Clinical Policy: rifaximin (Xifaxan)
Reference Number: HIM.PA.68
Effective Date: 12/14
Last Review Date: 08/17
Line of Business: Health Insurance Marketplace

Coding Implications
Revision Log

See Important Reminder **at the end of this policy for important regulatory and legal information.**

Description
Rifaximin (Xifaxan®) is an oral rifamycin antibiotic.

FDA approved indication
Xifaxan is indicated:
- For the treatment of travelers' diarrhea (TD) caused by noninvasive strains of *Escherichia coli* in adult and pediatric patients 12 years of age and older
- For the reduction in risk of overt hepatic encephalopathy (HE) recurrence in adults
- For the treatment of irritable bowel syndrome with diarrhea (IBS-D) in adults

Limitation of use:
- TD: Do not use in patients with diarrhea complicated by fever or blood in the stool or diarrhea due to pathogens other than *Escherichia coli.*

Policy/Criteria
Provider must submit documentation (including office chart notes and lab results) supporting that member has met all approval criteria

I. Initial Approval Criteria

A. Travelers' Diarrhea (must meet all)**:**
1. Diagnosis of traveler's diarrhea;
2. Failure of one of the following regimens, unless contraindicated or clinically significant adverse effects are experienced (a or b):
   a. Ciprofloxacin 500 mg twice daily for 1-3 days;
   b. Levofloxacin 500 mg once daily for 1-3 days;
3. Failure of azithromycin 1000 mg single dose unless contraindicated or clinically significant adverse effects are experienced;
4. Dose does not exceed 600 mg/day (3 tables/day).

Approval duration: 200 mg 3 times daily for 3 days

B. Hepatic Encephalopathy (must meet all)**:**
1. Diagnosis of hepatic encephalopathy;
2. Failure of lactulose in the past 30 days at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
3. Dose does not exceed 1100 mg/day (2 tablets/day).

Approval duration: 550 mg 2 times daily for 6 months

C. Irritable Bowel Syndrome with Diarrhea (must meet all)**:**

1. Diagnosis of irritable bowel syndrome with diarrhea;
2. Failure of an antispasmodic agent (e.g., dicyclomine) at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
3. Failure of ≥ 10 day trial of loperamide at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
4. Dose does not exceed 1650 mg/day (3 tablets/day).

Approval duration: 550 mg 3 times daily for 14 days

D. Other diagnoses/indications

1. Refer to HIM.PHAR.21 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized);

II. Continued Therapy

A. Travelers' Diarrhea (must meet all)**:**

1. May not be renewed as maximum allowed treatment duration is 3 days. Review initial approval criteria for new cases of travelers' diarrhea unrelated to original medication request.

B. Hepatic Encephalopathy (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Documentation of positive response to therapy;
3. Xifaxan is being used concurrently with lactulose, unless contraindicated or clinically significant adverse effects are experienced;
4. Dose does not exceed 1100 mg/day (2 tablets/day).

Approval duration: 12 months

C. Irritable Bowel Syndrome with Diarrhea (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Documentation of positive response to therapy;
3. Member has not had ≥ two 14-day treatment course in the last 6 months;
4. Dose does not exceed 1650 mg/day (3 tablets/day).

Approval duration: 14 days

D. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to HIM.PA.21 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – HIM.PA.21 or evidence of coverage documents

IV. Appendices/General Information

Appendix A: Abbreviation Key
FDA: Food and Drug Administration
HE: hepatic encephalopathy
IBS-D: irritable bowel syndrome with diarrhea
TD: travelers' diarrhea

V. References

1. Xifaxan Prescribing Information. Raleigh, NC: Salix Pharmaceuticals, Inc.; November 2015. Available at: https://shared.salix.com/shared/pi/xifaxan550-pi.pdf. Accessed April 11, 2017.
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. Vilstrup H, Amodio P, Bajaj J, et al. Hepatic encephalopathy in chronic liver disease: 2014 practice guideline by AASLD-EASL. Hepatology. 2014; 60 (2): 715-735.
6. Weinberg DS, Smalley W, Heidelbaugh JJ, Shahnaz S. American Gastroenterological Association Institute guideline on the pharmacological management of irritable bowel syndrome. Gastroenterology. 2014; 147: 1146-1149.
7. Lacy BE, Chey WD, Lembo AJ. New and emerging treatment options for irritable bowel syndrome. Gastroenterol Hepatol. 2015; 11(4 Suppl 2): 1-19.
8. Ford AC, Moayyedi P, Lacy BE et al. American College of Gastroenterology monograph on the management of irritable bowel syndrome and chronic idiopathic constipation. Am J Gastroenterol. 2014 Aug;109 Suppl 1:S2-26; quiz S27. doi: 10.1038/ajg.2014.187.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Changed guideline to new format.	08/16	08/16
Removed age requirement as age is not an absolute contraindication for all diagnoses. For travelers' diarrhea: added levofloxacin as a trial option and removed BID dosing for azithromycin per IDSA For traveler's diarrhea: removed Patient does not exhibit symptoms of severe or systemic bacterial infection, including fever and bloody stools (i.e. invasive infection); For hepatic encephalopathy: Removed "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 not tolerated." Replaced with general statement of use at the max indicated dose.	04/17	08/17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
For hepatic encephalopathy: Removed "Concurrent use of lactulose at adequate dosing in the past 90 days (as evidenced by claims history)" replaced with use of lactose in the past 30 days per IDSA. Updated approval duration to 6 months For IBS: Patient must meet Rome III diagnostic criteria for IBS		

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.