**SUMMARY OF PRODUCT CHARACTERISTICS**

1. **NAME OF THE MEDICINAL PRODUCT**

<Trade Name> <Strength> Tablet

1. **QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each tablet contains <Strength> albendazole.

<Regarding the approval>

For a full list of excipients see section 6.1

1. **PHARMACEUTICAL FORM**

Tablet

<Regarding the approval>

1. **CLINICAL PARTICULARS**
	1. **Therapeutic indications**

<Generic Name> is a broad-spectrum anthelmintic used for the treatment of the following infections:

Cestode infections (tapeworms):

<Generic Name> is indicated for the treatment of *Echinococcus multilocularis* and *E. granulosus* infections before or after surgery or where surgery is not suitable.

<Generic Name> is also indicated for the treatment of neurocysticercosis caused by larval forms of the pork tapeworm, *Taenia solium.*

Lymphatic filariasis:

<Generic Name> is indicated together with ivermectin and/or diethylcarbamazine for the elimination of lymphatic filariasis.

Treatment is given to the entire eligible population in endemic areas through a mass drug administration programme.

Other nematode infections (roundworms):

<Generic Name> is indicated for the treatment of nematode infections including ascariasis, capillariasis, enterobiasis, hookworm infections (necatoriasis and ancylostomiasis), strongyloidiasis, trichostrongyliasis, trichuriasis, cutaneous larva migrans and trichinellosis.

<Generic Name> can also be used, alone or in combination with other medicines, for the control of soiltransmitted helminthiasis (ascariasis, trichuriasis and hookworm infections) through mass drug administration programmes.

* 1. **Posology and method of administration**

*Cestode infections (tapeworms):*

Adults

* In adults over 60 kg, the dose is 400 mg twice a day.
* In adults up to 60 kg, the dose is 15 mg/kg daily in 2 divided doses (maximum 800 mg daily).

*For cystic echinococcosis*

 <Generic Name> is taken for a course of 28 days followed by 14 tablet-free days. Up to 3 courses may be given.

*For alveolar echinococcosis*

<Generic Name> is taken for a course of 28 days followed by 14 tablet-free days, and treatment cycles may need to be continued for months or years.

*For neurocysticercosis*

 <Generic Name> is taken for 8–30 days.

Children

Only limited data are available on the use of <Generic Name> in children for cestode infections.

*Nematode infections*

Doses for the treatment of nematode infections are shown in the following table.

|  |  |  |
| --- | --- | --- |
| **Infection** | **Dose and frequency** | **Treatment duration** |
| **Adult and child over 2 years** | **Child 1–2 years** |
| Ascariasis Enterobiasis Hookworm infections Trichostrongyliasis  | 400 mg once | 200 mg once | Single dose |
| Trichuriasis, moderate  | 400 mg once | 200 mg once | Single dose |
| Trichuriasis, severe  | 400 mg once daily | 200 mg once daily | 3 days |
| Strongyloidiasis  | 400 mg once or twice daily | Not recommended | 3 days |
| Trichinellosis  | 400 mg once daily | Not recommended | 3 days |
| Capillariasis  | 400 mg once daily | Not recommended | 10 days |
| Cutaneous larva migrans  | 400 mg once or twice daily | Not recommended | 3-7 days |

*Mass drug administration*

For the elimination of *lymphatic filariasis* and the controlof *soil-transmitted helminthiasis* (ascariasis, trichuriasis, or hookworm disease), <Generic Name> is taken once or twice a year as needed (see WHO guidelines).

* *Adults* and children aged over 2 years: In adults and children aged over 2 years, the dose of <Generic Name> for mass drug administration is 400 mg once a year.
* *Children aged 1–2 years:* In children aged 1–2 years, the dose of <Generic Name> for the controlofsoil-transmitted helminthiasis is 200 mg.
* <Generic Name> is not used in children below 2 years for the elimination of lymphatic filariasis*.*

## *Special populations*

## Renal impairment

## No dose adjustment is required.

## Hepatic impairment

## Caution should be used if <Generic Name> is given to patients with liver disease, since albendazole is metabolised by the liver and has been associated with idiosyncratic hepatotoxicity.

## Method of administration

## For oral use. <Generic Name> is not a chewable tablet but may be crushed or swallowed whole.

## For young children or patients not able to swallow the tablets whole, the tablets may be crushed and added to a small amount of semi-solid food or liquid, all of which should be consumed immediately.

For intestinal infections, where absorption into the blood is not required, albendazole should be given on an empty stomach. For systemic effect, albendazole should be given with or after a meal.

* 1. **Contraindications**

Hypersensitivity to the active substance or to any excipients listed in section 6.1.

* 1. **Special warnings and precautions for use**

Uncovering pre-existing neurocysticercosis

Treatment with albendazole may uncover pre-existing neurocysticercosis, particularly in areas with high taenia infection. Patients may experience neurological symptoms such as 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, and appropriate steroid and anticonvulsant therapy should be started.

