Clinical Policy: Rifabutin (Mycobutin), Rifabutin/Omeprazole/Amoxicillin (Talicia)

Reference Number: ERX.NPA.135
Effective Date: 03.01.20
Last Review Date: 02.22
Line of Business: Commercial, Medicaid

Revision Log

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

Description

Rifabutin (Mycobutin®) is a derivative of rifamycin, an antimycobacterial agent.

Rifabutin/omeprazole/amoxicillin (Talicia®) is a three-drug combination of rifabutin; omeprazole, a proton pump inhibitor; and amoxicillin, a penicillin-class antibacterial.

FDA Approved Indication(s)

Mycobutin is indicated for the prevention of disseminated *Mycobacterium avium* complex (MAC) disease in patients with advanced HIV infection.

Talicia is indicated for the treatment of *Helicobacter pylori* infection in adults.

Policy/Criteria

Provider must submit documentation (including such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Mycobutin and Talicia are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. *Mycobacterium avium* Complex Prophylaxis (must meet all)**:**

1. Request is for Mycobutin;
2. Prescribed by or in consultation with an HIV or infectious disease specialist;
3. Age ≥ 18 years;
4. Failure of azithromycin or clarithromycin, unless clinically significant adverse effects are experienced or both are contraindicated;
5. If request is for brand Mycobutin, member must use generic rifabutin unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed 300 mg (2 capsules) per day.

Approval duration: 12 months

B. *Helicobacter pylori* Infection (must meet all)**:**

1. Diagnosis of *H. pylori* infection;
2. Prescribed by or in consultation with a gastroenterologist or infectious disease specialist;
3. Age ≥ 18 years;
4. Failure of a first-line treatment regimen (see *Appendix B*), unless contraindicated, clinically significant adverse effects are experienced, or culture and sensitivity report shows resistance or lack of susceptibility of *H. pylori* to all first-line treatment regimens;
5. For Mycobutin (off-label) requests, both of the following (a and b):
   a. Prescribed in combination with amoxicillin and a proton pump inhibitor;
   b. If request is for brand Mycobutin, member must use generic rifabutin unless contraindicated or clinically significant adverse effects are experienced;

6. For Talicia requests, member must instead use the individual components (i.e., generic rifabutin, amoxicillin, omeprazole) concurrently, unless contraindicated or clinically significant adverse effects are experienced;
7. Dose does not exceed one of the following (a or b):
   a. Mycobutin: 300 mg (2 capsules) per day;
   b. Talicia: 150 mg rifabutin (12 capsules) per day.

Approval duration:
Mycobutin – 10 days
Talicia – 14 days

C. Tuberculosis (off-label) (must meet all)**:**
1. Diagnosis of tuberculosis infection in member with HIV;
2. Request is for Mycobutin;
3. Prescribed by or in consultation with an HIV or infectious disease specialist;
4. Documentation of current or anticipated treatment with protease inhibitors, non-nucleoside reverse transcriptase inhibitors (NNRTIs), or integrase strand transfer inhibitors (INSTIs) other than elvitegravir for the treatment of HIV infection;
5. Age ≥ 18 years;
6. If request is for brand Mycobutin, member must use generic rifabutin unless contraindicated or clinically significant adverse effects are experienced;
7. Dose does not exceed one of the following (a or b):
   a. 300 mg (2 capsules) per day;
   b. 600 mg (4 capsules) per day and member is being treated with efavirenz.

Approval duration: 12 months

D. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. *Mycobacterium avium* Complex Prophylaxis (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for brand Mycobutin, member must use generic rifabutin unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, new dose does not exceed 300 mg (2 capsules) per day.

Approval duration: 12 months

B. *Helicobacter pylori* Infection
1. Re-authorization is not permitted. Members must meet the initial approval criteria.

Approval duration: Not applicable

C. Tuberculosis (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Documentation of current treatment with protease inhibitors, NNRTIs, or INSTIs other than elvitegravir for the treatment of HIV infection;
3. If request is for brand Mycobutin, member must use generic rifabutin unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, new dose does not exceed one of the following (a or b):
   a. 300 mg (2 capsules) per day;
   b. 600 mg (4 capsules) per day and member is being treated with efavirenz.

