**ABZENDAZOLE Tablets, USP**

Revised: March 2018

**2.3 Monitoring for Safety Before and During Treatment**

- **Hydatid Disease**: Monitor liver enzymes (transaminases) at the beginning of each 28-day cycle of therapy, and every 2 weeks while on therapy with albendazole in all patients. Monitor blood counts at the beginning of each 28-day cycle of therapy, and every 2 weeks while on therapy with albendazole in all patients.
- **Neurocysticercosis**: Obtain a complete reproductive potential prior to therapy and at one month after end of therapy. Discontinue albendazole therapy immediately if pregnancy test in women of reproductive potential is positive.

**3. DOSAGE FORMS AND STRENGTHS**

- **Tablet**: 50 mg

**4. CONTRAINDICATIONS**

- **Bone Marrow Suppression**: Patients who have been treated with high doses of antituberculosis therapy (isoniazid, rifampin, ethambutol, or streptomycin) or patients who have received corticosteroids in high doses or for long periods of time, and patients with megakaryocytic hypoplasia, and patients who have received high-dose chemotherapeutic agents should not receive albendazole. Patients with hepatic failure or cirrhosis should not receive albendazole.

**5. WARNINGS AND PRECAUTIONS**

- **Hepatic Effects**: Elevations of liver enzymes in approximately 16% of patients. These elevations have been generally observed to be reversible after discontinuation of therapy.
- **Neurological Effects**: Patients with neurological involvement may experience seizures, increased intracranial pressure, or increased intracranial pressure.

**6. ADVERSE REACTIONS**

- **Gastrointestinal**: Nausea, vomiting, diarrhea.
- **Musculoskeletal and Connective Tissue Disorders**: Myalgia, arthralgia.

**7. HANDLING**

- **Praziquantel**: In the fed state, the rate of absorption/conversion and elimination of albendazole sulfoxide appeared to be increased by about 50% in healthy subjects. (7.1)
- **Dexamethasone**: Steady-state concentrations of albendazole in plasma were increased by 56% higher when dexamethasone was administered with albendazole. (7.1)
- **Theophylline**: Concomitant administration of theophylline with albendazole resulted in a 2-fold increase in the area under the concentration-time curve of albendazole sulfoxide by about 50% in healthy subjects. (7.1)

**8.5 Geriatric Use**

- In patients aged 65 and older with either hydatid disease or neurocysticercosis, there were no significant differences in age when compared with younger patients. (8.5)

**8.6 Patients with Impaired Renal Function**

- Patients with end-stage renal disease receiving hemodialysis or peritoneal dialysis had normal concentrations of albendazole sulfoxide after 14 days of therapy. (8.6)

**9. OVERDOSE**

- **In case of overdose, symptomatic therapy and general supportive measures are recommended.**

**Table 1: Albendazole Dosage**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Patient Weight</th>
<th>Dose</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydatid Disease</td>
<td>60 kg or greater</td>
<td>400 mg twice daily</td>
<td>28-day cycle followed by 14-day interval, for a total of 56 cycles</td>
</tr>
<tr>
<td>Neurocysticercosis</td>
<td>60 kg or greater</td>
<td>10 mg/kg twice daily</td>
<td>8 to 30 days</td>
</tr>
</tbody>
</table>

**Table 2: Adverse Reaction Incidence for 1% or Greater in Hydatid Disease and Neurocysticercosis**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Albendazole sulfoxide</th>
<th>Theophylline</th>
<th>Dexamethasone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypersensitivity reactions</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Meningeal signs</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Headache</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**References**

1. Albendazole Tablets, USP.
2. Vaness Leddy 4/3/18
3. FDA/ANDA# VV-137911
4. NOA/ANDA# 208094
5. NDA/ANDA# 208094
6. PR# N/A
7. Rev: Revised March 2018

**Abbreviations**

- FDA: Food and Drug Administration
- NDA: New Drug Application
- ANDA: Abbreviated New Drug Application
- PR: Priority Review
- N/A: Not Applicable

**Pharmaceuticals**

- VivaZeta
- Microsoft Word

**Outdent Configuration**

- Flat: 257 mm x 280 mm
- Folded: 23 mm x 299 mm
11 DESCRIPTION

Albendazole is an orally administrated anthelmintic drug. Chemically, it is methyl 5-(1-naphthyl)-2-benzimidazolecarboxylate. Its molecular formula is C_{14}H_{17}N_{3}O_{2}. Its molecular weight is 265.34. It has the following chemical structure:

H
\|\n\|\nN
\|\nCH₂
\|\n\|\nH

Albendazole, USP is a white to faintly yellowish powder. It is freely soluble in anhydrous forms acid and slightly soluble in ethanol. Practically insoluble in water. Each white to off-white, film-coated tablet contains 200 mg of albendazole, USP.

12 CLINICAL PHARMACOLOGY

12.1 Mechanisms of Action

Albendazole is the synthetic, antihelminthic drug of the class benzimidazoles (see Clinical Pharmacology (12.4)).

12.2 Pharmacokinetics

12.2.1 Absorption

Albendazole is poorly absorbed from the gastrointestinal tract due to its low aqueous solubility. Albendazole concentrations are negligible or undetectable in plasma as it is rapidly converted to the sulfate metabolite prior to reaching the systemic circulation. The systemic anthelmintic activity has been attributed to the primary metabolite, albendazole sulfoxide. Oral bioavailability appears to be enhanced when albendazole is consumed with a fatty meal (estimated fat content 41 grams) as evidenced by higher (up to 5-fold on average) plasma concentrations of albendazole sulfoxide compared to the fasted state.

