

## **SUMMARY OF PRODUCT CHARACTERISTICS**

## 1. NAME OF FINISHED PHARMACEUTICAL PRODUCT

DISWORM (Albendazole Oral Suspension 200mg/5ml)

## 2. Strength (composition):

Each 5 ml contains:

Albendazole USP 200 mg

## 3. Pharmaceutical dosage form:

Oral Suspension

Rose colour suspension having uniform consistency and free from gritty particles.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

#### Intestinal and skin infections

- Threadworms (*Enterobius vermicularis*),
- Roundworms (*Ascaris lumbricoïdes*),
- Hookworms (*Ankylostoma duodenale*, *Necator americanus*),
- Whipworms (*Trichuris trichuria*),
- Anguillulosis (*Strongyloides stercoralis*),
- Taeniasis (*Taenia saginata*, *Taenia solium*),
- Giardiasis (*Giardia intestinalis* or *duodenalis*) in children,

#### Systemic infections

- Trichinosis (*Trichinella spiralis*).

### 4.2 Posology and method of administration

#### Posology

Indications	Daily dose	Treatment duration
<b>Intestinal and skin infections (short-term treatment with lower dose)</b>		
Oxyurosis	Children from 1 to 2 years: 5 ml suspension (200 mg) in one single dose Adults and children older than 2 years*: 400 mg, 1 single tablet or 10 ml of suspension in single dose Strict hygiene measures should be taken and family environment	Single dose to be repeated 7 days after.

	should also be treated.	
Roundworms Hookworms Whipworms	Children from 1 to 2 years: 5 ml of suspension (200 mg) Adults and children older than 2 years*: 400 mg, 1 single tablet or 10 ml of suspension in single dose.	Single dose. **
Anguillulosis (associated with parasitosis)	Taeniasis with others Adults and children older than 2 years *: 400 mg, 1 tablet or 10 ml of suspension daily	1 daily dose during 3 days. **
Giardiasis	Children older than 2 years*: 1 tablet or 10 ml of suspension daily.	1 daily dose during 5 days.
<b>Systemic infections (long-term treatment with higher doses)</b>		
Trichinosis	Children*: 15 mg/kg/day divided into two daily doses Adults: 1 tablet or 10 ml of suspension twice daily	2 daily doses (morning & evening) during 10 to 15 days depending on the severity of the symptoms and on the onset of treatment.

\* For children under 6 years, tablet form of 400 mg is inappropriate due to wrong route risk, and only suspension form should be used.

\*\*If the worm control performed 3 weeks after the treatment is positive, a second treatment should be administered.

### **Special populations**

#### **Elderly people:**

Data concerning patients from 65 years old are limited. Reports suggest that no adaptation of the posology is required in elderly people. However, albendazole should be used with care in patients with a liver dysfunction.

#### **Liver failure:**

Albendazole is rapidly metabolized by the liver, the main metabolite, albendazole sulfoxide, is pharmacologically active. Hence, liver failure might result in significant effect on the pharmacokinetics of albendazole sulfoxide.

Patients with abnormal liver function tests (transaminases) prior to treatment with albendazole should be closely monitored. The treatment should be stopped in case of significant increase in liver enzymes or in case of clinically significant decrease in blood formula numeration.

#### **Renal failure:**

As the elimination of albendazole and its main metabolite, albendazole sulfoxide are negligible, it is unlikely that the clearance of these compounds are modified in patients with renal failure. No dose adaptation of posology is required. However, patients with renal failure should be closely monitored.

#### **Method of administration**

Oral route.

#### **4.3 Contraindications**

Hypersensitivity to albendazole or to any of the components

Pregnancy and women of childbearing age who do not use an efficient contraceptive method

Breastfeeding

#### **4.4 Special warnings and precautions for use**

Neurologic symptoms

A treatment with albendazole might reveal a pre-existing neurocysticercosis, in particular in regions of strong infestation with taeniasis. Patients might feel neurological symptoms such as convulsions, increase in intracranial pressure and focal signs resulting from the inflammatory reactions following the death of the parasite in the brain. Symptoms might appear shortly after the treatment; an adapted treatment with corticoids and anticonvulsants should be immediately started.

**Precaution for use when using albendazole for systemic infections (long-term treatment with higher doses):**

##### ***Liver disorders***

Albendazole might result in a slight to moderate increase in liver transaminases, normalizing generally when stopping the treatment. Serious cases of hepatitis have also been reported when treating systemic helminth infections (long-term treatment with higher doses). Tests of the liver function should be carried out prior to starting the treatment and at least every second week during the treatment. Albendazole shall be stopped in case of increase in hepatic enzymes (more than twice normal). If reintroducing the treatment is indispensable, this should be done after normalization of liver enzymes. Moreover, a close monitoring should be carried out, keeping in mind that potential relapses might appear because an allergic mechanism cannot be discarded.

