

## **1 NAME OF THE MEDICINAL PRODUCT**

Mebendazole Tablets 100mg  
Almus Threadworm 100mg Tablets Two Years Plus

## **2 QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each tablet contains mebendazole Ph. Eur. 100mg

### Excipients with known effect

Sunset yellow (E110)

Lactose

For the full list of excipients, see section 6.1.

## **3 PHARMACEUTICAL FORM**

Tablet

Orange, flat, bevelled edged tablet with a breakline on one side.

## **4 CLINICAL PARTICULARS**

### **4.1 Therapeutic indications**

For the treatment of threadworm (*Enterobius vermicularis*) infestation.  
There is no evidence that this is effective in the treatment of cyticercosis.

## **4.2 Posology and method of administration**

### Posology

*Adults, the elderly and children over 2 years:*

Take one tablet.

Tablets may be chewed or swallowed whole. Crush the tablet before giving it to a young child. Always supervise a child while they are taking this medicine. Care should be taken to avoid re-infection and it is strongly recommended that all members of the family are treated at the same time. It is highly recommended that a second tablet is taken after two weeks, if re-infection is suspected.

*Children under 2 years:*

Not recommended.

### Method of administration

Oral

## **4.3 Contraindications**

Mebendazole is contraindicated in pregnant women and in patients who have shown hypersensitivity to the active substance or any of the excipients listed in section 6.1.

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

Mebendazole is not recommended in the treatment of children under 2 years.

If symptoms do not disappear within a few days, consult your doctor.

A case-control study of a single outbreak of Stevens-Johnson syndrome /toxic epidermal necrolysis (SJS/TEN) suggested a possible association with the

concomitant use of metronidazole with mebendazole. Although there are no additional data on this potential interaction, concomitant use of Mebendazole and metronidazole should be avoided.

Convulsions in children, including in infants below one year of age, have been reported very rarely during post-marketing experience with Mebendazole. Mebendazole tablets should only be given to very young children if their worm infestation interferes significantly with their nutritional status and physical development.

Glomerulonephritis and agranulocytosis have been very rarely reported with dosages substantially above those recommended and with treatment for prolonged periods of time.

This medicine contains Sunset Yellow (E110) – may cause allergic reactions.

This medicine contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially ‘sodium-free’.

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

Concomitant treatment with cimetidine may inhibit the metabolism of mebendazole in the liver, resulting in increased plasma concentrations of the drug.

Concomitant use of mebendazole and metronidazole should be avoided (see section 4.4)

#### **4.6 Fertility, Pregnancy and lactation**

##### Pregnancy

Since Mebendazole is contra-indicated in pregnancy, patients who think they are or may be pregnant should not take this preparation.

#### Breast-feeding

Limited data from case reports demonstrate that a small amount of mebendazole is present in human milk following oral administration. Therefore, caution should be exercised when mebendazole is administered to breast-feeding women.

#### Fertility

The effect on human fertility has not been evaluated.

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

Mebendazole does not affect mental alertness or driving ability.

### **4.8 Undesirable effects**

Throughout this section adverse reactions are reported. Adverse reactions are adverse events that were considered to be reasonably associated with the use of Mebendazole based on the comprehensive assessment of the available adverse event information. A causal relationship with Mebendazole cannot be reliably established in individual cases. Further, because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

At the recommended dose, Mebendazole is generally well tolerated. However, patients with high parasitic burdens when treated with Mebendazole have manifested diarrhoea and abdominal pain

The safety of mebendazole was evaluated in 6276 subjects who participated in 39 clinical trials for the treatment of single or mixed parasitic infestations of the gastrointestinal tract. In these 39 clinical trials, no adverse drug reactions

(ADRs) occurred in  $\geq 1\%$  of mebendazole-treated subjects.

ADRs identified from clinical trials and post-marketing experience with mebendazole are included in Table 1. The displayed frequency categories use the following convention:

Very common  $(\geq 1/10)$   
 Common  $(\geq 1/100 \text{ and } < 1/10)$   
 Uncommon  $(\geq 1/1000 \text{ and } < 1/100)$   
 Rare  $(\geq 1/10,000 \text{ and } < 1/1000)$   
 Very rare  $(< 1/10,000)$   
 Not known (cannot be estimated from the available date).