Approval duration: Up to a total duration of 12 months

D. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to ERX.PA.01 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 – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
INSTI: integrase strand transfer inhibitor
MAC*: Mycobacterium avium* complex
NNRTI: non-nucleoside reverse transcriptase inhibitor

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
azithromycin	**MAC:** 1,200 mg PO once weekly or 600 mg PO twice weekly	500 mg/day
clarithromycin	**MAC:** 500 mg PO BID	1.5 g/day
clarithromycin triple regimen	***H. pylori* infection:** 14 days: PPI (standard or double dose) BID; Clarithromycin 500 mg; Amoxicillin 1,000 mg or metronidazole 500 mg TID (if penicillin allergy)	See dosing regimen
bismuth quadruple regimen	***H. pylori* infection:** 10-14 days: PPI (standard dose) BID; bismuth subcitrate (120-300 mg) or subsalicylate (300 mg) QID; tetracycline 500 mg QID; metronidazole 250 mg QID or 500 mg TID-QID	See dosing regimen
concomitant regimen	***H. pylori* infection:** 10-14 days: PPI (standard dose) BID; Clarithromycin 500 mg; Amoxicillin 1,000 mg; Metronidazole or tinidazole 500 mg	See dosing regimen
sequential regimen	***H. pylori* infection:** 5-7 days of BID PPI (standard dose) + amoxicillin 1,000 mg; followed by 5-7 days of BID PPI, clarithromycin 500 mg + metronidazole/tinidazole	See dosing regimen
hybrid regimen	***H. pylori* infection:** 7 days of BID PPI (standard dose) + amoxicillin 1,000 mg; followed by 7 days of BID PPI, amoxicillin + clarithromycin 500 mg + metronidazole/tinidazole	See dosing regimen
levofloxacin triple regimen	***H. pylori* infection:** 10-14 days:	See dosing regimen

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	PPI (standard dose) BID; levofloxacin 500 mg QD; amoxicillin 1,000 mg BID	
levofloxacin sequential regimen	***H. pylori* infection:** 5-7 days of BID PPI (standard dose) + amoxicillin 1,000 mg; followed by 5-7 days of BID PPI, amoxicillin + metronidazole/tinidazole + QD levofloxacin 500 mg	See dosing regimen
rifabutin triple	***H. pylori* infection:** 10 days of BID PPI (standard dose) + amoxicillin 1,000 mg BID + rifabutin 300 mg QD	See dosing regimen

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Mycobutin: clinically significant hypersensitivity to rifabutin or to any other rifamycins
  - Talicia: hypersensitivity to the components of Talicia; patients receiving rilpivirine-containing products, delavirdine or voriconazole
- Boxed warning(s): none reported

Appendix D: General Information

- There is no evidence that rifabutin is an effective prophylaxis against Mycobacterium tuberculosis.

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Rifabutin (Mycobutin)	MAC prophylaxis	300 mg PO QD or 150 mg PO BID	300 mg/day
	Tuberculosis infection in patients co-infected with HIV	300 mg (approximately 5 mg/kg) PO QD in combination with other agents for up to 12 months	300 mg/day (600 mg/day if treatment with efavirenz)
	H. pylori infection (off-label)	300 mg PO QD with amoxicillin 1 g PO BID and proton pump inhibitor PO BID	300 mg/day
Rifabutin/ omeprazole/ amoxicillin (Talicia)	*H. pylori* infection	Four capsules PO Q8H for 14 days	150 mg rifabutin (12 capsules)/day

VI. Product Availability

Drug Name	Availability
Rifabutin (Mycobutin)	Capsule: 150 mg
Rifabutin/omeprazole/ amoxicillin (Talicia)	Delayed-release capsule: omeprazole 10 mg, (equivalent to 10.3 mg of omeprazole magnesium) amoxicillin 250 mg, and rifabutin 12.5 mg

VII. References

1. Mycobutin Prescribing Information. New York, New York: Pharmacia & Upjohn Co; September 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/050689s026lbl.pdf. Accessed September 23, 2021.
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2020. Available at: http://www.clinicalpharmacology-ip.com/. Accessed September 23, 2021.

3. U.S. Department of Health and Human Services. Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents. Available at: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/Adult_OI.pdf. Accessed September 23, 2021
4. Talicia Prescribing Information. Raleigh, NC: RedHill Biopharma Inc.; November 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/213004s002lbl.pdf. Accessed September 23, 2021.
5. Chey WD, Leontiadis GI, Howden CW, et al. ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. American Journal of Gastroenterology: 2017 January 10; doi: 10.1038/ajg.2016.563.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	12.03.19	02.20
1Q 2021 annual review: added missing "off-label" for Mycobutin for *H. pylori* infection; added criteria if request is for Mycobutin, medical justification supports inability to use generic rifabutin in initial and continuation criteria; references reviewed and updated.	11.06.20	02.21
1Q 2022 annual review: modified medical justification language to member must use language per updated template; clarified tuberculosis off-label criteria set apples to members with HIV and added additional option for current treatment with INSTIs other than elvitegravir (due to drug interactions) in addition to the previous options for protease inhibitors or NNRTIs; references reviewed and updated.	09.23.21	02.22
For tuberculosis off-label indication, revised to allow current or anticipated HIV therapy and dosing limitations to allow for potential drug interactions with efavirenz.	03.02.22	

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or 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.