### ***Medullar depression***

Cases of medullar depression have been reported during treatment of systemic helminth infections (long-term treatment with higher doses). Numerations of blood formula should be performed when starting the treatment and then after two weeks of treatment with albendazole.

Patients with a liver disease, including liver echinococcosis, seem more likely to develop a medullar depression, leading to pancytopenia, medullar aplasia, agranulocytosis and leucopenia. Then, an increase monitoring of the blood formula is recommended in patients showing a liver disease.

Albendazole shall be stopped in case of significant decrease in the number of blood cells

In the treatment of trichinosis, few data are available with albendazole in children under 6 years of age.

In the treatment of trichinosis, because of the activity, in particular on the intestinal forms and of the larvae in the early phase of the tissue migration, it is recommended to administer albendazole as early as possible at the start of the infestation in order to decrease the symptoms and the complications. This treatment remains inactive on the encysted larvae in chronic forms and when it is initiated belatedly.

### ***Contraception***

Before initiating the treatment with albendazole, the doctor should inform the patient of the embryotoxic, teratogenic and aneugenic risks of albendazole, of the necessity of an efficient contraception and of the potential consequences on pregnancy if it occurs during the course of the treatment with albendazole.

### **4.5 Interaction with other medicinal products and other forms of interaction**

Enzymes inducers anti-convulsants, ritonavir and rifampicine may have the potential to reduce plasma concentrations of albendazole and of its active metabolite, albendazole sulfoxide with a risk of decrease in its efficacy. Clinical monitoring of the therapeutic efficacy and the potential adaptation of the posology of albendazole during the course of the treatment with an enzymatic inducer and after stopping.

### **4.6 Fertility, pregnancy and lactation**

#### **Female patients**

Given the aneugenic, embryotoxic and teratogenic potential of albendazole, all the precautions should be taken in order to avoid pregnancy in these female patients. Treatment with albendazole should not be initiated before a negative result to a pregnancy test performed right before the treatment initiation. Women of childbearing age should use an efficient contraceptive method during the treatment and 6 months after stopping the treatment.

### **Male patients and their female partners**

All precaution should be taken in order to avoid pregnancy in the partners of male patients treated with albendazole. It is not known if the presence of albendazole in sperm can cause teratogenic or Genotoxic effects on human embryo/foetus. Men or their female partners of childbearing age must be informed of the obligation to use an efficient contraceptive method during all the course of the treatment with albendazole and during 3 months after stopping the treatment. Men whose partners are pregnant should be informed of the obligation to use a condom in order to reduce the exposition of their partner to albendazole.

### **Pregnancy**

Studies in animal showed teratogenic embryotoxic effects in rat and rabbit at doses close to those used in men in clinical trials, the data on the use of albendazole during the first term of pregnancy are limited. Albendazole is contraindicated during pregnancy, especially because there are therapeutic alternatives that are better assessed in terms of safety in pregnant woman. Female patients should be informed of the necessity to consult their doctor immediately in case of pregnancy. This is based on prenatal monitoring targeted on malformations described in animal (skeletal, cranofacial, limbs).

### **Fertility**

In rat or mouse, studies have showed testicular toxicity of albendazole. Albendazole has an aneugenic activity, which is a risk factor for alteration of fertility in man.

### **Breastfeeding**

Albendazole is present in human breast milk after a single dose of 400 mg. Because of its aneugenic activity, a risk for the new born child cannot be excluded. In case of a single dose, breastfeeding should be stopped at the time of intake and for at least 5.5 half-lives (about 48

hours) after stopping the treatment. Before initiating breastfeeding, pump all the available breast milk and dispose of it; in case of repeated intakes, breastfeeding is contraindicated.

#### 4.7 Effects on ability to drive and use machines

When driving or using machines, it should be kept in mind that dizziness have been reported after using albendazole.

#### 4.8 Undesirable effects

The frequency of side effects from very common to rare have been determined based on the data from the clinical trials. The frequencies of the other side effects are mainly based on the post-marketing data and are referred to the reported observations rather than the real frequencies.

The side effects listed below are classified by organ system and frequency, according to the following convention:

##### Intestinal and skin infections (short-term treatment with low doses)

<b>Systemic class organs</b>	<b>Uncommon</b>	<b>Unknown frequency</b>
<i>Immune system disorders</i>		Hypersensitivity reaction, including skin rash, itching and hives
<i>Nervous system disorders</i>	Headaches Dizziness	
<i>Gastro-intestinal disorders</i>	Gastro-intestinal symptoms (epigastric or abdominal pains, nausea, vomiting) and diarrhoea	
<i>Hepatobiliary disorders</i>		Increase in liver enzymes
<i>Skin and subcutaneous tissue disorders</i>		Polymorphic erythema Stevens-Johnson syndrome

