nh healthy families

MEDICAL NECESSITY GUIDELINE

DEPARTMENT: Pharmacy	**DOCUMENT NAME:** rifaximin (Xifaxan®)
PAGE: 1 of 5	**REFERENCE NUMBER:** NH.PMN.47
EFFECTIVE DATE: 11/11	**REPLACES DOCUMENT:**
RETIRED:	**REVIEWED:** 11/11, 12/14, 08/16, 07/17
PRODUCT TYPE: All	**REVISED:** 11/12, 11/13, 09/16

IMPORTANT REMINDER

This Clinical Policy has been developed by appropriately experienced and licensed health care professionals based on a thorough review and consideration of generally accepted standards of medical practice, peer-reviewed medical literature, government agency/program approval status, and other indicia of medical necessity.

The purpose of this Clinical Policy is to provide a guide to medical necessity. Benefit determinations should be based in all cases on the applicable contract provisions governing plan benefits ("Benefit Plan Contract") and applicable state and federal requirements, as well as applicable plan-level administrative policies and procedures. To the extent there are any conflicts between this Clinical Policy and the Benefit Plan Contract provisions, the Benefit Plan Contract provisions will control.

Clinical policies are intended to be reflective of current scientific research and clinical thinking. This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

Description: Xifaxan is an oral rifamycin antibiotic. It has clinical utility in the treatment of infections caused by various gram-positive and gram-negative aerobes and anaerobes. The drug has virtually no systemic absorption, so its use is generally limited to treating GI infections.

Brand: Rifaximin (Xifaxan®): 200 mg tablets, 550 mg tablets

FDA Labeled Indications:

1. Treatment of travelers' diarrhea caused by noninvasive strains of *E. coli*
2. Reduction of overt hepatic encephalopathy recurrence

Criteria for Approval:

Travelers' Diarrhea

A. Patients age ≥ 12 years.
B. Documented treatment failure with quinolone antibiotic (e.g ciprofloxacin 500mg twice daily for 1-3 days) or azithromycin (recommended dosing 500mg daily for 3

days or 1000mg single dose) unless contraindicated.

C. Bacterial infection that is caused by non-invasive E. coli only. Rifaximin is not indicated for traveler's diarrhea caused by other pathogens, including Shigella, Salmonella or Campylobacter species.
D. Patient does not exhibit symptoms of severe or systemic bacterial infection, including fever and bloody stools (i.e. invasive infection).
E. OR Clinically unacceptable risk with a change in therapy to a preferred drug.

NOTE: Treatment with sulfonamides, neomycin, ampicillin, doxycycline, tetracycline, trimethoprim alone, or trimethoprim-sulfamethoxazole is no longer recommended as first line therapy for travelers' diarrhea due to worldwide resistance.

Irritable Bowel Syndrome with Diarrhea (IBS-D) (must meet all):

A. Diagnosis of irritable bowel syndrome with diarrhea (IBS-D);
B. Age ≥ 18 years;
C. Failure of adherent use of one of the following regimens in the past 90 days (as evidenced by claims history): loperamide (10-day trial) or a PDL bile acid sequestrant, unless contraindicated;
D. Request does not exceed FDA approved maximum recommended dose and health plan approved daily quantity limit.

Hepatic Encephalopathy

A. Patients age ≥ 18 years.
B. Documented adherent use of lactulose at dosing of 30-45 ml 3 to 4 times daily. Dosage should be titrated to

produce 2 to 3 soft formed stools daily, unless contraindicated or intolerance **AND**

C. Concurrent use of lactulose at adequate dosing in the past 90 days (as evidenced by claims history)

D. OR Clinically unacceptable risk with a change in therapy to a preferred drug.

NOTE: Rifaximin has not been studied in patients with MELD (model for end stage liver disease) scores > 25. There is increased systemic exposure in patients with more severe hepatic dysfunction. In trials, 91% of patients use lactulose with rifaximin concomitantly.

