Bharat Parenterals Limited
Registered Office & Works:
Vill. Haripura, Ta. Savli, Dist. Vadodara - 391520 (Guj.) India.
Tele Fax : (02667)-251679, 251680, 251669, 99099 28332.
E-mail: bplbrd@bplindia.in, info@bplindia.in, Web.: www.bplindia.in
CIN NO: U24231GJ1992PLC018237

ASCANTEL - SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. Name of the medicinal product

1.1. Name of the medicinal product:

Generic Name/INN Name: Albendazole Oral Suspension

Trade Name:

ASCANTEL

1.2 Strength:

Each 5 ml contains

Albendazole USP.... ....200 mg

Flavoured syrup base ...q.s.

Colour: Sunset Yellow FCF

1.3 Pharmaceutical form:

Oral Liquid

2. Qualitative and Quantitative Composition:

Sr. No	Name of Material	Spec.	Qty./ 5 ml of suspension (mg)	Qty./ Bottle of suspension (gm)	Qty. Taken as per Batch Size (Kg.)	Function
1.	Albendazole	USP	200.00	0.400	6.660	Active
2.	Sodium Methyl Paraben	BP	5.00	0.010	0.167	Preservative
3.	Sodium Propyl Paraben	BP	2.50	0.005	0.083	Preservative
4.	Citric Acid Monohydrate	BP	7.50	0.015	0.250	Buffering Agent
5.	Sucrose (Refined Sugar)	BP	2500.00	5.000	83.330	Sweetener
6.	Sodium carboxy methyl cellulose	BP	25.00	0.050	0.833	Suspending agent
7.	Polysorbate – 80	BP	7.50	0.015	0.250	Stabilizing agent
8.	Anhydrous Colloidal Silica	BP	15.00	0.03	0.500	Anti- Caking Agent
9.	Color Sunset Yellow Supra	IH	1.00	0.002	0.033	Coloring agent
10.	Flavor Orange Sweet	IH	75.00	0.15	0.033	Flavoring agent
11.	Purified Water	BP	Q. S.	Q. S.	Q. S.	Vehicle

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3. Pharmaceutical form:

Dosage Form: Oral-Liquid

Visual & Physical characteristics of the product:.

Albendazole Oral Suspension

Description: An orange coloured suspension filled in an amber colour Pet bottle.

Type of container & closure System:

15 ml amber colour Pet bottle.

4. Clinical particulars:

4.1 Therapeutic indications

Indicated in the treatment of single or mixed infestations of the following:

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*.

It is also indicated for the treatment of Hymenolepis nana and Taenia spp. (tapeworm) infections, when other susceptible helminths species are present.

Albendazole is indicated in giardiasis in children over 2 years of age.

Albendazole in higher doses is indicated for the treatment of hydatid disease.

4.2 Posology and method of administration

Age 12 to 24 months: 200 mg as a single dose.

Adults & children (over two years): 400 mg as a single dose in cases of *Enterobius vermicularis, Trichuris trichiura, Ascaris lumbricoides, Ancylostoma duodenale* and *Necator americanus*. In cases of strongyloidiasis or taeniasis, 400 mg as a single dose should be given for three consecutive days.

Giardiasis: 400 mg once daily for five days.

In hydatid disease (Echinococcosis): In the treatment of echinococcosis, it is given by mouth with meals in a dose of 400 mg twice daily for 28 days for patients weighing over 60 kg. A dose of 15 mg/kg body weight daily in two divided doses (to a maximum total daily dose of 800 mg) is used for patients weighing less than 60 kg. For cystic echinococcosis the 28- days course may be repeated after 14 days without treatment to a total of three treatment cycles. For alveolar echinococcosis, cycles of 28 days of treatment followed by 14 days without

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treatment may need to continue for months or years. When three courses of therapy have been given in the pre or post surgical setting, optimal killing of cyst contents is achieved.

4.3 Contraindications

Should not be administered during pregnancy or in women thought to be pregnant as it has been shown to be teratogenic and embryotoxic in some animals.

Contraindicated in persons who are known to be hypersensitive to Albendazole, other Benzimidazole derivatives or any component of product.

4.4 Special warnings and precautions for use

General precaution:

Confirmation of eradication of many intestinal and tissue parasites is necessary after treatment.

Use in Systemic Helminth Infections (longer duration of treatment at higher doses).

Hepatic Effects:

Mild to moderate elevations of liver enzymes have been reported with albendazole. Elevations of liver enzymes increase risk of hepatotoxicity and bone marrow suppression. In prolonged higher dose albendazole therapy for hydatid disease, there have been rare reports of severe hepatic abnormalities associated with jaundice and histological hepatocellular damage, which may be irreversible. Case reports of hepatitis have also been received. Enzyme abnormalities usually normalise on discontinuation of treatment.

