Clinical Policy: Rifabutin (Mycobutin), Rifabutin/Omeprazole/Amoxicillin (Talicia)
Reference Number: CP.PMN.223
Effective Date: 03.01.20
Last Review Date: 02.21
Line of Business: HIM, Medicaid

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 (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 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 both are contraindicated or clinically significant adverse effects are experienced;
      5. If request is for Mycobutin, medical justification supports inability to use generic rifabutin (e.g., contraindications to excipients in rifabutin);
      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 or 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, prescribed in combination with amoxicillin and a proton pump inhibitor;

6. For Talicia requests, medical justification supports inability to use the individual components (i.e., generic rifabutin, amoxicillin, omeprazole) concurrently (e.g., contraindications to the excipients);

7. If request is for Mycobutin, medical justification supports inability to use generic rifabutin (e.g., contraindications to excipients in rifabutin);

8. 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;
   2. Request is for Mycobutin;
   3. Prescribed by or in consultation with an HIV or infectious disease specialist;
   4. Documentation of current treatment with protease inhibitors or non-nucleoside reverse transcriptase inhibitors (NNRTIs) for the treatment of HIV infection;
   5. Age ≥ 18 years;
   6. If request is for Mycobutin, medical justification supports inability to use generic rifabutin (e.g., contraindications to excipients in rifabutin);
   7. Dose does not exceed 5 mg/kg per day.

**Approval duration: 12 months**

D. **Other diagnoses/indications**
   1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid and HIM.PA.154 for health insurance marketplace.

II. **Continued Therapy**

A. **Mycobacterium avium Complex Prophylaxis** (must meet all):
   1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   2. Member is responding positively to therapy;
   3. If request is for Mycobutin, medical justification supports inability to use generic rifabutin (e.g., contraindications to excipients in rifabutin);
   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 Centene benefit or member has previously met initial approval criteria;
   2. Documentation of current treatment with protease inhibitors or non-nucleoside reverse transcriptase inhibitors (NNRTIs) for the treatment of HIV infection;
   3. If request is for Mycobutin, medical justification supports inability to use generic rifabutin (e.g., contraindications to excipients in rifabutin);
   4. If request is for a dose increase, new dose does not exceed 5 mg/kg per day.
      **Approval duration: Up to a total duration of 12 months**

D. *Other diagnoses/indications* (must meet 1 or 2):
   1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
      **Approval duration: Duration of request or 12 months (whichever is less); or**
   2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid and HIM.PA.154 for health insurance marketplace.

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.PMN.53 for Medicaid and HIM.PA.154 for health insurance marketplace or evidence of coverage documents.

IV. Appendices/General Information
   *Appendix A: Abbreviation/Acronym Key*
   FDA: Food and Drug Administration
   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.*

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/ Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>azithromycin</td>
<td><strong>MAC</strong>: 1,200 mg PO once weekly or 600 mg PO twice weekly</td>
<td>500 mg/day</td>
</tr>
<tr>
<td>clarithromycin</td>
<td><strong>MAC</strong>: 500 mg PO BID</td>
<td>1.5 g/day</td>
</tr>
<tr>
<td>clarithromycin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>triple regimen</td>
<td><strong>H. pylori infection:</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>14 days:</td>
<td></td>
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<td></td>
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</tbody>
</table>
## CLINICAL POLICY
Rifabutin, Rifabutin/Omeprazole/Amoxicillin

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PPI (standard or double dose) BID; Clarithromycin 500 mg; Amoxicillin 1,000 mg or metronidazole 500 mg TID (if penicillin allergy)</td>
<td></td>
</tr>
<tr>
<td>bismuth</td>
<td>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</td>
<td>See dosing regimen</td>
</tr>
<tr>
<td>quadruple</td>
<td>regimens</td>
<td></td>
</tr>
<tr>
<td>concomitant</td>
<td>H. pylori infection: 10-14 days: PPI (standard dose) BID; Clarithromycin 500 mg; Amoxicillin 1,000 mg; Metronidazole or tinidazole 500 mg</td>
<td>See dosing regimen</td>
</tr>
<tr>
<td>sequential</td>
<td>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</td>
<td>See dosing regimen</td>
</tr>
<tr>
<td>regimen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>hybrid</td>
<td>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</td>
<td>See dosing regimen</td>
</tr>
<tr>
<td>levofloxacin</td>
<td>H. pylori infection: 10-14 days: PPI (standard dose) BID; levofloxacin 500 mg QD; amoxicillin 1,000 mg BID</td>
<td>See dosing regimen</td>
</tr>
<tr>
<td>triple regimen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>levofloxacin</td>
<td>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</td>
<td>See dosing regimen</td>
</tr>
<tr>
<td>sequential regimen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>rifabutin triple</td>
<td>H. pylori infection: 10 days of BID PPI (standard dose) + amoxicillin 1,000 mg BID + rifabutin 300 mg QD</td>
<td>See dosing regimen</td>
</tr>
</tbody>
</table>

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
Talia: 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

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifabutin (Mycobutin)</td>
<td>MAC prophylaxis</td>
<td>300 mg PO QD or 150 mg PO BID</td>
<td>300 mg/day</td>
</tr>
<tr>
<td></td>
<td>Tuberculosis infection in patients co-infected with HIV</td>
<td>5 mg/kg PO QD in combination with other agents for up to 12 months</td>
<td>5 mg/kg/day</td>
</tr>
<tr>
<td></td>
<td><em>H. pylori</em> infection (off-label)</td>
<td>300 mg PO QD with amoxicillin 1 g PO BID and proton pump inhibitor PO BID</td>
<td>300 mg/day</td>
</tr>
<tr>
<td>Rifabutin/omeprazole/amoxicillin (Talicia)</td>
<td><em>H. pylori</em> infection</td>
<td>Four capsules PO Q8H</td>
<td>150 mg rifabutin (12 capsules)/day</td>
</tr>
</tbody>
</table>

VI. Product Availability

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifabutin (Mycobutin)</td>
<td>Capsule: 150 mg</td>
</tr>
<tr>
<td>Rifabutin/omeprazole/amoxicillin (Talicia)</td>
<td>Delayed-release capsule: omeprazole 10 mg, (equivalent to 10.3 mg of omeprazole magnesium) amoxicillin 250 mg, and rifabutin 12.5 mg</td>
</tr>
</tbody>
</table>

VII. References
Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Description</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Policy created, adapted from HIM.PA.12; HIM.PA.12 to be retired; added Talicia and criteria set for H. pylori; references reviewed and updated.</td>
<td>12.03.19</td>
<td>02.20</td>
</tr>
<tr>
<td>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.</td>
<td>11.06.20</td>
<td>02.21</td>
</tr>
</tbody>
</table>

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.

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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.

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