BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

Albendazole oral

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

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

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Infectious Disease specialist

  2. Individual has a confirmed diagnosis of **ONE** of the following:
     a. Parenchymal neurocysticercosis due to active lesions caused by larval forms of the pork tapeworm, *Taenia solium*

     b. Cystic hydatid disease of the liver, lung, and peritoneum caused by the larval form of the dog tapeworm, *Echinococcus granulosus*

3. Individual has received and completed **ALL** the following baseline tests before initiation of treatment and with continued monitoring of the individual as clinically appropriate:
    a. Complete blood count
    b. Liver enzymes (transaminases)
    c. Retinal examination
    d. Negative pregnancy test in a woman of childbearing potential

4. There are **NO** FDA-label contraindications such as known hypersensitivity to the benzimidazole class of compounds or any component (e.g., thiabendazole, mebendazole, triclabendazole) of generic albendazole

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 a total of 3 cycles

- **Criteria for continuation of coverage (renewal request):** Generic albendazole is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Infectious Disease specialist

2. Individual's condition has not improved and/or has worsened while on therapy defined as **ONE** of the following:
    a. Neurocystircercosis: Continues to have nausea, vomiting, headache, visual problems, seizures, altered mental status, cysticerci are present and have not calcified
    b. Cystic hydatid disease: Cysticerci have not calcified, daughter cells are present, stage of cyst is either active or transitional

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

4. Individual has been adherent with the medication

5. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use as follows:
    a. Contraindications as listed in the criteria for initial therapy section
    b. Significant adverse effect such as:
        i. Bone marrow suppression
        ii. Liver enzyme elevations two times the upper limit of normal
        iii. Seizures in an individual being treated for neurocysticercosis
        iv. Increased intracranial pressure and focal signs in an individual being treated for neurocysticercosis
        v. Retinal damage in an individual being treated for retinal neurocysticercosis

PHARMACY COVERAGE GUIDELINE

Albendazole oral

Renewal duration:
For neurocysticercosis: 120 tablets per month for 1 month
For hydatid disease: Up to 112 tablets per 28 days for a total of 3 cycles

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**
2. **Off-Label Use of Cancer Medications**

Description:

Albendazole is indicated for the treatment of parenchymal neurocysticercosis due to active lesions caused by larval forms of the pork tapeworm, *Taenia solium* and is indicated for the treatment of cystic hydatid disease of the liver, lung, and peritoneum, caused by the larval form of the dog tapeworm, *Echinococcus granulosus*.

Albendazole is a synthetic benzimidazole antihelmintic 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.

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. 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.

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; and 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; and 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 and 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: 1) percutaneous treatment of the hydatid cysts with the PAIR (Puncture, Aspiration, Injection, Re-aspiration) technique; 2) Surgery; 3) Drug treatment; and 4) “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 months. WHO stages CE4 and CE5 have inactive cysts and are managed with observation.

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					

Resources:

Albendazole product information, revised by Camber Pharmaceuticals. 11-2022. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed December 12, 2024.

White AC. Cysticercosis: Clinical manifestations and diagnosis. In: UpToDate, Weller PF, Baron EL (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Literature current through November 2024. Topic last updated April 25, 2024. Accessed December 12, 2024.

White AC. Cysticercosis: Treatment. In: UpToDate, Weller PF, Baron EL (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Literature current through November 2024. Topic last updated December 13, 2023. Accessed December 12, 2024.

Moro PL, Reddy DN. Echinococcosis: Clinical manifestations and diagnosis. In: UpToDate, Weller PF, Baron EL (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Literature current through November 2024. Topic last updated May 21, 2024. Accessed December 12, 2024.

Moro PL, Reddy DN. Echinococcosis: Treatment . In: UpToDate, Weller PF, Baron EL (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Literature current through November 2024. Topic last updated October 17, 2024. Accessed December 12, 2024.

Regev A, Reddy KR. Diagnosis and management of cystic lesions of the liver. In: UpToDate, Chopra S, Robson KM (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Literature current through November 2024. Topic last updated July 30, 2024. Accessed December 12, 2024.

Weller PF. Anthelminthic therapies. In: UpToDate, Leder K, Baron EL (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Literature current through November 2024. Topic last updated April 25, 2024. Accessed December 12, 2024.