BlueCross BlueShield of Arizona
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PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 01/18/18**
SECTION: DRUGS	**LAST REVIEW DATE: 02/21/19**
	LAST CRITERIA REVISION DATE: 02/21/19
	ARCHIVE DATE:

ALBENZA® (albendazole) oral tablet and chewable 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.**

ALBENZA® (albendazole) oral tablet and chewable tablet (cont.)

Criteria:

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

  1. Prescriber is an Infectious Disease specialist

  2. A confirmed diagnosis of **ONE** of the following:
     - Parenchymal neurocysticercosis due to active lesions caused by larval forms of the pork tapeworm, *Taenia solium*
     - Cystic hydatid disease of the liver, lung, and peritoneum caused by the larval form of the dog tapeworm, *Echinococcus granulosus*

  3. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
     - Complete blood count
     - Pregnancy test in a woman of reproductive potential

  4. There are **NO** contraindications.
     - Contraindications include:
       - Known hypersensitivity to the benzimidazole class of compounds or any component of Albenza

  Initial approval duration:

  Patients weighing ≥ 60 kg: 400 mg twice daily
  Patients weighing < 60 kg: 15 mg/kg/day divided twice daily (maximum total daily dose 800 mg)

  For neurocysticercosis: 120 tablets per month for 1 month

  For hydatid disease: Up to 112 tablets per 28 days for 4 months

- **Criteria for continuation of coverage (renewal request):** Albenza (albendazole) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual continues to be seen by an Infectious Disease specialist

  2. Individual's condition has not improved or worsened while on therapy
     - Worsening is defined as:
       - Neurocystercercosis – continue to have nausea, vomiting, headache, visual problems, seizures, altered mental status, cysticerci are present and have not calcified
       - Cystic hydatid disease – cysticerci have not calcified, daughter cells are present, stage of cyst is either active or transitional

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3. The indication for use is one that requires a longer duration than the usual duration for either:
   - Neurocystercercosis
   - Cystic hydatid disease

4. Individual has been adherent with the medication

5. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use
   - Contraindications as listed in the criteria for initial therapy section
   - Significant adverse effect such as:
     - Bone marrow suppression
     - Liver enzyme elevation

6. There are no significant interacting drugs

Renewal duration:
For neurocysticercosis: 120 tablets per month for 1 month
For hydatid disease: Up to 112 tablets per 28 days for 4 months

Description:

Albenza (albendazole) is a synthetic benzimidazole antihelminthic drug. It is rapidly converted in the liver to the primary metabolite, albendazole sulfoxide, which is further metabolized to albendazole sulfone and other oxidative metabolites. The systemic anthelmintic activity has been attributed to the primary metabolite, albendazole sulfoxide. Albendazole binds to the colchicine-sensitive site of β-tubulin, inhibiting their polymerization into microtubules. The decrease in microtubules in the intestinal cells of the parasites decreases the absorption and uptake of glucose by the adult and larval forms of the parasites; it also depletes glycogen storage. Insufficient glucose results in inadequate energy for the production of adenosine trisphosphate (ATP) and the parasite eventually dies.

Background:

Cysticercosis (pork tapeworm):
- Cysticercosis is caused by the larval stage (metacestode) of the pork tapeworm *Taenia solium*

- Clinical manifestations depend upon whether the cysts are localized to the brain parenchyma, the extraparenchymal tissues, or extraneural sites
  - Parenchymal cysts (single or multiple lesions) are the most common form of neurocysticercosis (NCC)
    - Parenchymal cysts are associated with seizures and headache
    - The risk for seizures is highest in the setting of multiple cysts when the lesions are degenerating and surrounded by inflammation
  - Extraparenchymal NCC forms include intraventricular, subarachnoid, intraocular, and spinal disease

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        - Extraparenchymal cysts are associated with symptoms of elevated intracranial pressure (headache, nausea, and vomiting) and may be accompanied by altered mental status
        - Extraparenchymal forms of NCC generally carry a higher risk for complication or death than parenchymal disease
    - Extraneural cysticercosis may involve a wide range of tissues such as muscle or subcutaneous tissue involvement
        - Subcutaneous or intramuscular cysticerci causing symptoms due to inflammation can be excised or treated with nonsteroidal anti-inflammatory medication
            - Excision is reasonable for symptomatic solitary lesions
        - Asymptomatic patients with cysticerci in subcutaneous or intramuscular sites generally do not require specific therapy

- Other less common manifestations include mass effect, altered vision, focal neurologic signs, altered mental status, and meningitis

- Diagnosis of NCC is based on clinical presentation and radiographic imaging (CT scan, MRI).
    - Serologic testing of serum and CSF may be helpful in identifying anticysticercal antibodies or antigens

