Summary of Product Characteristics

1. Name of the medicinal product

Sivodazole Suspension

2. Qualitative and quantitative composition

Each 5 ml contains :

Albendazole BP 200 mg

In Flavoured Palatable base q.s.

Colour: Sunset yellow

3. Pharmaceutical form

Suspension; Liquid

4. Clinical particulars

4.1 Therapeutic indications

Albendazole is Broad spectrum gastrointestinal anthelmintic indicated for the treatment of:

Enterobius vermicularis (threadworm/pinworm)

Oxyuris vermicularis

Trichuris trichuria (whipworm)

Ascaris lumbricoides (large roundworm)

Ancylostoma duodenale (common hookworm)

Necator americanus (American hookworm)

4.2 Posology and method of administration

For oral administration. Shake the bottle before use. An oral syringe may be used to measure doses less than 5ml.

The usual adult dose is as a single dose in both adults and children over two years of age. The usual dose in children between one and two years of age is 10 mL of Albendazole

suspension as a single dose. In heavy mixed infestation involving Strongyloides or Taeniasis, a single daily dose may be inadequate and the dose may be given for three consecutive days.

4.3 Contraindications

Albendazole is known to be teratogenic and embryotoxic in animals. The safety of albendazole during pregnancy has not been established, and it should not be taken by pregnant women at any stage of their pregnancy or by women who are likely to become pregnant, during or shortly after the course of therapy.

It is similarly contra-indicated in patients with a known history of hypersensitivity to albendazole or constituents.

4.4 Special warnings and precautions for use

It has been noted that leucopaenia has occurred when used for periods longer than recommended.

4.5 Interaction with other medicinal products and other forms of interaction

Praziquantel has been reported to increase the plasma levels of the albendazole active metabolite.

4.6 Fertility, pregnancy and lactation

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

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.

4.7 Effects on ability to drive and use machines

No or negligible influence on driving.

4.8 Undesirable effects

The adverse event profile of albendazole differs between hydatid disease and neurocysticercosis. Adverse events occurring with a frequency of ≥1% in either disease are described in the table below.

These symptoms were usually mild and resolved without treatment. Treatment discontinuations were predominantly due to leukopenia (0.7%) or hepatic abnormalities (3.8% in hydatid disease). The following incidence reflects events that were reported by investigators to be at least possibly or probably related to albendazole.

Adverse Event	Hydatid Disease	Neurocysticercosis
Abnormal Liver Function Tests	15.6	<1.0
Abdominal Pain	6.0	0
Nausea/ Vomiting	3.7	6.2
Headache	1.3	11.0
Dizziness/Vertigo	1.2	<1.0
Raised Intracranial Pressure	0	1.5
Meningeal Signs	0	1.0
Reversible Alopecia	1.6	<1.0
Fever	1.0	0

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.

4.9 Overdose

If poisoning or excessive overdosage is suspected it is recommended, on general principles, that vomiting be induced or gastric lavage be performed, and such symptomatic supportive therapy be administered as appears indicated.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Albendazole binds to the colchicine-sensitive site of β-tubulin inhibiting their polymerization into microtubules. The decrease in microtubules in the intestinal cells of the parasites decreases their absorptive 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 trisphosphate (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.

5.2 Pharmacokinetic properties

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 sulfoxide 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 coadministered with a fatty meal (estimated fat content 40 g) as evidenced by higher (up to 5-fold on average) plasma concentrations of albendazole sulfoxide as compared to the fasted state.

Maximal plasma concentrations of albendazole sulfoxide are typically achieved 2 to 5 hours after dosing and are on average 1.31 mcg/mL (range 0.46 to 1.58 mcg/mL) following oral doses of albendazole (400 mg) in 6 hydatid disease patients, when administered with a fatty meal. Plasma concentrations of albendazole sulfoxide increase in a dose-proportional manner over the therapeutic dose range following ingestion of a fatty meal (fat content 43.1 g). The mean apparent terminal elimination half-life of albendazole sulfoxide typically ranges from 8 to 12 hours in 25 normal subjects, as well as in 14 hydatid and 8 neurocysticercosis patients.

Following 4 weeks of treatment with albendazole (200 mg three times daily), 12 patients' plasma concentrations of albendazole sulfoxide were approximately 20% lower than those observed during the first half of the treatment period, suggesting that albendazole may induce its own metabolism.

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.

Albendazole is rapidly converted in the liver to the primary metabolite, albendazole sulfoxide, which is further metabolized to albendazole sulfone and other primary oxidative 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.

Special Populations

Patients with Impaired Renal Function

The pharmacokinetics of albendazole in patients with impaired renal function have not been studied. However, since renal elimination of albendazole and its primary metabolite, albendazole sulfoxide, is negligible, it is unlikely that clearance of these compounds would be altered in these patients.

Biliary Effects

In patients with evidence of extrahepatic obstruction (n = 5), the systemic availability of albendazole sulfoxide was increased, as indicated by a 2-fold increase in maximum serum concentration and a 7-fold increase in area under the curve. The rate of absorption/conversion and elimination of albendazole sulfoxide appeared to be prolonged with mean Tmax and serum elimination half-life values of 10 hours and 31.7 hours, respectively. Plasma concentrations of parent albendazole were measurable in only 1 of 5 patients.

Pediatrics

Following single-dose administration of 200 mg to 300 mg (approximately 10 mg/kg) albendazole to 3 fasted and 2 fed pediatric patients with hydatid cyst disease (age range 6 to 13 years), albendazole sulfoxide pharmacokinetics were similar to those observed in fed adults.

Elderly Patients

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.

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

Refined Sugar, Sodium Carboxymethyl Cellulose, Xanthan gum, Sodium methyl hydroxybenzoate, Sodium propyl hydroxybenzoate, Polysorbate-80, Colloidal Anhydrous

Silica, Citric acid monohydrate, Aspartame, Sodium EDTA, Sodium Benzoate, Colour Sunset yellow supra, Flavour Sweet Orange No. 1 and Purified Water

6.2 Incompatibilities

None known

6.3 Shelf life

30 months

6.4 Special precautions for storage

Do not store above 30°C.

Keep out of the reach of children

6.5 Nature and contents of container

Pet bottle 10ml

6.6 Special precautions for disposal and other handling

Any product remaining at the end of treatment should be discarded.

7. Marketing authorisation holder

Not Applicable

8. Marketing authorisation number(s)

Not Applicable

9. Date of first authorisation/renewal of the authorisation

Not Applicable

10. Date of revision of the text

Not Applicable