Maximal plasma concentrations of albendazole sulfoxide were achieved 2 hours to 5 hours after dosing and were on average 1310 ng/mL, range 400 ng/mL to 1800 ng/mL, following oral doses of albendazole (400 mg) in 6 healthy male patients, when administered with a fatty meal. Plasma concentrations of albendazole sulfoxide were above 50% of the albendazole dose in 5 of 6 patients following ingestion of a high-fat meal (fat content 43.1 grams). The mean apparent terminal elimination half-life of albendazole sulfoxide ranged from 35 hours to 73 hours in 25 healthy subjects, as well as 14 healthy and 8 necrobiotic patients.

Following 4 weeks of treatment with albendazole (200 mg three times daily), 10 patients' plasma concentrations of albendazole sulfoxide were approximately 25% lower than those observed during the first half of the treatment period, suggesting that albendazole may induce its own metabolism.

12.2.2 Distribution

Albendazole sulfoxide is 75% bound to plasma protein and is widely distributed throughout the body. It has been detected in urine, bile, liver, cyst wall, cyst fluid, and cerebral spinal fluid (CSF). Concentrations in plasma were 3-fold to 10-fold and 2-fold to 4-fold higher than those simultaneously determined in cyst fluid and CSF, respectively.

12.2.3 Metabolism and Excretion

Albendazole is rapidly converted in the liver to the primary metabolite, albendazole sulfoxide, which is further metabolized to albendazole sulfone and other primary and secondary metabolites that have been identified in human urine. Following oral administration, albendazole has not been detected in human urine. Urinary excretion of albendazole sulfoxide is a minor elimination pathway with less than 1% of the dose recovered in the urine. Biliary elimination presumably accounts for a portion of the elimination as evidenced by biliary concentrations of albendazole sulfoxide similar to those achieved in plasma.

12.3 Pharmacokinetics

12.3.1 Pediatrics

Following single-dose administration of 200 mg to 300 mg (approximately 10 mg/kg) albendazole to 3 lamellar and 2 helminthic patients with hydatid cyst disease (age range 6 to 13 years), albendazole sulfoxide pharmacokinetic profiles were similar to those observed in adult patients.

12.3.2 Geriatrics

Although no studies have investigated the effect of age on albendazole sulfoxide pharmacokinetics, data in 26 healthy elderly patients (up to 79 years) suggest pharmacokinetics similar to those observed in young healthy subjects.

12.4 Microbiology

Mechanism of Action

Albendazole binds to the colchicine-sensitive site of β tubulin inhibiting its polymerization into microtubules. The decrease in microtubules in the microtubules of the parasites decreases their motility function, especially the uptake of glucose by the adult and larval forms of the parasites, and also depletes glycogen storage. Insufficient glucose results in insufficient energy for the production of adenosine triphosphate (ATP) and the parasite eventually dies.

Mechanism of Resistance

Parasitic resistance to albendazole is caused by changes in amino acids that result in changes in the β tubulin protein. This causes reduced binding of the drug to β tubulin. In the specified treatment indications albendazole appears to be active against the larval forms of the following organisms:

- Echinococcus granulosus
- Dientamoeba vulvovaginalis

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term carcinogenicity studies were conducted in mice and rats.

No evidence of increased incidence of tumors was found in the mice or rats at up to 400 mg/kg/day or 20 mg/kg/day respectively (2 times and 0.2 times the recommended human dose). Long-term carcinogenicity studies were conducted in mice and rats.

14 CLINICAL STUDIES

14.1 Treatment of Hydatid Disease

14.1.1 In the treatment of hydatid cysts, albendazole is usually administered along with surgery, if indicated. Albendazole has been shown to reduce the size of cysts, reduce symptoms, and minimize the risk of infection.

14.1.2 Albendazole may cause fetal harm, therefore, obtain a pregnancy test in women of reproductive potential prior to initiating therapy.

15 ADVERSE REACTIONS

15.1 In the treatment of hydatid disease, side effects have been minimal and are usually mild. Common reactions include:

- Nausea
- Vomiting
- Abdominal pain
- Diarrhea
- Headache

In rare cases, serious adverse reactions may occur:

- Hypersensitivity reactions
- Neurotoxicity
- Hepatotoxicity

15.2 In the treatment of neurocysticercosis, the most common side effects are:

- Headache
- Dizziness
- Nausea

15.3 Serious adverse reactions may include:

- Seizures
- Neurotoxicity
- Hepatotoxicity

15.4 In the treatment of dermatitosis, the most common side effects are:

- Skin rash
- Pruritus

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

Albendazole Tablets, USP are available as follows:

200 mg — Each white to off-white, round, film-coated tablet debossed with ‘A210’ on one side and plain on the other contains 200 mg of albendazole, USP. Tablets are supplied in bottles of 2 (NDC 0591-2712-02) and 28 (NDC 0591-2712-96) with a child-resistant closure.

Dispense in a tight, light-resistant container as defined in the USP.

16.2 Storage and Handling

Store at 20°C to 25°C (68°F to 77°F) [See USP Controlled Room Temperature].

17 PATIENT COUNSELING INFORMATION

Patients should be advised that:

- Some people, particularly children, may experience difficulties swallowing the albendazole tablets.
- Take albendazole tablets with food.

- Albendazole may cause fetal harm, therefore, obtain a pregnancy test in women of reproductive potential prior to initiating therapy.
- Advise women of reproductive potential to use effective birth control while on albendazole tablets and for one month after completing treatment.

- During albendazole tablets therapy, monitor blood counts and liver enzymes every 2 weeks because of the possibility of harm to the liver or bone marrow.

Manufactured by:

Watson Pharma Private Limited
Verna, Salcette Goa 403 722 INDIA

Distributed by:

Actavis Pharma, Inc.
Parke-Davis, 40500 USA

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