BlueCross BlueShield of Arizona
An Independent Licensee of the Blue Cross and Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 11/16/17
LAST REVIEW DATE: 11/16/17
LAST CRITERIA REVISION DATE:
ARCHIVE DATE:

BENZNIDAZOLE oral tablet

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

BENZNIDAZOLE oral tablet (cont.)

Description:

- Benznidazole Tablets, a nitroimidazole antimicrobial, is indicated in pediatric patients 2 to 12 years of age for the treatment of Chagas disease (American trypanosomiasis), caused by *Trypanosoma cruzi*.

- Chagas disease is a parasitic infection that can be transmitted through different routes, including contact with the feces of a certain insect, blood transfusions, or from a mother to her child during pregnancy. The disease can cause serious heart illness, and it also can affect swallowing and digestion. There may be approximately 300,000 persons in the U.S. with Chagas disease.

- The safety and efficacy of benznidazole were demonstrated in 2 placebo-controlled studies of 235 patients (ages 6 – 12 years) with chronic Chagas disease. Both studies measured anti-*T. cruzi* IgG antibodies changing from positive to negative.

    - In the first study, 60% of patients treated with benznidazole vs. 13.5% treated with placebo were seronegative (Difference = 46.5; 95% CI: 24.5, 64.4).
    - In the second study, 54.7% of patients treated with benznidazole vs. 4.6% treated with placebo were seronegative (Difference = 50.1; 95% CI: 35.8, 63.4).
    - In addition, a study of the safety and pharmacokinetics of benznidazole in pediatric patients 2 - 12 years of age provided information for dosing recommendations down to 2 years of age.

- Benznidazole is contraindicated in patients with a history of hypersensitivity reaction to benznidazole or other nitroimidazole derivatives, disulfiram usage within the last two weeks, and alcoholic beverage consumption during and for at least three days after therapy.

- Other warnings and precautions of benznidazole include potential for genotoxicity and carcinogenicity, embryo-fetal toxicity, hypersensitivity skin reactions, central and peripheral nervous system effects, and hematological manifestations of bone marrow depression.

- The most common adverse reactions with benznidazole use were abdominal pain, rash, decreased weight, headache, nausea, vomiting, neutropenia, urticaria, pruritus, eosinophilia, and decreased appetite.

- The recommended dosage of benznidazole is 5 mg/kg to 8 mg/kg orally administered in two divided doses separated by approximately 12 hours, for a duration of 60 days.

BENZNIDAZOLE oral tablet (cont.)

Benznidazole

Medication class:
Anthelmintics

FDA-approved indication(s):
- In pediatric patients 2 to 12 years of age for the treatment of Chagas disease (American trypanosomiasis), caused by *Trypanosoma 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.

Recommended Dose:
- Pediatric Patients 2 to 12 years of age: The total daily dose is 5 mg/kg to 8 mg/kg orally administered in two divided doses separated by approximately 12 hours for a duration of 60 days.
- See Full Prescribing Information for important administration instructions.

Available Dosage Forms:
- Tablets: 100 mg (functionally scored)
- Tablets: 12.5 mg

Warnings and Precautions:
- Potential Risk for Genotoxicity and Carcinogenicity.
- Embryo-Fetal Toxicity: Can cause fetal harm. Pregnancy testing is recommended for females of reproductive potential. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception.
- Hypersensitivity skin reactions have been reported with benznidazole. In case of skin reactions, presenting with additional symptoms of systemic involvement such as lymphadenopathy, fever and/or purpura, discontinuation of treatment is recommended.
- Treatment with Benznidazole Tablets can potentially cause paresthesia or symptoms of peripheral neuropathy. In cases where neurological symptoms occur, immediate discontinuation of treatment is recommended.
- There have been hematological manifestations of bone marrow depression, such as neutropenia, thrombocytopenia, anemia, and leukopenia.

BENZNIDAZOLE oral tablet (cont.)

Criteria:

- **Criteria for initial therapy:** Benznidazole is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is an Infectious Disease specialist

  2. Individual is 2 to 12 years of age

  3. A confirmed diagnosis of Chagas disease (American trypanosomiasis), caused by *Trypanosoma cruzi* confirmed by one of the following tests:
     - Detection of circulating *T. cruzi* trypomastigotes on microscopy;
     - Detection of *T. cruzi* DNA by polymerase chain reaction assay;
     - Two positive diagnostic serologic tests* using different techniques (e.g., enzymelinked immuno assay, indirect fluorescent antibody) and antigens (e.g., whole parasitelysate, recombinant antigens) showing IgG antibodies to *T. cruzi*

  4. Dose (weight-based) does not exceed 400 mg/day.

  5. There are **NO** contraindications.
     - Contraindications include:
       - History of hypersensitivity reaction to benznidazole or other nitroimidazole derivatives
       - Disulfiram usage within the last two weeks
       - Alcoholic beverage consumption during and for at least three days after therapy

  Initial approval duration: 60 days total

Resources:

Benznidazole. Package Insert. Revised by manufacturer 8/2017. Accessed 11-03-17.

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:	Dosage Form:
Directions for Use:	Quantity: / Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.