National Agency for Food & Drug Administration & Control (NAFDAC)

Registration & Regulatory Affairs (R & R) Directorate

SUMMARY OF PRODUCT CHARACTERISTICS

ABENDAZOLE 400MG TABLE

1. NAME OF THE MEDICINAL PRODUCT

Dalat (Albendazole) 400mg Tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Uncoated tablet
contains: Albendazole 400 mg tablet Excipients:

Albendazole
Excipients:
Lactose, Maize starch, Methyl paraben, Propyl Paraben, Sodium Saccharine, PVPK30, Sunset Yellow, banana flavour, magnesium stearate, Aerosil.

3. PHARMACEUTICAL FORM

Oral Tablet

4. Clinical particulars

4.1 Therapeutic indications

Albendazole are indicated in the treatment of single or mixed infestations of intestinal and tissue parasites as a Single dose or short-term courses, in adults and children over 2 years of age.

Albendazole have shown clinically to be effective in the treatment of infections caused by: Enterobius vermicularis (pinworm/threadworm), Ascaris lumbricoides (roundworm), Ancylostoma duodenale and Necator americanus (hookworms), Trichuris trichiura (whipworm), Strongyloides stercoralis, animal hookworm larvae causing cutaneous larva migrans, and the liver flukes Opisthorchis viverrini and Clonorchis sinensis. Albendazole is also indicated for the treatment of Hymenolepis nana and Taenia spp. (tapeworm) infections, when other susceptible helminths species are present. Treatment courses should be extended to 3 days.

4.2 Posology and method of administration.

Albendazole 400mg tablets may be swallowed with a drink of water Adults and Children (over two years):

Enterobius vermicularis, Ascaris lumbricoides, Ancylostoma duodenale, Necator americanus and Trichuris trichiura: 400mg Albendazole as a single dose, taken on an empty stomach.

Suspected or confirmed Strongyloides stercoralis infestation: Albendazole 400mg once daily, taken on an empty stomach for three consecutive days. Patients should then be appropriately followed for at least 2 weeks to confirm cure.

Cutaneous larva migrans: 400mg once daily, taken with food for one to three days has been reported to be effective.

Suspected or confirmed Taenia spp. or Hymenolepis nana infestation, when other susceptible helminths species are present: Albendazole 400mg once daily, taken on an empty stomach for three consecutive days. If the patient is not cured after three weeks, a second course of Albendazole treatment is indicated. In cases of proven H. nana infestation, retreatment in 10-21 days is recommended.

Method of administration

Albendazole 400mg tablets may be swallowed with a drink of water Adults and Children (over two years):

4.3 Contraindications

Albendazole has been shown to be teratogenic and embryotoxic in rats and rabbits as such should not be administered during pregnancy or in women thought to be pregnant Women childbearing age should be advised to take effective precautions against conception during and within one month of completion of treatment with Albendazole (see Use in Pregnancy, Category D). Albendazole is contraindicated in persons who are known to be hypersensitive to albendazole, other benzimidazole derivatives, or any component of the tablets.

4.4 Special warnings and precautions for use

Use in Systemic Helminth Infections (longer duration of treatment at higher doses) Mild to moderate elevations of liver enzymes have been reported with albendazole. In prolonged higher dose albendazole therapy for hydatid disease there have been rare reports of severe hepatic abnormalities associated with jaundice and histological hepatocelluler damage, which may be irreversible. Enzyme abnormalities usually normalize on discontinuation of treatment. Patients with abnormal liver function test results (transaminases) prior to commencing albendazole therapy should be carefully evaluated and therapy should be discontinued if liver enzymes are significantly increased (greater than twice the upper limit of normal) or full blood count decreased by a clinically significant level (see Adverse Reactions). Albendazole treatment may be restarted when liver enzymes have returned to normal limits, but patients should be carefully monitored for a recurrence. Case reports of hepatitis have also been received (see Adverse Reactions). Liver function tests should be obtained before the start of each treatment cycle and at least every two weeks during treatment. Albendazole has been shown to cause bone marrow suppression and therefore blood counts should be performed at the start and every two weeks during each 28-day cycle. Patients with liver disease, including hepatic echinococcosis, appear to be more susceptible to bone marrow suppression leading to pancytopenia, aplastic anaemia, agranulocytosis and leukopenia and therefore warrant closer monitoring of blood counts.

