SUMMARY OF PRODUCT CHARACTEISTICS (SPC)

1. NAME OF THE MEDICINAL PRODUCT

Albendazole Tablets 400 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each uncoated chewable tablet contains:

Albendazole USP 400 mg

Excipients q.s.

3. Pharmaceutical form

Chewable tablet

4. Clinical particulars

4.1 Therapeutic indications

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

Clinical studies have shown Albendazole 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 400 mg chewable tablets may be crushed, chewed, or swallowed whole.

Adults and Children (over two years):

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

- Suspected or confirmed *Strongyloides stercoralis* infestation: Albendazole 400 mg 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*: 400 mg 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: 400 mg 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.

- Mixed worm infestations including *Opisthorchis viverrini* and *Clonorchis sinensis*: 400 mg twice a day, taken with food for three days is effective. Patients should be re-examined 1 month after treatment to confirm fluke eradication.

4.3 Contraindications

Albendazole should not be administered during pregnancy or in women thought to be pregnant.

ALbendazole has been shown to be teratogenic and embryotoxic in rats and rabbits. Women of childbearing age should be advised to take effective precautions against conception during and within one month of completion of treatment with Albendazole.

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

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 28day 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.

Laboratory Tests:

White Blood Cell Count: Albendazole has been shown to cause occasional (less than 1% of treated patients) reversible reductions in total white blood cell count. Rarely, more significant reductions may be encountered including granulocytopenia, agranulocytosis, or pancytopenia. Blood counts should be performed at the start of each 28-day treatment cycle

and every 2 weeks during each 28-day cycle in all patients. Patients with liver disease, including hepatic echinococcosis, appear to be more at risk of bone marrow suppression and warrant closer monitoring of blood counts. Albendazole should be discontinued in all patients if clinically significant decreases in blood cell counts occur.

Liver Function: In clinical trials, treatment with albendazole has been associated with mild to moderate elevations of hepatic enzymes in approximately 16% of patients. These elevations have generally returned to normal upon discontinuation of therapy. There have also been case reports of acute liver failure of uncertain causality and hepatitis.

Liver function tests (transaminases) should be performed before the start of each treatment cycle and at least every 2 weeks during treatment. If hepatic enzymes exceed twice the upper limit of normal, consideration should be given to discontinuing albendazole therapy based on individual patient circumstances. Restarting albendazole treatment in patients whose hepatic enzymes have normalized off treatment is an individual decision that should take into account the risk/benefit of further albendazole usage. Laboratory tests should be performed frequently if albendazole treatment is restarted.

Patients with abnormal liver function test results are at increased risk for hepatotoxicity and bone marrow suppression. Therapy should be discontinued if liver enzymes are significantly increased or if clinically significant decreases in blood cell counts occur.

Theophylline: Although single doses of albendazole have been shown not to inhibit theophylline metabolism, albendazole does induce cytochrome P450 1A in human hepatoma cells. Therefore, it is recommended that plasma concentrations of theophylline be monitored during and after treatment with Albendazole.

Drug Interactions: ***Dexamethasone:*** Steady-state trough concentrations of albendazole sulfoxide were about 56% higher when 8 mg dexamethasone was coadministered with each dose of albendazole (15 mg/kg/day) in 8 neurocysticercosis patients.

Praziquantel: In the fed state, praziquantel (40 mg/kg) increased mean maximum plasma concentration and area under the curve of albendazole sulfoxide by about 50% in healthy subjects (n = 10) compared with a separate group of subjects (n = 6) given albendazole alone. Mean Tmax and mean plasma elimination half-life of albendazole sulfoxide were unchanged. The pharmacokinetics of praziquantel was unchanged following coadministration with albendazole (400 mg).

Cimetidine: Albendazole sulfoxide concentrations in bile and cystic fluid were increased (about 2-fold) in hydatid cyst patients treated with cimetidine (10 mg/kg/day) (n = 7)

compared with albendazole (20 mg/kg/day) alone (n = 12). Albendazole sulfoxide plasma concentrations were unchanged 4 hours after dosing.