##### Systemic infections (long-term treatment with higher doses)

<b>Systemic class organs</b>	<b>Very common</b>	<b>Common</b>	<b>Uncommon</b>	<b>Unknown frequency</b>
<i>Haematological and lymph</i>				<i>Medullar aplasia Leucopenia</i>

<i>system disorders</i>				<i>Pancytopenia Agranulocytosis</i>
<i>Immune system disorders</i>			<i>Hypersensitivity reactions including skin rash, itching, hives</i>	
<i>Nervous system disorders</i>	<i>Headaches</i>	<i>Dizziness</i>		
<i>Gastro-intestinal disorders</i>		<i>Gastro-intestinal disorders (abdominal pains, nausea and vomiting)</i>		
<i>Hepatobiliary disorders</i>	<i>Slight to moderate increase in liver enzymes</i>		<i>Hepatitis</i>	

#### 4.9 Overdose

In case of overdose, symptomatic treatment and medical monitoring are recommended.

### 5. PHARMACOLOGICAL PROPERTIES

#### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antiparasitics - antihelmintics, ATC code: P02CA03.

Albendazole is a benzimidazole carbamate. Albendazole is broad-spectrum antihelmintics, which is effective against a wide range of intestinal helminths.

Albendazole acts on helminths' cytoskeleton by the inhibition of tubulin polymerisation and thus, their introduction in the microtubules, blocking glucose absorption of parasites and resulting in their death.

Albendazole is also active on *Giardia intestinalis* (or *duodenalis*). It has an irreversible action that is targeted on the ventral disc of the trophozoites by acting on the polymerisation of tubulin and giardine, leading to a disorganization of the cytoskeleton and micro strips. The ability of adhesion to the enterocytes is decreased, resulting in an inhibition of the growth and multiplication of the parasite.

#### 5.2 Pharmacokinetic properties



### **Absorption and biotransformation**

Following the administration, the low proportion of albendazole is absorbed (< 5 %) is metabolised into albendazole sulfoxide and sulfone. The plasma concentration in sulfoxide, the main active circulating metabolite reaches its maximum about two and a half hours after its administration.

The systemic pharmacological effect of albendazole is increased if the dose is administered concomitantly with a fat-rich meal, improving absorption by about 5.

### **Elimination**

The plasma half-life of albendazole sulfoxide is 8 and a half hours.

Albendazole sulfoxide and its metabolites seem to be mainly eliminated by biliary route and for a lower proportion by urinary route.

### **Specific population**

Renal failure: albendazole pharmacokinetics has not been studied in patients with renal failure.

Haptic failure: albendazole pharmacokinetics has not been studied in patients with hepatic failure.

### **5.3 Preclinical safety data**

Degeneration of the seminiferous tubules has been reported in cancerogenesis studies at dose of 100 mg/kg/day in mouse and 20 mg/kg/day in rat. A decrease in the testicle weight has been observed in dog treated with 60 mg/kg/day during 6 months. These doses correspond respectively to 2.4; 0.24 and 2.5 times the maximum therapeutic dose (based on the human equivalence). Albendazole has not altered fertility in males or female rat up to the maximum dose of 30 mg/kg/day, or 0.36 times the maximum therapeutic dose (based on the human equivalence).

Albendazole appeared to be teratogenic and embryotoxic in rat and rabbit.

No carcinogenic potential has been shown during the carcinogenesis studies in rats (20 mg/kg/day) and in mice (400 mg/kg/day). Albendazole did show any genotoxic effects in *in vitro*

trials carried out on bacteria and mammal cells cultures, as well as in an *in vivo* micronucleus trial in rodents. A positive result has been reported in another micronucleus study in mouse, and is regarded as resulting from an aneugenic effect of albendazole.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of Excipients**

Sucrose

Xanthan gum

Methyl paraben sodium

Propyl paraben sodium

Sodium Benzoate

Glycerin

Polysorbate 80

Disodium Edetate

Citric acid

Aspartame

Erythrosine supra

Raspberry

Mixed fruit

Purified water

### **6.2 Incompatibilities**

Not applicable

### **6.3 Shelf life**

24 months

### **6.4 Special precautions for storage**

Store below 30°C. Protect from light and moisture.

Keep out of reach of children. Shake well before use.

### **6.5 Nature and contents of container**

10 ml Amber colour glass bottle.

## **7. Marketing authorization holder**

AS PHARMACEUTICALS,

No. 1/134, B4, Kuthubi Complex,

2<sup>nd</sup> Avenue, 6<sup>th</sup> Cross Street,

Vettuvankeni, Chennai – 600115, India

**8. Marketing authorisation number(s)**

MAD/IND/405

**9. Date of first registration/ renewal of the registration**

Date of first authorisation: 31.05.2018

**10. Date of revision of the text**

07/2023