Risk of retinal damage in patients with retinal neurocysticercosis

Cysticercosis may, in rare cases, involve the retina. Before initiating therapy for neurocysticercosis, the patient should be examined for the presence of retinal lesions. If such lesions are visualised, the need for anticysticeral therapy should be weighed against the possibility of retinal damage caused by albendazoleinduced changes to the retinal lesion.

Hepatic effects

Mild to moderate elevations of liver enzymes have been reported with albendazole. In prolonged higher dose albendazole therapy for hydatid disease there have been rare reports of severe hepatic abnormalities such as jaundice and histological hepatocellular damage, which may be irreversible. Enzyme abnormalities are usually reversible on discontinuation of treatment.

Patients with disturbed liver function tests prior to commencing albendazole therapy should be carefully evaluated, since the medicine is metabolised by the liver and has been associated with idiosyncratic hepatotoxicity. If enzymes are significantly increased (greater than twice the upper limit of normal) during treatment, <Generic Name> should be discontinued. <Generic Name> treatment may be reinstituted when levels have returned to normal limits, but liver function should be monitored frequently during repeat therapy.

Bone marrow suppression

Albendazole can cause bone marrow suppression and therefore blood counts are needed at the start and every two weeks during each 28 day cycle for treating echinococcosis. Patients with liver disease, including hepatic echinococcosis, may 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.

Excipients

<Regarding the approval>

It is important to consider the contribution of excipients from all the medicines that the patient is taking.

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

#### Dexamethasone, praziquantel and cimetidine may increase the plasma concentration of the active metabolite of albendazole, albendazole sulphoxide.

#### Ritonavir, phenytoin, carbamazepine and phenobarbital may have the potential to reduce plasma concentrations of the active metabolite of albendazole. The clinical relevance of this is unknown, but may result in decreased efficacy, especially in the treatment of systemic helminth infections. Patients should be monitored for efficacy and may require alternative dose regimens or therapies.

* 1. **Fertility, pregnancy and breastfeeding**

Women of childbearing potential

Pregnancy should be avoided in women treated with albendazole. Adequate contraceptive measures should be taken.

Pregnancy

There are no adequate and well-controlled studies of <Generic Name> administration in pregnant women. Animal studies have revealed evidence of teratogenicity in rats and rabbits (see section 5.3).

<Generic Name> should be used in pregnant women only if there are no alternatives and the potential benefit justifies the potential risk to the fetus.

Lactation

Albendazole acts primarily in the intestinal system of the mother and little is absorbed systemically; therefore, it is compatible with breastfeeding.

Fertility

There are no data on the effects of <Generic Name> on human male or female fertility. Animal studies indicate no effects of albendazole on fertility (see section 5.3).

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

#### Patients should be warned about the potential for dizziness (see sections 4.8) while taking albendazole and should be advised not to drive or operate machines if this occurs.

#### Undesirable effects

#### Data from clinical trials and post-marketing surveillance were used to estimate the frequency of adverse events linked to albendazole.

The adverse reactions considered related to albendazole are listed below by body system, organ class and absolute frequency. Frequencies are defined as very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1000 to <1/100), rare (≥1/10 000 to <1/1000), and very rare (< 1/10 000).

## *Short duration of treatment*

## Blood and the lymphatic system disorders

## Rare: Low red cell count

## Immune system disorders

## Rare: Hypersensitivity reactions including rash, pruritus and urticaria

## Nervous system disorders

## Uncommon: Headache, dizziness

## Gastrointestinal disorders

## Common: Upper gastrointestinal symptoms (e.g. epigastric or abdominal pain, nausea, vomiting)

## Uncommon: Diarrhea

## Hepatobiliary disorders

## Rare: Elevations of hepatic enzymes

## Skin and subcutaneous tissue disorders

## Uncommon: Itchiness, skin rashes

## Very rare: Erythema multiforme, Stevens-Johnson syndrome

## Musculoskeletal and connective tissue disorders

## Rare: Bone pain

## Renal and urinary disorders

## Rare: Proteinuria

## *Longer duration of treatment*

## Blood and the lymphatic system disorders

## Uncommon: Leucopenia

## Rare: Low red cell count

## Very rare: Pancytopenia, aplastic anaemia, agranulocytosis

## 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)

## Hepatobiliary disorders

## Very common: Mild to moderate elevations of hepatic enzyme

## Uncommon: Hepatitis1

## Skin and subcutaneous tissue disorders

## Common: Reversible alopecia (thinning of hair, and moderate hair loss)

## Very rare: Erythema multiforme, Stevens-Johnson syndrome

## Musculoskeletal and connective tissue disorders

## Rare: Bone pain

## Renal and urinary disorders

## Rare: Proteinuria

## General disorders

## Common: Fever

## 1 With prolonged albendazole treatment for hydatid disease there have also been reports of severe hepatic abnormalities, including jaundice and hepatocellular damage which may be irreversible

## Reporting of suspected adverse reactions

## Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Health care providers are asked to report any suspected adverse reactions via Health Product Vigilance Center; HPVC Thai FDA.

* 1. **Overdose**

In case of overdosage, symptomatic therapy and general supportive measures are recommended.

