hepatic encephalopathy.

References: 1. Garcia-Tsao G, Abraido JG, Berzigotti A, Bosch J. Portal hypertension bleeding in cirrhosis: risk stratification, diagnosis, and management. 2016 practice guidance by the American Association for the Study of Liver Diseases. *Hepatology*; 2017;65(1):310-335. 2. Vlstrup H, Amiod P, Bajaj J, et al. Hepatic encephalopathy in chronic liver disease: 2014 practice guideline by the American Association for the Study of Liver Diseases and the European Association for the Study of the Liver. *Hepatology*; 2014;60(2):715-735. 3. XIFAXAN. Prescribing Information. Salix Pharmaceuticals; 2023.

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