Monitor and perform liver function tests (hepatic transaminase concentrations) prior to each cycle of albendazole treatment and at least every 2 weeks during treatment. If liver enzymes are significantly increased (greater than twice the Upper Limit of Normal (ULN) or full blood count decreased by a clinically significant level, consider discontinuing the drug based. Decisions to reinstitute albendazole when hepatic enzymes return to pretreatment levels should be individualized taking into account the risks and benefits of further albendazole treatment. If the drug is reinstituted, perform laboratory tests frequently to monitor for recurrence.

Myelosuppression:

Can cause bone marrow suppression, aplastic anemia, and agranulocytosis in patients with or without underlying hepatic dysfunction. Reversible leukopenia has occurred in <1% of patients receiving the drug; granulocytopenia, pancytopenia, agranulocytosis, or

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thrombocytopenia reported rarely. Rare fatalities reported due to granulocytopenia or pancytopenia.

Albendazole has been shown to cause bone marrow suppression and therefore blood counts should be monitored at the start of each 28-day cycle and every two weeks during treatment. Closer monitoring of blood counts is recommended in patients with liver disease, including hepatic echinococcosis, since these individuals may be more susceptible to bone marrow suppression leading to pancytopenia, aplastic anemia, agranulocytosis, and leukopenia. Albendazole should be discontinued if clinically significant decreases in blood cell counts occur.

Precautions Related to Treatment of Neurocysticercosis:

Destruction of cysticercosis lesions by albendazole may cause irreparable retinal damage, even when corticosteroids are given. Prior to treatment of neurocysticercosis, examine patient for cysticercosis retinal lesions. In those with such lesions, weigh the need for treatment against the possibility of irreparable retinal damage.

Symptoms associated with an inflammatory reaction following death of the parasite within the brain may occur in patients receiving albendazole treatment for neurocysticercosis (e.g. seizures, raised intracranial pressure, hydrocephalus, focal signs). These should be treated with appropriate corticosteroid and anticonvulsant therapy. Oral or intravenous corticosteroids are recommended during the first week of treatment to prevent cerebral hypertension. Pre-existing neurocysticercosis may also be uncovered in patients treated with albendazole for other conditions. 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 minimise this possibility.

Use in Impaired Renal or Hepatic Function:

The use 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 albendazsole is metabolised by the liver and has been associated with idiosyncratic hepatotoxicity.

Use in Children:

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There is limited experience in children under 2 years of age, therefore use in this age group is not recommended.

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.

Grapefruit juice may increase the bioavailability of albendazole but less than the increase observed after a fatty meal.

Phenytoin, carbamazepine and phenobarbital appear to induce the oxidative metabolism of albendazole, resulting in significantly reduced concentrations of albendazole sulfoxide. This interaction is likely to be clinically significant when albendazole is used to treat systemic worm infections. The interaction is probably not clinically significant when albendazole is used for intestinal worm infections.

Chinese Ginseng may theoretically reduce the intestinal concentration of albendazole active metabolite.

Albendazole may theoretically inhibit theophylline metabolism and increase toxicity.

4.6 Fertility, pregnancy and lactation

Pregnancy: Category C

Albendazole has been shown to be teratogenic (to cause embryotoxicity and skeletal malformations) in pregnant rats and rabbits. The teratogenic response in the rat was shown at oral doses of 10 and 30 mg/kg/day (0.10 times and 0.32 times the recommended human dose based on body surface area in mg/m2, respectively) during gestation days 6 to 15 and in pregnant rabbits at oral doses of 30 mg/kg/day (0.60 times the recommended human dose based on body surface area in mg/m2) administered during gestation days 7 to 19. In the rabbit study, maternal toxicity (33% mortality) was noted at 30 mg/kg/day. In mice, no teratogenic effects were observed at oral doses up to 30 mg/kg/day (0.16 times the recommended human dose based on body surface area in mg/m2), administered during gestation days 6 to 15.

There are no adequate and well-controlled studies of albendazole administration in pregnant women. Albendazole should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

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Nursing Mothers: Albendazole is excreted in animal milk. It is not known whether it is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when albendazole is administered to a nursing woman.

Pediatric Use: Experience in children under the age of 6 years is limited. In hydatid disease, infection in infants and young children is uncommon, but no problems have been encountered in those who have been treated. In neurocysticercosis, infection is more frequently encountered. In 5 published studies involving pediatric patients as young as 1 year, no significant problems were encountered, and the efficacy appeared similar to the adult population.

4.7 Effects on ability to drive and use machines

No specific warning.

4.8 Undesirable effects

Adverse effects are usually mild and resolve without treatment.

Dermatologic Effects:

Reversible alopecia (thinning of hair, and moderate hair loss), itchiness and/or skin rashes, erythema multiforme and Stevens-Johnson syndrome

Gastrointestinal Effects:

Abdominal pain, diarrhoea, nausea, vomiting

Hematologic Effects:

Low red cell count, leucopenia, pancytopenia, aplastic anaemia and agranulocytosis

Hepatic Effects:

Transiently raised hepatic enzymes, hepatitis, acute liver failure, jaundice, hepatocellular damage

Immunologic Effects:

Hypersensitvity reactions including rash, pruritis and urticaria.

