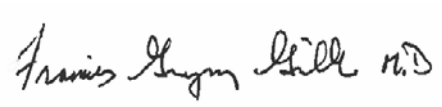


Prior Authorization Review Panel

CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: PA Health & Wellness	Submission Date: 02/01/2020
Policy Number: PA.CP.PMN.90	Effective Date: 01/01/2018 Revision Date: 01/15/2020
Policy Name: Benznidazole	
<p>Type of Submission – <u>Check all that apply</u>:</p> <ul style="list-style-type: none"> <input type="checkbox"/> New Policy <input checked="" type="checkbox"/> Revised Policy* <input type="checkbox"/> Annual Review - No Revisions <input type="checkbox"/> Statewide PDL - <i>Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.</i> 	
<p>*All revisions to the policy <u>must</u> be highlighted using track changes throughout the document.</p> <p>Please provide any changes or clarifying information for the policy below:</p> <p style="margin-left: 40px;">1Q 2020 annual review; aligned the maximum auth duration for Other diagnoses/indications to 60 days; references reviewed and updated.</p>	
Name of Authorized Individual (Please type or print): Francis G. Grillo, MD	Signature of Authorized Individual: 

Clinical Policy: Benznidazole

Reference Number: PA.CP.PMN.90

Effective Date: 10.17.17

Last Review Date: 01.15.20

[Revision Log](#)

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 (which may include office chart notes and lab results) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with PA Health & Wellness 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 \leq 18 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 PA.PA.CP.PMN.53.

II. Continued Therapy

A. Chagas Disease (must meet all):

1. Currently receiving medication via PA Health & Wellness benefit or member has met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
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 PA Health & Wellness benefit or member has met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
Approval duration: Duration of request or 60 days(whichever is less); or
2. Refer to PA.PA.CP.PMN.53.

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 – PA.PA.CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CDC: Centers for Disease Control and
Prevention

IgG: immunoglobulin G

T cruzi: *Trypanosoma cruzi*

WHO: World Health Organization

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.
 - Benznidazole tablets are contraindicated in patients who have taken disulfiram within the last two weeks. Psychotic reactions may occur in patients who are using benznidazole and disulfiram concurrently.
 - Consumption of alcoholic beverages or products containing propylene glycol is contraindicated in patients during and for at least 3 days after therapy with benznidazole tablets. A disulfiram-like reaction (abdominal cramps, nausea, vomiting, headaches, and flushing) may occur due to the interaction between alcohol or propylene glycol and benznidazole.
- Boxed warning(s): None reported

Appendix D: General Information

- Resources and Consultation

- Centers for Disease Control and Prevention (CDC)
 1. Parasitic Diseases: 404-718-4745, <https://www.cdc.gov/parasites/chagas/>
 - CDC recommended guidance document: Bern C, Montgomery SP, Herwaldt BL, et al. Evaluation and treatment of Chagas disease in the United States: a systematic review. JAMA 2007; 298:2171.
 2. CDC Drug Service: 404-639-3670
 3. CDC Emergency Operations Center: 770-488-7100
- World Health Organization (WHO)
 1. Outside the US: www.who.int/chagas/home_treatment/en/
- American Society of Tropical Medicine and Hygiene
 1. Directory of consultants: <http://www.astmh.org/education-resources/clinical-consultants-directory>

V. Dosage and Administration

Dosage and Administration						
Indication	Dosing Regimen					Maximum Dose
Chagas disease	Body Weight Range (kg)	Dose (mg)	# of 12.5 mg tablets	# of 100 mg tablets	Duration and Frequency of Therapy	400 mg/day
	<15 kg	50 mg	4 tablets	½ tablet	PO BID approximately 12 hours apart for 60 days	
	15 kg to <20 kg	62.5 mg	5 tablets			
	20 kg to <30 kg	75 mg	6 tablets	¾ tablet		
	30 kg to <40 kg	100 mg		1 tablet		
	40 kg to <60 kg	150 mg		1 ½ tablets		
	≥60 kg	200 mg		2 tablets		

VI. Product Availability

Tablets: 12.5 mg (not scored) or 100 mg (scored for halves or quarters)

VII. References

1. Benznidazole Prescribing Information. Florham Park, NJ: Exeltis USA, Inc.; August 2017. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209570lbl.pdf. Accessed December 30, 2019.
2. Benznidazole Drug Monograph. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2019. Available at: <http://www.clinicalpharmacology-ip.com/>.
3. Estani SS, Segura EL, Ruiz AM, et al. Efficacy of chemotherapy with benznidazole in children in the indeterminate phase of Chagas disease. 1998; Am J Trop Med Hyg 59: 526-529.
4. Sgambatti de Andrade, ALS, Zicker F, Mauricio de Oliveira. R, et al. Randomised trial of efficacy of benznidazole in treatment of early *Trypanosoma cruzi* infection. 1996; Lancet 348: 1407-1413.

5. Perez-Molina JA, Molina I. Chagas disease: Seminar. Lancet. June 30, 2017.
[http://dx.doi.org/10.1016/S0140-6736\(17\)31612-4](http://dx.doi.org/10.1016/S0140-6736(17)31612-4).
6. Bern C. Chagas disease. N Engl J Med 2015; 373: 456-66. DOI: 10.1056/NEJMra1410150.
7. Bern C, Montgomery SP, Herwaldt BL, et al. Evaluation and treatment of Chagas disease in the United States: A systematic review. JAMA 2007; 298:2171.
8. Formulary (Benznidazole, nifurtimox): Infectious Diseases Laboratory. Centers for Disease Control and Prevention. Available at <https://www.cdc.gov/laboratory/drugservice/formulary.html#tnifurtimox>. Last updated May 18, 2018. Accessed November 7, 2018.
9. American Trypanosomiasis. DPDx - Laboratory identification of parasitic diseases of public health concern. Centers for Disease Control and Prevention. Available at <https://www.cdc.gov/dpdx/trypanosomiasisamerican/index.html>. Last updated April 30, 2019. Accessed December 30, 2019.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2019 annual review; references reviewed and updated.	01/19	
1Q 2020 annual review; aligned the maximum auth duration for Other diagnoses/indications to 60 days; references reviewed and updated.	01/2020	