Summary of Product Characteristics

1. Name of the medicinal product

Sivodazole

2. Qualitative and quantitative composition

Each uncoated chewable tablet contains:

Albendazole BP 400 mg

Excipients q.s.

Colour: Sunset yellow

3. Pharmaceutical form

Chewable Tablet

4. Clinical particulars

4.1 Therapeutic indications

Albendazole' is a benzimidazole carbamate anthelmintic for use in the treatment of hydatid cysts caused by:

Echinococcosis:

Albendazole Tablets shows greatest efficacy in the treatment of liver, lung and peritoneal cysts. Experience with bone cysts and those in the heart and central nervous system is limited.

Cystic Echinococcosis (caused by Echinococcus granulosus)

Albendazole Tablets is used in patients with cystic echinococcosis:

1. Where surgical intervention is not feasible.

2. Prior to surgical intervention.

3. Post-operatively if pre-operative treatment was too short, if spillage has occurred or if viable material was found at surgery.

4. Following percutaneous drainage of cysts for diagnostic or therapeutic reasons.

Alveolar Echinococcosis (caused by Echinococcus multilocularis)

Albendazole Tablets is used in patients with alveolar echinococcosis:

1. In inoperable disease, particularly in cases of local or distant metastasis.

2. Following palliative surgery.

3. Following radical surgery or liver transplantation.

4.2 Posology and method of administration

Dosages are dependent on the parasite involved, the weight of the patient, and the severity of the infection:

Cystic Echinococcosis

Patients weighing >60 kg Total daily dose: 800 mg given in two divided doses of 400 mg for a total of 28 days.

Patients weighing <60 kg Total daily dose: 12 mg/kg given in two equally divided doses (maximum dose 800 mg/day) as above.

This 28-day treatment period may be repeated after a 14-day period without treatment for a total of three cycles.

Alveolar Echinococcosis

Patients weighing >60 kg Total daily dose: 800 mg given in two equally divided doses for cycles of 28 days with 14 days between cycles.

Patients weighing <60 kg Total daily dose: 12 mg/kg given in two equally divided doses (maximum dose 800 mg/day) as above.

Treatment may need to be prolonged for months or years. Continuous treatment at the same dose has been used for periods of up to 20 months.

For oral use. The tablet should be chewed

4.3 Contraindications

Albendazole should not be administered during pregnancy or in women thought to be pregnant. Women of childbearing age should be advised to take effective precautions, with non hormonal contraceptive measures, against conception during and within one month of completion of treatment with Albendazole Tablets. Albendazole is contraindicated in patients with a known history of hypersensitivity to the active substance or to any of the product excipients.

4.4 Special warnings and precautions for use

Albendazole has been associated with mild to moderate elevations of hepatic enzymes. Hepatic enzymes generally normalise on discontinuation of treatment. Case reports of hepatitis have also been received. Liver function tests should be obtained before the start of each treatment cycle and at least every two weeks during treatment. If hepatic enzymes are significantly increased (greater than twice the upper limit of normal), albendazole should be discontinued. Treatment may be restarted when hepatic enzymes have returned to normal limits, but patients should be monitored for recurrence.

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 leucopenia and therefore warrant closer monitoring of blood counts. Albendazole should be discontinued if clinically significant decreases in blood cell counts occur.

Precautions:

In order to avoid administering albendazole during early pregnancy, women of childbearing age should:

- initiate treatment only after a negative pregnancy test. These tests should be repeated at least once before initiating the next cycle.
- be advised to take effective precautions against conception during and within one month of completion of treatment with albendazole for a systemic infection.

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.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Tablet to be chewed.

4.5 Interaction with other medicinal products and other forms of interaction

Albendazole has been shown to induce liver enzymes of the cytochrome P450 system responsible for its own metabolism.

Drugs that can reduce the effectiveness of albendazole – monitor effect - other dose regimens or therapies may be required.

• Anticonvulsants (eg phenytoin: fosphenytoin: carbamazepine: phenobarbital: primidone)

• Levamisole

• Ritonavir

Drugs that may increase levels of the active metabolite of albendazole – monitor to possible increased albendazole adverse effects.

• Cimetidine

• Dexamethasone (continuous use raises albendazole levels by 50%)

• Praziquantel

Grapefruit juice also increases the plasma levels of albendazole sulfoxide.

Other possible interactions Because of possible alterations in cytochrome P450 activity, there is a theoretical risk of an interaction with the following

• Oral contraceptives

• Anticoagulants

• Oral hypoglycaemics

• Theophylline Care should be exercised when albendazole is given to patients taking these medicines.

4.6 Fertility, pregnancy and lactation

Albendazole Tablets should not be administered during pregnancy or in women thought to be pregnant (see contraindications).

It is not known whether albendazole or its metabolites are secreted in human breast milk. Thus albendazole Tablets should not be used during lactation unless the potential benefits are considered to outweigh the potential risks associated with 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

Very common: Mild to moderate elevations of hepatic enzymes, Headache.

Common: Dizziness, gastrointestinal disturbances, reversible alopecia, fever.

Uncommon: Leucopenia, hypersensitivity reactions including rash, pruritus and urticaria, hepatitis,

Very rare: Erythema multiforme, stevens-Johnson syndrome, mild to moderate elevations of hepatic enzymes, pancytopenia, aplastic anaemia, agranulocytosis.

4.9 Overdose

In case of overdosage, symptomatic therapy (gastric lavage) and general supportive measures should be undertaken.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Anthelmintics, Antinematodal agents, Benzimidazole derivative; 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

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.

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 population

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.

6. Pharmaceutical particulars

6.1 List of excipients

Maize Starch, Lactose, Colour Sunset Yellow Supra, Sodium Methyl Hydroxybenzoate, Sodium Propyl Hydroxybenzoate, Saccharin Sodium, Sucrose, Purified Water, Purified Talc, Magnesium Stearate and Flavour Orange Dry.

6.2 Incompatibilities

None known

6.3 Shelf life

36 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

20x1x1 Tablets Alu-PVC Blister Pack

1x1 Tablet Alu-PVC Blister Pack

10x10 Tablets Alu-PVC Blister Pack

Not all pack sizes may be marketed.

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