- Ocular cysticercosis should be excluded by an ophthalmologic examination in all patients with NCC prior to initiating therapy as inflammation around degenerating cysticerci can threaten vision by causing chorioretinitis, retinal detachment, or vasculitis

- Treatment considerations:
    - Antiepileptics should be used in patients with NCC who present with seizures and may also be appropriate for patients who do not present with seizures but who are at high risk for seizures
    - Corticosteroids should be used in patients who are receiving treatment with antiparasitic therapy to reduce inflammation associated with the dying organisms
    - Antiparasitic medications **should not be used in**:
        - The absence of viable parasites – therapy does not affect whether a lesion will calcify
        - Patients with diffuse cerebral edema associated with multiple inflamed cysticerci (cysticercal encephalitis), these patients should receive corticosteroid therapy alone
            - Enhanced parasite killing can exacerbate host inflammatory response and lead to diffuse cerebral edema and potential transtentorial herniation
        - Patient with calcified cysts (in the absence of viable lesions)
    - Antiparasitic medications **should be used in** patients with:
        - Single enhancing cyst or multiple cysts
        - Subarachnoid cysts
        - Involvement of the extraocular muscles or optic nerve
    - Treatment with nonsteroidal anti-inflammatory drug is used for patients with symptomatic subcutaneous or intramuscular lesions
        - If symptoms persist, excision of solitary lesions can be considered

- Optimal therapy for patients with symptomatic NCC depends upon the location, number, and type of cysts
    - For patients with a single enhancing lesion, treatment for 7 days
    - For patients with multiple cystic lesions, treatment for 10-14 days

- For patients with subarachnoid disease, treatment for at least 28 days

- If a determination has been made that antiparasitic therapy is indicated, albendazole is preferred over praziquantel
  - Prarziquantel is effective for intestinal tapeworm infections

Echinococcosis (dog tapeworm):

- Echinococcal disease is a parasitic infection with the metacestode stage of the tapeworm of the genus *Echinococcus*

- There are 4 known species of *Echinococcus*
  - *Echinococcus granulosus,* causing cystic echinococcosis (CE)
  - *Echinococcus multilocularis,* causing alveolar echinococcosis (AE)
  - *Echinococcus vogeli* causing polycystic echinococcosis (PE)
  - *Echinococcus oligarthrus* causing unicystic echinococcosis (UE)
- The two most important forms relevant to humans, are CE and AE

- CE is caused by infection with the larval stage of *Echinococcus granulosus*, a tapeworm found in dogs (definitive host) and sheep, cattle, goats, and pigs (intermediate hosts)
  - Most infections of CE in humans are asymptomatic
  - CE causes slowly enlarging cysts in the liver, lungs, and other organs that often grow unnoticed and neglected for years

- AE is caused by infection with the larval stage of *Echinococcus multilocularis*, a tapeworm found in foxes, coyotes, and dogs (definitive hosts); small rodents are intermediate hosts
  - AE poses a greater health risk than CE, it causes parasitic tumors that can form in the liver, lungs, brain, and other organs
    - If left untreated, AE can be fatal

- CE and AE may be diagnosed with a combination of imaging and serology
  - CE and AE are visualized with ultrasound, computed tomography (CT) and/or magnetic resonance imaging (MRI) scans
  - Ultrasound allows classification of the cysts as active, transitional, or inactive based on biologic activity; such categorizations may influence the choice of treatment

- The World Health Organization (WHO) classification characterizes cysts by type and size
  - WHO categories CE1 and CE2 are active cysts
  - Class CE3 consists of cysts that are thought to be degenerating (transitional group)
    - There are two types of CE3:
      - CE3a featuring the "water-lily" sign for floating membranes
      - CE3b which is predominantly solid with daughter cysts
    - Establishing whether daughter cysts are present is important for guiding treatment
  - Classes CE4 and CE5 are considered inactive

- There are 4 options for the treatment of cystic echinococcosis:

- Percutaneous treatment of the hydatid cysts with the PAIR (Puncture, Aspiration, Injection, Re-aspiration) technique
- Surgery
- Drug treatment
- "Watch and wait"

- Albendazole is recommended as the preferred drug therapy for WHO stages CE1 through CE3b either alone or with PAIR
  - Mebendazole and praziquantel are less effective

- Optimal duration of treatment is uncertain
  - 1-3 months may be appropriate, while some may need up to 6 month

- WHO stages CE4 and CE5 have inactive cysts and are managed with observation

***Enterobiasis (pinworm)*:**

- *Enterobius vermicularis* (pinworm) is one of the most common nematode infections worldwide
  - Enterobiasis occurs in both temperate and tropical climates; it is the most common helminthic infection in the United States and Western Europe