Theophylline: The pharmacokinetics of theophylline (aminophylline 5.8 mg/kg infused over 20 minutes) was unchanged following a single oral dose of albendazole (400 mg) in 6 healthy subjects.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term carcinogenicity studies were conducted in mice and rats. In the mouse study, albendazole was administered in the diet at doses of 25, 100, and 400 mg/kg/day (0.1, 0.5, and 2 times the recommended human dose based on body surface area in mg/ m^2, respectively) for 108 weeks. In the rat study, albendazole was administered in the diet at doses of 3.5, 7, and 20 mg/kg/day (0.04, 0.08, and

0.21 times the recommended human dose based on body surface area in mg/m^2, respectively) for 117 weeks. There was no evidence of increased incidence of tumors in the treated mice and rats when compared to the control group.

In genotoxicity tests, albendazole was found negative in an Ames Salmonella/Microsome Plate mutation assay with and without metabolic activation or with and without pre-incubation, cell-mediated Chinese Hamster Ovary chromosomal aberration test and in vivo mouse micronucleus test. In the in vitro BALB/3T3 cells transformation assay, albendazole produced weak activity in the presence of metabolic activation while no activity was found in the absence of metabolic activation.

Albendazole did not adversely affect male or female fertility in the rat at an oral dose of 30 mg/kg/day (0.32 times the recommended human dose based on body surface area in mg/ m^2).

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

Use in Pregnancy:

Albendazole is contraindicated during pregnancy, and for one month prior to conception. In order to avoid administering albendazole during early pregnancy, women of child bearing

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 (30 mg/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 (10 mg/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 the 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 machines

Dizziness is reported as a common reaction. Patients should be advised that if affected they should not drive, operate machinery or take part in activities where this could put them or others at risk.

4.8 Undesirable effects

Data from large clinical studies were used to determine the frequency of very common to rare undesirable reactions. The frequencies assigned to all otherundesirable reactions (i.e. those occurring at < 1/1000) were mainly determined using post-marketing data and refer to a reporting rate rather than a true frequency.

The following convention has been used for the classification of frequency:

Very common ≥1/10

Common ≥1/100 to <1/10

Uncommon ≥ 1/1000 to < 1/100

Rare ≥ 1/10,000 to < 1/1000

Very rare < 1/10,000

Blood and the lymphatic system disorders

Uncommon: Leucopenia

Very rare: Pancytopenia, aplastic anaemia, agranulocytosis

Patients with liver disease, including hepatic echinococcosis, appear to be more susceptible to bone marrow suppression (see ‘4.2 Posology and Method of Administration’ and ‘4.4 Special Warnings and Precautions for Use’).

Immune system disorders

Uncommon: Hypersensitivity reactions including rash, pruritus and urticaria

Nervous system disorders

Very common: Headache

Common: Dizziness

Gastrointestinal disorders

Common: Gastrointestinal disturbances (abdominal pain, nausea, vomiting)

Gastrointestinal disturbances have been associated with albendazole when treating patients with echinococcosis.

Hepato-biliary disorders

Very common: Mild to moderate elevations of hepatic enzymes

Uncommon: Hepatitis

Skin and subcutaneous tissue disorders

Common: Reversible alopecia (thinning of hair, and moderate hair loss)

Very rare: Erythema multiforme, Stevens-Johnson syndrome

General disorders and administrative site conditions

Common: Fever

4.9 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 and general supportive measures are recommended.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antihelminthic

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 primarymetabolite, which is thought to be the active moiety in effectiveness againstsystemic 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 takenwith 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

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6. Pharmaceutical particulars

6.1 List of excipients

Lactose Monohydrate

Microcrystalline Cellulose

Maize Starch

Povidone(PVP-K-30)

Methyl Hydroxybenzoate

Propyl Hydroxybenzoate

Purified water

Aspartame

Magnesium Stearate

Purified Talc

Dry Flavour Orange

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store at temperature not exceeding 30°C. Keep out of reach of children.

6.5 Nature and contents of container

1 tablet packed in Alu PVC blister, such 1 blister packed in carton along with package insert.

6.6 Special precautions for disposal and other handling

No special instructions for use/handling.

7. MARKETING AUTHORISATION HOLDER

Name	**Brawn Laboratories Limited.**
Location (address)	13, N.I.T. Industrial Area, FARIDABAD-121 001, (HARYANA)
Country	INDIA
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Website	www.brawnlabs.com

8. Marketing authorization number(s)

06303/08103/REN/2021

9. Date of first authorization/renewal of the authorization

Jul 25, 2021

10. Date of revision of the text

N/A