Clinical Policy: Rifabutin (Mycobutin)

Reference Number: CP.PMN.223
Effective Date: 03.01.20
Last Review Date: 02.25
Line of Business: Commercial, HIM, 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.

FDA Approved Indication(s)

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

Policy/Criteria

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

It is the policy of health plans affiliated with Centene Corporation® that rifabutin and Mycobutin 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 MAC prophylaxis in member with HIV;
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* (off-label) (must meet all)**:**

** For Talicia® requests, see CP.PMN.277 Ulcer Therapy Combinations*

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. Prescribed in combination with amoxicillin and a proton pump inhibitor;

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 300 mg (2 capsules) per day for 10 days.

Approval duration: 10 days

C. Tuberculosis (off-label) (must meet all)**:**

1. Diagnosis of tuberculosis infection in member with HIV;
2. Prescribed by or in consultation with an HIV or infectious disease specialist;
3. 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;
4. Age ≥ 18 years;.
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 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 (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
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 (off-label) (must meet all):

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member has not received more than 12 months of therapy;
3. Documentation of current 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;
4. If request is for brand Mycobutin, member must use generic rifabutin unless contraindicated or clinically significant adverse effects are experienced;
5. 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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

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

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,	See dosing regimen

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	amoxicillin + clarithromycin 500 mg + metronidazole/tinidazole	
levofloxacin triple regimen	***H. pylori* infection:** 10-14 days: PPI (standard dose) BID; levofloxacin 500 mg QD; amoxicillin 1,000 mg BID	See dosing regimen
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

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): Clinically significant hypersensitivity to rifabutin or to any other rifamycins
- 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

Indication	Dosing Regimen	Maximum Dose
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

VI. Product Availability

Capsule: 150 mg

VII. References

1. Mycobutin Prescribing Information. New York, New York: Pharmacia & Upjohn Co; September 2021. Available at: labeling.pfizer.com/ShowLabeling.aspx?id=635. Accessed October 22, 2024.
2. Clinical Pharmacology [database online]. Elsevier, Inc. Updated periodically. Available at: https://www.clinicalkey.com/pharmacology/. Accessed October 30, 2024.

3. U.S. Department of Health and Human Services. Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents. Reviewed October 29, 2024. Available at: https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-opportunistic-infections/whats-new. Accessed October 30, 2024.
4. 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.
5. Chey, WD, Howden, CW, Moss, SF, et al. ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. The American Journal of Gastroenterology. September 2024. 119(9): 1730-1753.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q21 annual review: added "off-label" for Mycobutin for *H. pylori* infection; added redirection to generic rifabutin in initial and continuation criteria; references to HIM.PHAR.21 revised to HIM.PA.154; 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 applies to members with HIV and added additional option for current treatment with integrase strand transfer inhibitors (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	
Per February SDC and prior clinical guidance, removed Talicia from policy (new policy created for ulcer therapy combinations).	02.17.22	05.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.06.22	
1Q 2023 annual review: no significant changes; references reviewed and updated.	10.25.22	02.23
1Q 2024 annual review: no significant changes; added specific requirement that "request is for MAC prophylaxis in member with HIV" to support labeled indication; for off-label use in tuberculosis, added to continuation of therapy the following to support existing approval duration: "member has not received more than 12 months of therapy"; for added clarity with requests for H.pylori added the following note "for Talicia requests, see CP.PMN.277 Ulcer Therapy Combinations"; references reviewed and updated.	10.20.23	02.24
1Q 2025 annual review: no significant changes; added Commercial line of business; in policy description added reference to generic to clarify that criteria would apply; references reviewed and updated.	10.22.24	02.25

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.