PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

XIFAXAN 550MG ONLY
(rifaximin)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization ***Ref # 681-A***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Xifaxan and other antibacterial drugs, Xifaxan when used to treat infection should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Hepatic Encephalopathy

Xifaxan is indicated for reduction in risk of overt hepatic encephalopathy (HE) recurrence in adults.

In the trials of Xifaxan for HE, 91% of the patients were using lactulose concomitantly. Differences in the treatment effect of those patients not using lactulose concomitantly could not be assessed.

Xifaxan has not been studied in patients with MELD (Model for End-Stage Liver Disease) 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.

Irritable Bowel Syndrome with Diarrhea

Xifaxan is indicated for the treatment of irritable bowel syndrome with diarrhea (IBS-D) in adults.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed to reduce the risk of overt hepatic encephalopathy (HE) recurrence
  AND
  - The requested drug is being used as add-on therapy to lactulose

OR

- The patient has the diagnosis of irritable bowel syndrome with diarrhea (IBS-D)
  AND
  - If the patient has previously received treatment with the requested drug, the patient is experiencing a recurrence of symptoms AND
  - The patient has not already received an initial 14-day course of treatment AND two additional 14-day courses of treatment with the requested drug

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Xifaxan 550 mg is indicated for reduction in risk of overt hepatic encephalopathy (HE) recurrence and for the treatment of irritable bowel syndrome with diarrhea (IBS-D) in adults.

The recommended dose of Xifaxan (rifaximin) for travelers' diarrhea is 200 mg taken orally three times a day for three days. Treatment with a higher rifaximin dosage (400 mg three times daily) did not provide additional clinical benefit.[2] This criteria only targets Xifaxan 550 mg tablet, which exceeds the recommended dose for travelers' diarrhea. Therefore, coverage for travelers' diarrhea will not be addressed in this criteria.

The Hepatic Encephalopathy in Chronic Liver Disease: 2014 Practice Guideline by AASLD and EASL states lactulose is the first choice for treatment of episodic overt hepatic encephalopathy (OHE). Lactulose is generally used as initial treatment for OHE. A large meta-analysis of trial data did not completely support lactulose as a therapeutic agent for treatment of OHE, but for technical reasons, it did not include the largest trials, and these agents continue to be used widely. The guideline also recommends rifaximin is an effective add-on therapy to lactulose for prevention of overt hepatic encephalopathy (OHE) recurrence. A multinational study with patients having two earlier OHE bouts to maintain remission showed the superiority of rifaximin versus placebo (in the background of 91% lactulose use). No solid data support the use of rifaximin alone. Rifaximin added to lactulose is the best-documented agent to maintain remission in patients who have already experienced one or more bouts of OHE while on lactulose treatment after their initial episode of OHE. Therefore, coverage will be considered when a patient is currently taking lactulose.[4] To allow coverage without disruption in therapy, the duration of approval will be 12 months if the coverage criteria is met.

The recommended dose of Xifaxan for IBS-D is one 550 mg tablet taken orally three times a day for 14 days. Patients who experience a recurrence of symptoms can be retreated up to two times with the same dosage regimen. The safety and efficacy of Xifaxan for the treatment of IBS-D was evaluated in 3 randomized, multi-center, double-blind, placebo-controlled studies in adult patients. In Trials 1 and 2, patients received Xifaxan 550 mg three times a day for 14 days, or placebo, and followed for a 10-week treatment-free period. Trial 3 evaluated repeat treatment in adults with IBS-D for up to 46 weeks.[1] To confirm Xifaxan is being used appropriately, coverage for patients who have previously received treatment with Xifaxan will be considered if the patient is experiencing a recurrence of symptoms and the patient has not already received an initial 14-day course of treatment and two additional 14-day courses of treatment with Xifaxan. Since Xifaxan is not indicated for use beyond 14 days to treat IBS-D symptoms, the duration of approval will be 14 days if coverage criteria is met.

REFERENCES

1. Xifaxan [package insert]. Bridgewater, NJ: Salix Pharmaceuticals, Inc; October 2020.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: UpToDate, Inc.; 2021; Accessed March 5, 2021.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. https://www.micromedexsolutions.com. Accessed March 2, 2021.
4. Vilstrup H, Amodio 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.

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Reviewed:	Medical Affairs (KP) 06/2010, 05/2011, 06/2011, 10/2011, (LMS) 10/2012, 10/2013, 10/2014; (LCB) 05/2015, 10/2015; (RR) 04/2019; (CHART) 03/26/20; (CHART) 03/25/21 External Review: 08/2010, 06/2011, 03/2012, 04/2013, 04/2014, 04/2015, 06/2015, 02/2016, 12/2016, 12/2017, 06/2018, 06/2019, 06/2020, 06/2021

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed to reduce the risk of overt hepatic encephalopathy (HE) recurrence? [If no, then skip to question 3.]	Yes	No
2	Is the requested drug being used as add-on therapy to lactulose? [No further questions.]	Yes	No

3	Does the patient have the diagnosis of irritable bowel syndrome with diarrhea (IBS-D)? [If no, then no further questions.]	Yes	No
4	Has the patient previously received treatment with the requested drug? [If no, then no further questions.]	Yes	No
5	Is the patient experiencing a recurrence of symptoms? [If no, then no further questions.]	Yes	No
6	Has the patient already received an initial 14-day course of treatment AND two additional 14-day courses of treatment with the requested drug?	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 2	Go to 3	
2.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you are taking lactulose. Your request has been denied based on the information we have. [Short Description: Not being used as add-on therapy to lactulose.]
3.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet any of these conditions: - You have irritable bowel syndrome with diarrhea (IBS-D) - The drug is used to lower the risk of overt hepatic encephalopathy (HE) recurrence Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
4.	Go to 5	Approve, 14 days	
5.	Go to 6	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions: - You have used this drug before - You have had a recurrence of symptoms Your request has been denied based on the information we have. [Short Description: Continuation of therapy; No recurrence of symptoms]
6.	Deny	Approve, 14 days	You do not meet the requirements of your plan. Your plan covers this drug when you have not already had three total 14-day courses of treatment with this drug. Your request has been denied based on the information we have. [Short Description: Exceeded max number of courses of therapy]