Albendazole should be discontinued if clinically significant decreases in blood cell counts occur. Symptoms associated with an inflammatory reaction following death of the parasite may occur in patients receiving albendazole treatment for neurocysticercosis (e.g. seizures, raised intracranial pressure, focal signs). These should be treated with appropriate steroid and anticonvulsant therapy. Oral or intravenous corticosteroids are recommended to prevent cerebral hypertensive episodes during the first week of treatment. Pre-existing neurocysticercosis may also be uncovered in patients treated with albendazole for other conditions, particularly in areas with high taenosis infection. 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.

There is a risk that treatment of Taenia solium infections may be complicated by cysticercosis, and appropriate measures should be taken to minimize this possibility. Confirmation of eradication of many intestinal and tissue parasite is necessary after treatment. Use in Impaired Renal or Hepatic Function The use of Albendazole in patients with impaired renal or hepatic function has not been studied. However, caution should be used in patients with pre-existing liver disease, since Albendazole is metabolised by the liver and has been associated with idiosyncratic hepatotoxicity.

In Children There is limited experience with Albendazole, therefore use in children under 2 years of age is not recommended.

Carcinogenicity and Mutagenicity No evidence of carcinogenic activity was observed in mice given albendazole in the diet at doses up to 400mg/kg/day for 25 months. In rats, dietary administration of doses of 3.5, 7 and 20mg/kg/day did not affect the total incidence of adrenocortical tumours (adenoma plus carcinoma), however, in females there was an increased incidence of adrenocortical carcinomas. Mutagenicity tests with bacterial cells and an assay of chromosomal damage in vivo have shown no clear evidence that albendazole has genotoxic activity. A cell transformation assay showed a slight dose-related increase in the transformation rate of cultured mouse cells in the presence of metabolic activation.

4.5 Interaction with other medicinal products and other forms of interaction

Cimetidine, praziquantel and dexamethasone have been reported to increase the plasma levels of the albendazole active metabolite. Ritonavir, phenytoin, carbamazepine and phenobarbital may have the potential to reduce plasma concentrations of the active metabolite of albendazole; albendazole sulfoxide. The clinical relevance of this is unknown, but may result in decreased efficacy, especially in the treatment of systemic helminth infections. Patients should be monitored for efficacy and may require alternative dose regimens or therapies

4.6 Pregnancy and Lactation

Albendazole is contraindicated during pregnancy, and for one month prior to conception. In order to avoid administering albendazole during early pregnancy, women of childbearing age should initiate treatment during the first week of menstruation or after a negative pregnancy test.

The use of Albendazole in human pregnancy has not been studied, but in animal studies it is teratogenic in more than one species. In animal studies oral treatment with maternotoxic doses of albendazole (30mg/kg/day) during the period of organogenesis was associated with multiple malformations in rats and ectrodactyly in rabbits. In one study in rats, an oral dose (10mg/kg/day) similar to the human therapeutic dose was not maternotoxic, but was associated with microphthalmia and microfetalis. The latter occurred alone and together with multiple malformations including cranioschisis, talipes and renal agenesis.

There is no information on the possible effect of albendazole on human foetus.
Use in Lactation: Adequate human and animal data on use during lactation are not available. Therefore, breast feeding should be discontinued during and for a minimum of 5 days after treatment.

4.7 Effects on ability to drive and use machine

None known

4.8 Undesirable effects

ADVERSE REACTIONS

The following adverse events were observed during clinical studies. It should however be noted that causality has not necessarily been established for these events.

Common (≥1%) Abdominal pain was the most frequently reported symptom (1%) during short term dosing, however this frequency was not significantly different from that in placebo-treated patients.

Uncommon (>0.1% and < 0.1%) Diarrhoea, nausea, vomiting, dizziness, itchiness and/or skin rashes were reported. There was no significant difference in the percentage of patients experiencing diarrhoea, compared to placebotreated patients.

Rare (< 0.1%) Rarely reported events included bone pain, proteinuria, and low red cell count. Leucopenia and transiently raised hepatic enzymes were reported in studies with laboratory monitoring, however no definite relationship to the drug was shown.

Hypersensitvity reactions including rash, pruritis and urticaria have been reported very rarely.

During prolonged higher dose albendazole therapy of hydatid disease there have also been reports of severe hepatic abnormalities, including jaundice and hepatocellular damage which may be irreversible.

Post-Marketing Data During post-marketing surveillance, the following reactions have been reported additionally in temporal association with Albendazole.

