

1.17

## Summary Product Characteristics (SPC):

### Summary Product Characteristics (SPC)

#### 1. Proposed trade name of the pharmaceutical product

Nilworm Suspension

#### 2. Qualitative and quantitative composition

Each 5 ml contains:

Albendazole BP                      200 mg

Flavoured syrup base                      q.s.

Colour: Erythrosine

#### 3. Pharmaceutical form

Suspension (Liquid dosage form)

#### 4. Clinical Particulars

##### 4.1 Therapeutic indications

Albendazole Suspension BP 200 mg are used for the treatment of Single or mixed infestations of intestinal nematodes

- Pinworm (Enterobiasis)
- Roundworm (ascariasis)
- Old world hookworm (Ankylostomiasis)
- New world hookworm (Nectoriasis)
- Whipworm (Strongyloidiasis)

Infestation with Taeniasaginata, Taeniasolium and Echinococcus.

##### 4.2 Posology and method of administration

Posology:

Route of administration: Oral route of administration

Average dose and dose range for adults and children:

10 ml of NILWORM suspension 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 5 ml (200 mg) of NILWORM 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 Contra-indications**

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. Albendazole is contra-indicated in patients with a known history of hypersensitivity to the active substance.

### **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.

### **4.5 Interaction with other medicaments 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 Pregnancy and lactation**

##### Pregnancy:

Pregnancy Category C. Albendazole has been shown to be teratogenic (to cause embryotoxicity and skeletal malformations) in pregnant rats and rabbits. 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.

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.

Pregnancy category C in United State and Category D in the Australia.

##### Lactation:

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

##### Fertility:

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<sup>2</sup>).

#### **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 other undesirable 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	$\geq 1/10$
Common	$\geq 1/100$ to $< 1/100$
Rare	$\geq 1/10,000$ 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.

#### 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)

## General disorders and administrative site conditions

Common: Fever

### **4.9 Overdosage**

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**

#### **General properties**

Nilworm Suspension contains Albendazole as an active ingredients and Broad-spectrum anthelmintic - Benzimidazole derivatives

ATC Class: P02CA03

#### Mode of action:

Albendazole causes degenerative alterations in the tegument and intestinal cells of the worm by binding to the colchicine-sensitive site of tubulin, thus inhibiting its polymerization or assembly into microtubules. The loss of the cytoplasmic microtubules leads to impaired uptake of glucose by the larval and adult stages of the susceptible parasites, and depletes their glycogen stores. Degenerative changes in the endoplasmic reticulum, the mitochondria of the germinal layer, and the subsequent release of lysosomes result in decreased production of adenosine triphosphate (ATP), which is the energy required for the survival of the helminth. Due to diminished energy production, the parasite is immobilized and eventually dies.

#### Pharmacodynamics

Albendazole is a benzimidazole carbamate with anthelmintic effects against tissue parasites.

Albendazole exhibits larvicidal, ovicidal and vermucidal 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: Albendazole is poorly absorbed (<5% ) following oral administration. In man, the full extent of albendazole absorption following oral administration has not been established. However, it is known that albendazole is poorly absorbed 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 (approximately 5 fold) if albendazole is administered with a fatty meal.

Distribution: 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 cerebrospinal fluid (CSF). Concentrations in plasma were 3-fold to 10-fold and 2-fold to 4-fold higher than those simultaneously determined in cyst fluid and CSF,

respectively.

**Metabolism:** 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.

**Excretion:** The plasma half-life of albendazole sulfoxide is 8½ hours. Albendazole sulphoxide and its metabolites appear to be principally eliminated in bile, with only a small proportion appearing in the urine.

### **5.3 Preclinical safety data**

No new study was conducted with this type of application,

## **6. Pharmaceutical Particulars**

### **6.1 List of Excipients**

Sugar, Sodium methyl paraben, Sodium propyl paraben, Propylene glycol, Colloidal silicone dioxide, Polysorbate 80, Xanthan gum, Colour erythrosine, Flavour aniseed no 1, Citric acid, Purified water.

### **6.2 Incompatibility**

Not Compatibility

### **6.3 Shelf Life**

2 Years

### **6.4 Special Precaution**

Store in dark place at a temperature not exceeding 30°C

### **6.5 Nature and content of container**

10 ml Amber coloured PET Bottle

### **6.6 Special precaution for disposal and other handling**

No special requirement.

### **6.7 Marketing authorisation holder**

Oasis Laboratories (P) Ltd.

E-18, Selaqui Industrial Area,

Dehradun (Uttarakhand) 248011, India

### **6.8 Date of 1st authorization/ renewal of the authorization**

Not applicable

### **6.9 Date of revision of the text**

Not applicable