Clinical Policy: Benznidazole
Reference Number: CP.PMN.90
Effective Date: 10.17.17
Last Review Date: 02.19
Line of Business: Commercial, HIM, Medicaid

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

Description
Benznidazole is a nitroimidazole antimicrobial.

FDA Approved Indication(s)
Benznidazole is indicated in pediatric patients 2 to 12 years of age for the treatment of Chagas disease (American trypanosomiasis), caused by Trypanosoma cruzi (T. cruzi).

This indication is approved under accelerated approval based on the number of treated patients who became Immunoglobulin G (IgG) antibody negative against the recombinant antigens of T. cruzi. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

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.

It is the policy of health plans affiliated with Centene Corporation® that benznidazole is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Chagas Disease (must meet all):
      1. Diagnosis of Chagas disease confirmed by one of the following tests (a, b, or c):
         a. Detection of circulating T. cruzi trypomastigotes on microscopy;
         b. Detection of T. cruzi DNA by polymerase chain reaction assay;
         c. Two positive diagnostic serologic tests* using different techniques (e.g., enzyme-linked immunoassay, indirect fluorescent antibody) and antigens (e.g., whole-parasite lysate, recombinant antigens) showing IgG antibodies to T. cruzi;
      2. Prescribed by or in consultation with an infectious disease specialist;
      3. Age 2 to ≤ 12 years;
      4. Dose (weight-based) does not exceed 400 mg per day.

   Approval duration: 60 days total

*If two commercial diagnostic IgG tests are unavailable, providers should consult their state health department for guidance; if results are discordant, a third assay may be needed. Chagas disease is a reportable disease in some states. Donor screening tests and Immunoglobulin M serology tests are not considered diagnostic tests.
B. 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.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy
   A. Chagas Disease (must meet all):
      1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
      2. Member has not yet received 60 or more days of benznidazole therapy;
      3. If request is for a dose increase, new dose does not exceed 400 mg per day.
   
   Approval duration: 60 days total

   B. 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 6months (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.CPA.09 for commercial, HIM.PHAR.21 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.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information
   Appendix A: Abbreviation/Acronym Key
   CDC: Centers for Disease Control and Prevention  
   IgG: immunoglobulin G
   WHO: World Health Organization
   T cruzi: Trypanosoma cruzi

   Appendix B: Therapeutic Alternatives
   Not applicable

   Appendix C: Contraindications/Boxed Warnings
   • Contraindication(s): Benznidazole tablets are contraindicated in patients with a history of hypersensitivity reaction to benznidazole or other nitroimidazole derivatives. Reactions have included severe skin and soft tissue reactions.
   • Boxed warning(s): None reported

   Appendix D: General Information
   • Resources and Consultation
V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
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<tbody>
<tr>
<td>Chagas disease</td>
<td></td>
<td>400 mg/day</td>
</tr>
<tr>
<td>Body Weight Range (kg)</td>
<td>Dose (mg)</td>
<td># of 12.5 mg tablets</td>
</tr>
<tr>
<td>&lt;15 kg</td>
<td>50 mg</td>
<td>4 tablets</td>
</tr>
<tr>
<td>15 kg to &lt;20 kg</td>
<td>62.5 mg</td>
<td>5 tablets</td>
</tr>
<tr>
<td>20 kg to &lt;30 kg</td>
<td>75 mg</td>
<td>6 tablets</td>
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<tr>
<td>30 kg to &lt;40 kg</td>
<td>100 mg</td>
<td>1 tablet</td>
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<tr>
<td>40 kg to &lt;60 kg</td>
<td>150 mg</td>
<td>1 ½ tablets</td>
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<tr>
<td>≥60 kg</td>
<td>200 mg</td>
<td>2 tablets</td>
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</table>

VI. Product Availability
Tablets: 12.5 mg (not scored) or 100 mg (scored for halves or quarters)

VII. References


<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
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<tbody>
<tr>
<td>Policy created.</td>
<td>10.17.17</td>
<td>02.18</td>
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<tr>
<td>1Q 2019 annual review; no significant changes, references reviewed and updated.</td>
<td>11.13.18</td>
<td>02.19</td>
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**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.

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy.

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