Neurologic Effects:

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Dizziness, headache, symptoms associated with treatment for neurocysticercosis (e.g. seizures, raised intracranial pressure, hydrocephalus, focal signs).

Ophthalmic Effects:

Albendazole induced retinal damage in patients with pre-existing cysticercosis retinal lesions.

Renal Effects:

Proteinuria

Others:

Bone pain and fever

5. Pharmacological properties:

5.1 Pharmacodynamics properties:

Albendazole is a benzimidazole carbamate anthelmintic drug similar to mebendazole. It is a broad-spectrum anthelmintic, which is highly effective against a wide range of intestinal helminths including a variety of intestinal nematodes, cestodes and trematodes. It is also effective against tissue helminth infections, such as cutaneous larva migrans and has also been used in the high dose, long term treatment of tissue helminth infections including hydatid cysts and cysticercosis.

The antihelminthic action of albendazole is thought to be mainly intra-intestinal due to low absorption (less than 5%) after oral administration. However, at higher albendazole doses, sufficient amount is absorbed and metabolised to the active sulphoxide metabolite, to have a therapeutic effect against tissue parasites.

Albendazole exhibits larvicidal, ovicidal and vermicidal activity, and is thought to act via inhibition of tubulin polymerization. This causes a cascade of metabolic disruption, including energy depletion, which immobilizes and then kills the susceptible helminth.

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5.2 Pharmacokinetic properties

Absorption:

In man, the full extent of albendazole absorption following oral administration has not been established. However, it is known that albendazole is poorly absorbed (<5%) with most of an oral dose remaining in the gastrointestinal tract. The poor absorption is believed to be due to the low aqueous solubility of albendazole. Absorption is significantly enhanced (up to 5 fold) if albendazole is administered with a fatty meal compared with fasted state.

Metabolism:

Albendazole rapidly undergoes extensive first-pass metabolism in the liver, and is generally not detected in plasma or in urine. Albendazole sulphoxide is the primary metabolite, which is thought to be the active moiety in effectiveness against systemic tissue infections (anthelmintic activity). Peak plasma concentrations of albendazole sulfoxide attained 2–5 hours after a dose. Albendazole sulphoxide is further metabolized to albendazole sulfone and other primary oxidative metabolites.

Distribution:

Albendazole sulfoxide is widely distributed throughout the body including into urine, bile, liver, cyst wall, cyst fluid, and cerebrospinal fluid (CSF). It is about 70% bound to plasma protein.

Elimination:

Albendazole sulphoxide and its metabolites appear to be principally eliminated in bile, with only a small proportion (<1% of albendazole sulfoxide) appearing in the urine. The plasma half life of albendazole sulphoxide is 8-12 hours.

Special population:

Patients with extra hepatic obstruction: Increased albendazole sulfoxide serum concentration and prolonged half-life. Elimination half-life may be 31.7 hours.

5.3 Preclinical safety data

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

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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).

6. Pharmaceutical particulars:

6.1. List of Excipients:

The list of excipients is as follows:

Sr. No.	Ingredients	Specification
1.	Sodium Methyl Paraben	BP
2.	Sodium Propyl Paraben	BP
3.	Citric Acid Monohydrate	BP
4.	Sucrose (Refined Sugar)	BP
5.	Purified Water	BP
6.	Sodium carboxy methyl cellulose	BP
7.	Anhydrous Colloidal Silica (Aerosil)	BP
8.	Polysorbate – 80	BP
9.	Color Sunset Yellow	IH
10.	Flavor Orange Sweet	IH

6.2 Incompatibilities:

Not applicable

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ASCANTEL - SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

6.3. Shelf life:

24 months

6.4. Special precautions for storage:

Store below 25°C. Protect from light & Moisture. Keep out of reach of children.

Prescription Only Medicine.

6.5. Nature and contents of container:

15 ml amber colour Pet bottle.

6.6. Special precautions for disposal:

No special requirement.

7. Applicant

Name and Address of Applicant

M/s. Biomedicine Sckivs Pharm.Nig Ltd,

Premise Address: No. 16, Anionwu Street Odoakpu, P.O.BOX:7846, Onitsha Nigeria,

Tel: +234803507884, +2348024517997.

E-mail: sckivspharm@yahoo.com

Name and Address of manufacturer:

M/s. BHARAT PARENTERALS LIMITED

Survey No. 144 &146, Jarod Samlaya Road,

Village: Haripura, Ta. Savli, Dist. Vadodara – 391520

Gujarat, INDIA.

Tel.91-2667-251680

Fax: 91-2667-251679

E-mail: ra@bplindia.in

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