# PHARMACOLOGICAL PROPERTIES

# Pharmacodynamic properties

# Pharmacotherapeutic group: Antihelmintics, benzimidazole derivatives

# ATC code: P02CA03.

# Mechanism of action

# Albendazole is a benzimidazole derivative that causes degenerative alterations in the tegument and intestinal cells of the parasite and blocks their energy production, ultimately leading to immobilisation and death of the parasite. It works by binding to the colchicine-sensitive site of tubulin, thus inhibiting its assembly into microtubules. As cytoplasmic microtubules are critical in promoting glucose uptake, the glycogen stores of the parasites are depleted.

### **Pharmacokinetic properties**

### The absorption characteristics of <Generic Name> have been determined in healthy volunteers for albendazole and summarised in the following tables;

|  |  |
| --- | --- |
| **Characteristic** | **Arithmetic mean ± Standard deviation (Geometric mean)** |
| Maximum concentration (Cmax)  | 84 ± 89 (56)  |
| Area under the curve (AUC0-∞), a measure of the extent of absorption  | 314 ± 368   |
| Time to attain maximum concentration (Tmax)  |  4.0 (1.33 – 5.0)  |

Pharmacokinetics of albendazole

|  |
| --- |
| **General** |
|   | Albendazole concentrations are negligible or undetectable in plasma as it is rapidly converted into the sulfoxide metabolite prior to reaching the systemic circulation. The systemic anthelmintic activity has been attributed to this primary metabolite, albendazole sulfoxide. Maximal plasma concentrations of albendazole sulfoxide are typically achieved 2 to 5 hours after dosing.  |
| **Absorption**   |
| Absolute bioavailability  | NA\*  |
| Oral bioavailability  | Albendazole is poorly absorbed from the gastrointestinal tract (<5%) due to its low aqueous solubility.  |
| Food effect  | Absorption is significantly enhanced (approximately 5-fold) if albendazole is administered with a fatty meal.  |
| **Distribution**   |
| Volume of distribution (mean)  | NA\*  |
| Plasma protein binding *in vitro*  | Albendazole sulfoxide is 70% bound to plasma protein.  |
| Tissue distribution  | Albendazole sulfoxide is widely distributed throughout the body; it has been detected in urine, bile, liver, cyst wall, cyst fluid, and cerebral spinal fluid.  |
| **Metabolism**   |
|   | Albendazole rapidly undergoes extensive first-pass metabolism in the liver to albendazole sulfoxide, and is generally not detected in plasma. Albendazole sulfoxide is further metabolized to albendazole sulfone and other primary oxidative metabolites.  |
| Active metabolite(s)  | Albendazole sulfoxide  |
| **Elimination**   |
| Elimination half life  | The terminal elimination half-life of albendazole sulfoxide typically ranges from 8 to 12 hours.  |
| Mean systemic clearance (Cl/F)  |   |
| Excretion  | Following oral administration, albendazole has not been detected in human urine. Albendazole sulphoxide and its metabolites appear to be principally eliminated in bile, with only a small proportion appearing in the urine.  |
| Pharmacokinetic linearity  | Plasma concentrations of albendazole sulfoxide increase in a doseproportional manner over the therapeutic dose range following ingestion of a fatty meal.  |
| Drug interactions *(in vitro*)  |   |
| Transporters  | NA\*  |
| Metabolizing enzymes  | NA\*  |

\* Information not available

*Special populations*

Renal impairment

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.

Liver impairment

In patients with evidence of extrahepatic obstruction, the systemic availability of albendazole sulfoxide was increased 7-fold.

Elderly patients

Although no studies have investigated the effect of age on albendazole sulfoxide pharmacokinetics, data suggest that the pharmacokinetics is similar to those in young healthy subjects.

Paediatrics

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

* 1. **Preclinical safety data**

General toxicity

Studies of up to 6 months in mice, rats and dogs recognised the haematopoietic system and the liver as target organs of toxicity.

Genotoxicity

In genotoxicity tests, albendazole was found negative in an Ames Salmonella/microsome plate mutation assay, 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.

Carcinogenicity

Long-term carcinogenicity studies in mice and rats found no evidence of increased incidence of tumours was found in the mice or rats at up to 400 mg/kg/day and 20 mg/kg/day, respectively.

Toxicity to reproduction

Albendazole did not affect male or female fertility in the rat at an oral dose level of 30 mg/kg/day.

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 during gestation days 6 to 15, and in pregnant rabbits at oral doses of 30 mg/kg/day 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 administered during gestation days 6 to 15.

# PHARMACEUTICAL PARTICULARS

# List of excipients

# <Regarding the approval>

# Incompatibilities

# Not applicable.

* 1. **Shelf life**

<Regarding the approval>

* 1. **Special precautions for storage**

<Regarding the approval>

* 1. **Nature and contents of container**

<Regarding the approval>

* 1. **Special precautions for disposal**

<Regarding the approval>

1. **MARKETING AUTHORISATION HOLDER**

<Regarding the approval>

1. **MARKETING AUTHORISATION NUMBER(S)**

<Regarding the approval>

1. **DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

<Regarding the approval>

# DATE OF REVISION OF THE TEXT 1

# <Regarding the approval>

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1 Ref: albendazole, WHO, May 2021