

Apply the latest ACG clinical guideline recommendations into your clinical practice when managing patients with HE



XIFAXAN earned the highest possible GRADE recommendation (LoE: strong, high quality) by the American College of Gastroenterology (ACG) as an add-on therapy to lactulose to reduce the risk of overt HE recurrence after a patient has an episode while on lactulose alone

See below for a full summary of the ACG clinical guideline recommendations for outpatient prevention of HE recurrence.

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.
- 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.

Please see additional Important Safety Information throughout and accompanying full [Prescribing Information](#).

Guidance on Prevention of Overt HE Recurrence

Outpatient management approach: from initial discharge to ongoing maintenance

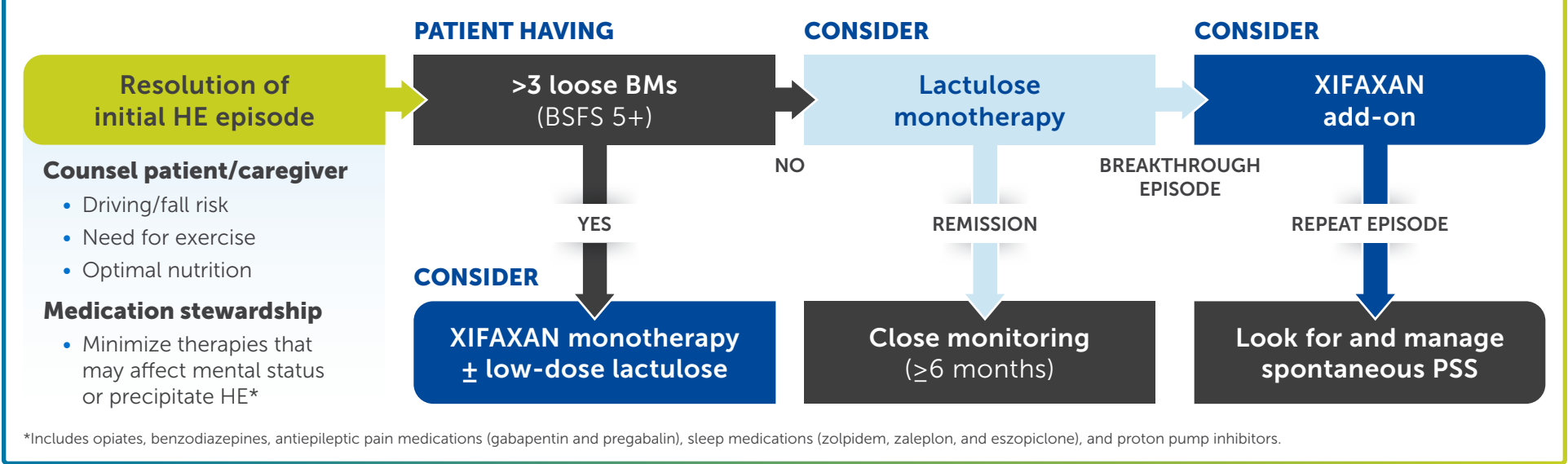


Figure adapted from Bajaj JS et al. *Am J Gastroenterol.* 2026;121(3):588-618. Licensed under CC BY.

ACG Guideline Recommendations†	Strength‡	Quality§
After initial overt HE episode, recommend outpatient first-line therapy with lactulose titrated to 2-3 soft BMs daily for prevention of HE recurrence	Strong	High
In patients treated with lactulose for HE, suggest using BSFS with BM frequency for titration to reduce readmissions	Conditional	Very Low
In patients with cirrhosis and overt HE, suggest rifaximin therapy in the outpatient setting to prevent HE recurrence	Conditional	Low
In patients with overt HE on lactulose maintenance therapy who experience recurrence, recommend addition of rifaximin treatment	Strong	High
In patients with overt HE and persistent symptoms despite lactulose and rifaximin, suggest zinc supplementation in those with low blood zinc levels	Conditional	Very Low
Suggest implementing health information technology interventions, such as electronic clinical reminders, when feasible, to optimize HE management	Conditional	Very Low
Suggest shunt embolization in patients with refractory HE on optimized medical therapy who have adequate hepatic function and no contraindications	Conditional	Very Low

†GRADE methodology was used to assess the quality of evidence and provide the strength of each recommendation.
‡Strong: most patients should receive the recommended course of action; Conditional: a shared decision-making model through discussion regarding the available evidence and alternative options is appropriate.
§High: very confident in estimate of effect; Moderate: moderate confidence in estimate of effect; Low: limited confidence in estimate of effect; Very Low: very little confidence in estimate of effect.

Proper Nutrition and Exercise Are Essential to Help Prevent HE Episodes

The relationship between HE and muscle health highlights the importance of evaluating patients’ nutrition, muscle strength, and physical fitness

ACG Guideline Recommendations*	Strength†	Quality‡
In outpatients with HE, recommend a protein intake target of 1.2-1.5 g/kg/d	Strong	Moderate
In individuals with HE, recommend BCAA supplementation if protein needs cannot be met by food alone	Strong	Moderate
For patients with cirrhosis, suggest a late-night snack to reduce frailty and HE	Conditional	Very Low
In patients with HE, suggest against protein restriction because it increases muscle breakdown and does not reduce the duration of HE	Conditional	Very Low
In patients with HE, suggest exercise interventions to reduce the risk for falls, lower portal pressure, and increase the capacity of skeletal muscle for ammonia metabolism	Conditional	Low

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Work together with patients and their loved ones to keep them informed about HE-associated risks and to help prevent future episodes



Oral and written advice to avoid driving should be given to patients (and their caregivers) with recent (<3 months) overt HE episodes



All patients with HE (and their caregivers) should receive HE-based educational materials



Caregivers should be screened for burnout and provided necessary support



Patients with HE are at an increased risk of exercise-induced injury, which can be mitigated through supervision

IMPORTANT SAFETY INFORMATION (*continued*)

- 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.
Please see additional Important Safety Information throughout and accompanying full [Prescribing Information](#).



FOLLOW GUIDELINE-RECOMMENDED CARE FOR YOUR ADULT PATIENTS AT RISK OF OVERT HE RECURRENCE
[Access](#) the full ACG clinical guideline for HE and a complete list of recommendations

ACG, American College of Gastroenterology; BCAA, branched chain amino acid; BM, bowel movement; BSFS, Bristol Stool Form Scale; LoE, level of evidence; PSS, portosystemic shunt.
Reference: Bajaj JS et al. *Am J Gastroenterol*. 2026;121(3):588-618.