CHEMTEL

(Albendazole Tablets USP 400 mg)

Summary of Product Characteristics (SmPC)

1. Name of the medicinal product

CHEMTEL

(Albendazole Tablets USP 400 mg)

2. Qualitative and Quantitative Composition

Each Chewable tablet contains:

Albendazole USP 400 mg

3. Pharmaceutical Form

Tablet

4. Clinical Particulars

Albendazole is indicated for the treatment of the following infections:

Neurocysticercosis

Albendazole is indicated for the treatment of parenchymal neurocysticercosis due to active lesions caused by larval forms of the pork tapeworm, Taenia solium.

Lesions considered responsive to albendazole therapy appear as nonenhancing cysts with no surrounding edema on contrast-enhanced computerized tomography. Clinical studies in patients with lesions of this type demonstrate a 74% to 88% reduction in number of cysts; 40% to 70% of albendazole-treated patients showed resolution of all active cysts.

Hydatid Disease

Albendazole 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.

This indication is based on combined clinical studies which demonstrated non-infectious cyst contents in approximately 80-90% of patients given albendazole for 3 cycles of therapy of 28 days each. Clinical cure (disappearance of cysts) was seen in approximately 30% of these patients, and improvement (reduction in cyst diameter of ≥25%) was seen in an additional 40%.

NOTE: When medically feasible, surgery is considered the treatment of choice for hydatid disease. When administering albendazole in the pre- or post-surgical setting, optimal killing of cyst contents is achieved when 3 courses of therapy have been given.

4.2 Posology and method of administration

Dosage and administration

The amount of medicine that you take depends on the strength of the medicine. Also, the number of doses you take each day, the time allowed between doses, and the length of time you take the medicine depend on the medical problem for which you are using the medicine.

For oral dosage form (tablets):

Adults

For hydatid disease:

60 kg or more: 400 mg orally twice a day with meals.

Less than 60 kg: 15 mg/kg/day orally, given in divided doses twice a day with meals (maximum dose: 800 mg/day)

Duration: 28-day cycle followed by a 14-day albendazole-free interval, for a total of 3 cycles When administering albendazole in the presurgical or postsurgical setting, optimal killing of cyst contents is achieved when 3 courses of therapy have been given.

For neurocysticercosis:

60 kg or more: 400 mg orally twice a day with meals

Less than 60 kg: 15 mg/kg/day orally, given in divided doses twice a day with meals (maximum dose: 800 mg/day)

Duration: 8 to 30 days.

Children

For hydatid disease:

Cystic hydatid disease of the liver, lung, and peritoneum due to Echinococcus granulosus:

60 kg or more: 400 mg orally twice a day with meals.

Less than 60 kg: 15 mg/kg/day orally, given in divided doses twice a day with meals (maximum dose: 800 mg/day).

Duration: 28-day cycle followed by a 14-day albendazole-free interval, for a total of 3 cycles.

When administering albendazole in the presurgical or postsurgical setting, optimal killing of cyst contents is achieved when 3 courses of therapy have been given.

For neurocysticercosis:

Parenchymal neurocysticercosis:

60 kg or more: 400 mg orally twice a day with meals

Less than 60 kg: 15 mg/kg/day orally, given in divided doses twice a day with meals (maximum dose: 800 mg/day)

Duration: 8 to 30 days.

4.3 Contraindications

Hypersensitivity to benzimidazole derivatives or any component in the formulation. Albendazole is contraindicated in pregnancy.

4.4 Special warning and special precaution for use:

Warnings:

Rare fatalities associated with the use of albendazole have been reported due to granulocytopenia or pancytopenia. Albendazole has been shown to cause bone marrow suppression, aplastic anemia, and agranulocytosis in patients with and without underlying hepatic dysfunction. Blood counts should be monitored at the beginning of each 28-day cycle of therapy, and every 2 weeks while on therapy with albendazole in all patients. Patients with liver disease, including hepatic echinococcosis, appear to be more at risk for bone marrow suppression leading to pancytopenia, aplastic anemia, agranulocytosis, and leukopenia attributable to albendazole and warrant closer monitoring of blood counts. Albendazole should be discontinued in all patients if clinically significant decreases in blood cell counts occur.

Albendazole should not be used in pregnant women except in clinical circumstances where no alternative management is appropriate. Patients should not become pregnant for at least 1 month following cessation of albendazole therapy. If a patient becomes pregnant while taking this drug, albendazole should be discontinued immediately. If pregnancy occurs while taking this drug, the patient should be apprised of the potential hazard to the fetus.