- The life cycle of *Enterobius* begins with egg deposition by the worms on perianal folds
  - Autoinfection occurs by scratching the perianal area and transferring infective eggs to the mouth with contaminated hands
  - Person-to-person transmission can occur by eating food touched by contaminated hands or by handling contaminated clothes or bed linens

- Most *Enterobius* infections are asymptomatic
  - The most common symptom is perianal itching, predominantly at night
  - If the worm burden is high, abdominal pain, nausea, and vomiting can develop

- Diagnosis is done by examination of cellophane tape for eggs after pressing the tape to perianal skin
  - Examination of the stool is not necessary since worms and eggs are not generally passed in stool

- Treatment options for enterobiasis consist of pyrantel pamoate, mebendazole, or albendazole
  - Simultaneous treatment of the entire household is necessary, given high transmission rates among families
  - All bedding and clothes should be washed
  - Other measures include clipping of fingernails, frequent handwashing, and baths, for reducing reinfection and spread of infection

- Pyrantel pamoate
  - 11 mg/kg; maximum 1 g; repeat in 2 weeks
  - The most frequently used medication as it is inexpensive and available over the counter
  - Has an efficacy of close to 100% if 2 doses are given 2 weeks apart
  - Adverse effects can include anorexia, nausea, vomiting, abdominal cramps, diarrhea, neurotoxic effects, and transient increases in hepatic enzymes

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- Other agents:
  - Single dose have relatively high cure rates, a second dose repeated at 2 weeks achieves a cure rate close to 100% and helps prevent recurrence due to reinfection
  - Mebendazole 100 mg orally once; repeat in 2 weeks
  - Albendazole 400 mg orally once on empty stomach; repeat in 2 weeks
  - Ivermectin has efficacy against *E. vermicularis* but is not generally used for this indication
    - In one study, 2 doses of ivermectin 200 mcg/kg given at an interval of 10 days resulted in a cure of 100% for enterobiasis

Definitions:

World Health Organization classification of cystic echinococcosis and treatment stratified by cyst stage

WHO stage	Description	Stage	Size	Preferred treatment	Alternate treatment
CE1	Unilocular unechoic cystic lesion with double line sign	Active	<5 cm	Albendazole alone	PAIR
			>5 cm	Albendazole + PAIR	PAIR
CE2	Multiseptated, "rosette-like" "honeycomb" cyst	Active	Any	Albendazole + either modified catheterization or surgery	Modified catheterization
CE3a	Cyst with detached membranes (water-lily sign)	Transitional	<5 cm	Albendazole alone	PAIR
			>5 cm	Albendazole + PAIR	PAIR
CE3b	Cyst with daughter cysts in solid matrix	Transitional	Any	Albendazole + either modified catheterization or surgery	Modified catheterization
CE4	Cyst with heterogenous hypoechoic/hyperechoic contents; no daughter cysts	Inactive	Any	Observation	-
CE5	Solid plus calcified wall	Inactive	Any	Observation	-
PAIR = Puncture, Aspiration, Injection, Re-aspiration					

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Resources:

Albenza (albendazole) product information accessed 01-10-19 at DailyMed: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=e8941166-b77d-45aa-a6e8-04f1c0afd845

Albendazole product information accessed 01-10-19 at DailyMed: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=0a4ce2e1-db3d-4b24-98aa-0519fbaff547

Albenza (albendazole). Package Insert. Revised by manufacturer 06-2015. Accessed 12-06-2017.

UpToDate: Anthelminthic therapies. Current through Nov 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/anthelminthic-therapies?source=search_result&search=neurocysticercosis&selectedTitle=4~20

UpToDate: Clinical manifestations and diagnosis of cysticercosis. Current through Nov 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/clinical-manifestations-and-diagnosis-of-cysticercosis?source=search_result&search=neurocysticercosis&selectedTitle=1~20

UpToDate: Treatment of cysticercosis. Current through Nov 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/treatment-of cysticercosis?source=search_result&search=neurocysticercosis&selectedTitle=2~20
UpToDate: Clinical manifestations and diagnosis of echinococcosis. Current through Nov 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/clinical-manifestations-and-diagnosis-of-echinococcosis?source=search_result&search=neurocysticercosis&selectedTitle=7~20

UpToDate: Treatment of echinococcosis. Current through Nov 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/treatment-of-echinococcosis?source=see_link#H3785987

UpToDate: Intestinal tapeworms. Current through Nov 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/intestinal-tapeworms?source=see_link

UpToDate: Hookworm infection. Current through Nov 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/hookworm-infection?source=see_link#H11

UpToDate: Enterbiasis (pinworm) and trichuriasis (whipworm). Current through Nov 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/enterobiasis-pinworm-and-trichuriasis-whipworm?search=pinworms&source=search_result&selectedTitle=1~28&usage_type=default&display_rank=1

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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.