Use in intestinal infections and Cutaneous larva migrans (short duration treatment at lower dose): Headache has been reported uncommonly (≥ 0.1% and <1%) in treatment with albendazole. Erythema multiforme and Stevens-Johnson syndrome have been reported very rarely (<0.01%)

Use in systemic helminth infections (longer duration of treatment at higher doses): Headache has been reported very commonly (≥10%). Reversible alopecia (thinning of hair, and moderate hair loss) and fever have been reported commonly (≥1% and <10%) Hepatitis has been uncommonly associated with albendazole treatment. Blood disorders such as pancytopenia, aplastic anaemia and agranulocytosis have been associated very rarely with albendazole treatment. Patients with liver disease, including hepatic echinococcosis, appear to be more susceptible to bone marrow suppression (see Precautions). There have been very rare cases of Erythema multiforme and StevensJohnson syndrome.

4.9 Overdose

Significant toxicity and mortality were shown in animal studies 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. In case of overdosage, symptomatic therapy and general supportive measures are recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

Pharmacotherapeutic group: Benzimidazole derivatives with anthelmintic effects against tissue parasites

ATC Code: P02CA03

Albendazole is a benzimidazole carbamate with anthelmintic effects against tissue parasites. Albendazole exhibits larvicidal, ovicidal and vermicidal activity, and it is thought to exert its anthelmintic effect by inhibiting tubulin polymerisation. This causes the disruption of the helminth metabolism, including energy depletion, which immobilises and then kills the susceptible helminth.

Albendazole is effective in the treatment of tissue parasites including cystic echinococcosis and alveolar echinococcosis caused by infestation of Echinococcus granulosus and Echinococcus multilocularis, respectively.

In the treatment of cysts due to E. multilocularis, a minority of patients were considered to be cured and a majority had an improvement or stabilisation of disease due to albendazole.

5.2 Pharmacokinetic properties

Absorption and Metabolism

In man, albendazole is poorly absorbed (<5%) following oral administration. Albendazole rapidly undergoes extensive first-pass metabolism in the liver, and is generally not detected in plasma. Albendazole sulfoxide is the primary metabolite, which is thought to be the active moiety in effectiveness against systemic tissue infections. The plasma half-life of albendazole sulfoxide is 8½ hours.

Following oral administration of a single dose of 400 mg albendazole, the pharmacologically active metabolite, albendazole sulfoxide, has been reported to achieve plasma concentrations from 1.6 to 6.0 micromol/litre when taken with breakfast. The systemic pharmacological effect of albendazole is augmented if the dose is administered with a fatty meal, which enhances the absorption by approximately 5-fold.

Excretion

Albendazole sulfoxide and its metabolites appear to be principally eliminated in bile, with only a small proportion appearing in the urine. Elimination from cysts has been shown to occur over several weeks following high and prolonged dosing.

Special Patient Populations

Elderly

Although no studies have investigated the effect of age on albendazole sulfoxide pharmacokinetics, data in 26 hydatid cyst patients (up to 79 years) suggest pharmacokinetics similar to those in young healthy subjects. The number of elderly patients treated for either hydatid disease or neurocysticercosis is limited, but no problems associated with an older population have been observed.

Renal Impairment

The pharmacokinetics of albendazole in patients with impaired renal function have not been studied.

Hepatic Impairment

The pharmacokinetics of albendazole in patients with impaired hepatic function have not been studied

5.3 Preclinical safety data

Carcinogenicity and Mutagenicity

No evidence of carcinogenic activity was observed in mice given albendazole in the diet at doses up to 400mg/kg/day for 25 months. In rats, dietary administration of doses of 3.5, 7 and 20mg/kg/day did not affect the total incidence of adrenocortical tumours (adenoma plus carcinoma), however, in females there was an increased incidence of adrenocortical carcinomas. Mutagenicity tests with bacterial cells and an assay of chromosomal damage in vivo have shown no clear evidence that albendazole has genotoxic activity. A cell transformation assay showed a slight dose-related increase in the transformation rate of cultured mouse cells in the presence of metabolic activation.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose, Maize starch, Methyl paraben, Propyl Paraben, Sodium Saccharine, PVPK30, Sunset Yellow, banana flavour, magnesium stearate, Aerosil.

6.2 Incompatibilities

Unknown

6.3 Shelf life

36 months

6.4 Special precautions for storage

Do not store above 30°C. Store in a dry place

6.5 Nature and contents of container <and special equipment for use, administration or implantation>

1 tablets to be packed in a blister made up of rigid nontoxic PVC and printed aluminum foil. Such 1 blister are packed in a carton along with a leaflet.

6.6 Special precautions for disposal

Any unused product or waste material should be disposed of in accordance with local requirements.

7. APPLICANT/MANUFACTURER

Daily Need Industries Limited

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