Precautions:

General:

Patients being treated for neurocysticercosis should receive appropriate steroid and anticonvulsant therapy as required. Oral or intravenous corticosteroids should be considered to prevent cerebral hypertensive episodes during the first week of anticysticeral therapy.

Pre-existing neurocysticercosis may also be uncovered in patients treated with albendazole for other conditions. Patients may experience neurological symptoms (e.g. seizures, increased intracranial pressure and focal signs) as a result of an inflammatory reaction caused by death of the parasite within the brain. Symptoms may occur soon after treatment; appropriate steroid and anticonvulsant therapy should be started immediately.

Cysticercosis may, in rare cases, involve the retina. Before initiating therapy for neurocysticercosis, the patient should be examined for the presence of retinal lesions. If such lesions are visualized, the need for anticysticeral therapy should be weighed against the possibility of retinal damage caused by albendazole-induced changes to the retinal lesion.

Information for Patients:

Patients should be advised that:

- Some people, particularly young children, may experience difficulties swallowing the tablets whole. In young children, the tablets should be crushed or chewed and swallowed with a drink of water.
- Albendazole may cause fetal harm, therefore, women of childbearing age should begin treatment after a negative pregnancy test.
- Women of childbearing age should be cautioned against becoming pregnant while on albendazole or within 1 month of completing treatment.
- During albendazole therapy, because of the possibility of harm to the liver or bone marrow, routine (every 2 weeks) monitoring of blood counts and liver function tests should take place.
- Albendazole should be taken with food.

4.5 Effects on ability to drive and use machines:

None known

4.6 Undesirable effects:

The following adverse events were observed at an incidence of <1%:

Blood and Lymphatic System Disorders

Leukopenia. There have been rare reports of granulocytopenia, pancytopenia, agranulocytosis, or thrombocytopenia. Patients with liver disease, including hepatic echinococcosis, appear to be more at risk of bone marrow suppression.

Immune System Disorders

Hypersensitivity reactions, including rash and urticaria.

Postmarketing Adverse Reactions

In addition to adverse events reported from clinical trials, the following events have been identified during world-wide post-approval use of albendazole. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made. These events have been chosen for inclusion due to a combination of their seriousness, frequency of reporting, or potential causal connection to albendazole.

Blood and Lymphatic System Disorders

Aplastic anemia, bone marrow suppression, neutropenia.

Hepatobiliary Disorders

Elevations of hepatic enzymes, hepatitis, acute liver failure.

Skin and Subcutaneous Tissue Disorders

Erythema multiforme, Stevens-Johnson syndrome.

Renal and Urinary Disorders

Acute renal failure.

The side effects of albendazole differ between hydatid disease and neurocysticercosis. The symptoms were generally mild and resolved without treatment. Treatment was discontinued primarily due to leukopenia (0.7%) or hepatic abnormalities (3.8% in hydatid disease).

Dermatologic:

Dermatologic side effects have included reversible alopecia (1.6% in hydatid disease; less than 1% in neurocysticercosis). Erythema multiforme and Stevens-Johnson syndrome have been reported during postmarketing experience.

Hypersensitivity:

Hypersensitivity side effects have included hypersensitivity reactions (including rash and urticaria) in less than 1% of patients.

Renal:

Renal side effects have included acute renal failure during postmarketing experience.

Hepatic:

Hepatic side effects have included abnormal liver function tests (15.6% in hydatid disease; less than 1% in neurocysticercosis) and hepatotoxicity (greater than or equal to 1%). Hepatic abnormalities, acute liver failure, elevations of hepatic enzymes, and hepatitis have been reported during postmarketing experience.

Hematologic:

Hematologic side effects have rarely included granulocytopenia, agranulocytosis, pancytopenia, and thrombocytopenia. Leukopenia has been reported in less than 1% of patients. Aplastic anemia, bone marrow suppression, and neutropenia have been reported during postmarketing experience.

Gastrointestinal:

Gastrointestinal side effects have included abdominal pain (6% in hydatid disease), nausea/vomiting (3.7% in hydatid disease; 6.2% in neurocysticercosis).

Nervous system:

Nervous system side effects have included headache (1.3% in hydatid disease; 11% in neurocysticercosis), dizziness/vertigo (1.2% in hydatid disease; less than 1% in neurocysticercosis), raised intracranial pressure (1.5% in neurocysticercosis), meningeal signs (1% in neurocysticercosis).