Approval:

Initial Approval:

Travelers' Diarrhea – 200 mg 3 times daily x 3 days
Hepatic Encephalopathy– 550 mg 2 times daily x 3 months
Irritable Bowel Syndrome with Diarrhea (IBS-D) – Approve for 14 days

Continued Approval:

A. Traveler's Diarrhea – There is no evidence to suggest additional benefit of treatment with rifaximin beyond 3 days

B. Hepatic Encephalopathy – Approve for 6 months if claims history shows concurrent lactulose use within the previous 90 days and documentation shows that patient has had no adverse events and has improved symptoms.

C. Irritable Bowel Syndrome with Diarrhea (IBS-D) (must meet all)–

a. Previously received medication via Centene benefit or member has previously met all initial approval criteria

b. Member has not had ≥ two 14-day treatment courses in the last 6 months

c. If request is for a dose increase, request does not exceed FDA approved maximum recommended dose and health plan approved daily quantity limit

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Special Instructions

> Please refer to prescribing information for dosing, precautions, and other clinical information.

> Due to concerns about inappropriate use of antibiotics leading to an increase in resistant organisms, prescribers should only consider treating travelers' diarrhea with rifaximin for infections that are proven or strongly suspected to be caused by *E. coli* bacteria.

> Rifaximin should not be used for travelers' diarrhea complicated by fever or blood in the stool or diarrhea due to pathogens other than *E. coli*.

> *Clostridium difficile*-associated diarrhea has been reported with use of nearly all antibacterial agents, including rifaximin

> Pregnancy Category C risk.

> MELD (Model for End Stage Liver Disease) i s a validated chronic liver disease severity scoring system

References:

1. Xifaxan® prescribing information. Accessed October, 2014.
2. Hill, DR, Ericsson, CD, Pearson, RD, et al. The practice of travel medicine: guidelines by the Infectious Diseases

Society of America. Clin Infect Dis 2006; 43:1499.
3. Bass, N M, Mullen, K D, Sanyal, A, et al. (2010). Rifaximin treatment in hepatic encephalopathy. The New England journal of medicine, 362(12), 1071-81.
4. Sharma, B C, Sharma, P, Agrawal, A, et al. (2009). Secondary prophylaxis of hepatic encephalopathy: an open-label randomized controlled trial of lactulose versus placebo. Gastroenterology, 137(3), 885-91, 891.e1.
5. Lactulose prescribing information. Clinical Pharmcology. Accessed October 2014. www.clinicalpharmacology.com
6. Ferenci, P. Treatment of Hepatic Encephalopathy in adults.Runyon B (Ed), UpToDate, Waltham, MA. Accessed October 2014.
7. Wanke, CA. Travelers' diarrhea. Calderwood SB (Ed), UpToDate, Waltham, MA. Accessed October 2014.

Revision Log	
Revision	**Date**
Modified "Criteria for Approval": Hepatic Encephalopathy "B.": Removed "treatment failure and"; modified "Dosage should be titrated to produce 2 to 3 soft formed stools daily". Removed "adjusted every 1-2 days to achieve".	11/12
Modified "Criteria for Approval": Travelers' Diarrhea "B.": Documented treatment failure with quinolone antibiotic (e.g. ciprofloxacin 500mg twice daily for 1-3 days) or azithromycin (recommended dosing 500mg daily for 3 days or 1000mg single dose) Updated reference section to reflect current literature search.	11/12
Added criteria C under approval criteria for hepatic encephalopathy. Lactulose was used concomitantly 91% of patients clinical trial for the approve of rifaximin for this indication and clinically, rifaximin should be used as an adjunct to lactulose and not a substitute (see reference 6).	11/13
Added requirement for history of lactulose use within past 90 days	11/13

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To the continued approval criteria to ensure that lactulose is being used concomitantly (see reference 6).	
Updated reference section to reflect current literature search.	11/13
Updated references.	12/14
Added "Clinically unacceptable risk with a change in therapy to a preferred drug" to criteria for approval	06/15
Annual Review, No Changes	08/16
Added approval criteria for Irritable Bowel Syndrome with Diarrhea	09/16
Annual Review, No changes	07/17

POLICY AND PROCEDURE APPROVAL

Pharmacy & Therapeutics Committee: Approval on file

V.P., Pharmacy Operations: Approval on file

Sr. V.P., Chief Medical Officer: Approval on file