Other:

Other side effects have included fever (1% in hydatid disease).

Ocular:

Ocular side effects have included retinal damage.

4.7 Overdose:

Significant toxicity and mortality were shown in male and female mice at doses exceeding 5,000 mg/kg; in rats, at estimated doses between 1,300 and 2,400 mg/kg; in hamsters, at doses exceeding 10,000 mg/kg; and in rabbits, at estimated doses between 500 and 1,250 mg/kg. In the animals, symptoms were demonstrated in a dose-response relationship and included diarrhea, vomiting, tachycardia, and respiratory distress.

One overdosage has been reported with albendazole in a patient who took at least 16 grams over 12 hours. No untoward effects were reported. In case of overdosage, symptomatic therapy (e.g., gastric lavage and activated charcoal) and general supportive measures are recommended.

5. Pharmacological Property:

5.1 Pharmacodynamic Properties:

Albendazole is a broad-spectrum anthelmintic. The principal mode of action for albendazole is by its inhibitory effect on tubulin polymerization which results in the loss of cytoplasmic microtubules.

Mode of action

Albendazole causes degenerative alterations in the tegument and intestinal cells of the worm by binding to the colchicine-sensitive site of tubulin, thus inhibiting its polymerization or assembly into microtubules. The loss of the cytoplasmic microtubules leads to impaired uptake of glucose by the larval and adult stages of the susceptible parasites, and depletes their glycogen stores. Degenerative changes in the endoplasmic reticulum, the mitochondria of the germinal layer, and the subsequent release of lysosomes result in decreased production of adenosine triphosphate (ATP), which is the energy required for the survival of the helminth. Due to diminished energy production, the parasite is immobilized and eventually dies.

5.2 Pharmacokinetic Properties:

Absorption

Albendazole is poorly absorbed from the GI tract; however, it is rapidly converted to its primary active metabolite, albendazole sulfoxide, prior to reaching systemic

circulation. Fatty meals enhance bioavailability, as indicated by up to a 5-fold increase in plasma concentration in albendazole sulfoxide. Albendazole sulfoxide plasma concentrations are dose-dependent. C_{max} is achieved in 2 to 5 h and ranges from 0.46 to 1.58 mcg/ml, when given with a fatty meal.

Distribution

Albendazole sulfoxide is 70% 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- to 10- fold and 2- to 4-fold higher than those simultaneously determined in cyst fluid and CSF, respectively. Limited in vitro and clinical data suggest that albendazole sulfoxide may be eliminated from cysts at a slower rate than observed in plasma.

Metabolism

After metabolism in the liver to albendazole sulfoxide, it is further metabolized to albendazole sulfone and other oxidative metabolites.

Excretion

Albendazole sulfoxide elimination half-life is 8 to 12 h. Biliary elimination of albendazole sulfoxide results in biliary concentrations similar to plasma concentration. Urinary excretion is a minor elimination pathway (less than 1%)

5.3 Preclinical safety data:

Not applicable

6. Pharmaceutical particulars:

6.1 List of excipients

- Mannitol BP
- Starch BP
- Gelatin BP
- Povidone K-30 BP
- Sugar BP
- Sodium Methylparaben BP
- Sodium Propylparaben BP
- Magnesium Stearate BP
- Colloidal Silicon Dioxide BP

- Sodium Lauryl Sulphate BP
- Purified Talc BP
- Orange (flavor)I.H.
- Trusil Orange Flavour I.H.
- Sunset Yellow FCF I.H.
- Purified Water BP

6.2 Incompatibilities:

Dexamethasone and praziquantel enhances effects of albendazole by increasing the serum levels. Albendazole may increase clearance of carbamazepine.

6.3 Shelf life:

36 Months.

6.4 Special precaution for storage:

Store at temperatures not exceeding 30°C. Keep in a cool, dry & dark place, protect from light.

6.5 Nature contents of container:

Blister Pack of 1 Tablets in a Carton

6.6 Instruction for use handling and disposal

Keep out of reach of children

7. Manufacturer Name

ALPA LABORATORIES LIMITED

33/2 A.B Road, Pigdamber,

Indore (M.P), India.

Pin Code- 453446

8. Marketing Authority

CHEZ RESOURCES PHARMA LIMITED

7, Calabar Street, Fegge, Onitsha,

Anambra State, Nigeria