Table 1: Adverse drug Reactions

System Organ Class	Adverse Drug Reactions			
	Frequency Category			
	Common ( $\geq 1/100$ to < 1/10)	Uncommon ( $\geq 1/1,000$ to < 1/100)	Rare ( $\geq 1/10,000$ to < 1/1,000)	Very rare ( $< 1/10,000$ )
<b>Blood and lymphatic system disorders</b>			Neutropenia <sup>b</sup>	Agranulocytosis <sup>a, c</sup>
<b>Immune system disorders</b>			Hypersensitivity including anaphylactic reaction and anaphylactoid reaction <sup>b</sup>	
<b>Nervous system disorders</b>			Convulsions <sup>b</sup> Dizziness <sup>a</sup>	
<b>Gastrointestinal disorders</b>	Abdominal pain <sup>a</sup>	Abdominal discomfort <sup>a, b</sup> , Diarrhoea <sup>a, b</sup> , Flatulence <sup>a</sup>		Nausea <sup>b</sup> ; Vomiting <sup>b</sup>
<b>Hepatobiliary disorders</b>			Hepatitis b; Abnormal liver function tests b	
<b>Skin and subcutaneous tissue disorders</b>			Rash <sup>a</sup> , Toxic epidermal necrolysis <sup>b</sup> ; Stevens-Johnson syndrome <sup>b</sup> ;	

			Exanthema <sup>b</sup> ; Angioedema <sup>b</sup> ; Urticaria <sup>b</sup> ; Alopecia <sup>b</sup>	
<b>Renal and urinary disorders</b>				Glomerulonephritis <sup>a, c</sup>

a ADR frequency data derived from Clinical Trials or Epidemiological Studies

b Adverse reactions reported during post-marketing surveillance.

c Observed in higher and prolonged doses

### **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. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at:

[www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard) or search for MHRA Yellow Card in the Google Play or Apple App Store.

## **4.9 Overdose**

In patients treated at dosages substantially higher than recommended or for prolonged periods of time, the following adverse reactions have been reported rarely: alopecia, reversible liver function disturbances, hepatitis, agranulocytosis, neutropenia and glomerulonephritis. With the exception of agranulocytosis and glomerulonephritis, these also have been reported in patients who were treated with mebendazole at standard dosages (see section 4.8).

### *Symptoms*

In the event of accidental overdosage, abdominal cramps, nausea, vomiting and diarrhoea may occur.

### *Management*

There is no specific antidote. Activated charcoal may be given if considered appropriate.

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: anthelmintic for oral administration, benzimidazole derivatives; ATC code: P02CA01

*In vitro* and *in vivo* work suggests that mebendazole blocks the uptake of glucose by adult and larval forms of helminths, in a selective and irreversible manner. Inhibition of glucose uptake appears to lead to endogenous depletion of glycogen stores within the helminth. Lack of glycogen leads to decreased formation of ATP and ultrastructural changes in the cells.

There is no evidence that mebendazole is effective in the treatment of cysticercosis.

### 5.2 Pharmacokinetic properties

#### *Absorption*

Following oral administration, approximately <10% of the dose reaches the systemic circulation, due to incomplete absorption and to extensive pre-systemic metabolism (first-pass effect). Maximum plasma concentrations are generally seen 2 to 4 hours after administration. Dosing with a high fat meal leads to a modest increase in the bioavailability of mebendazole.

#### *Distribution*

The plasma protein binding of mebendazole is 90 to 95%. The volume of distribution is 1 to 2 L/kg, indicating that mebendazole penetrates areas outside the vascular space. This is supported by data in patients on chronic mebendazole therapy (e.g., 40 mg/kg/day for 3-21 months) that show drug levels in tissue.

#### *Biotransformation*

Orally administered mebendazole is extensively metabolized primarily by the liver. Plasma concentrations of its major metabolites (amino and hydroxylated amino forms of mebendazole) are substantially higher than those of mebendazole. Impaired hepatic function, impaired metabolism, or impaired biliary elimination may lead to higher plasma levels of mebendazole.

#### *Elimination*

Mebendazole, the conjugated forms of mebendazole, and its metabolites likely undergo some degree of enterohepatic recirculation and are excreted in the

urine and bile. The apparent elimination half-life after an oral dose ranges from 3 to 6 hours in most patients.

#### *Steady-state Pharmacokinetics*

During chronic dosing (e.g., 40 mg/kg/day for 3-21 months), plasma concentrations of mebendazole and its major metabolites increase, resulting in approximately 3-fold higher exposure at steady-state compared to single dosing.

### **5.3 Preclinical safety data**

Acute oral toxicity of mebendazole in a number of species is low with a large margin of safety. Chronic oral toxicity studies in rats at 40 mg/kg/day and above, showed altered liver weights with some slight centrilobular swelling and hepatocellular vacuolation, and altered testicular weights with some tubular degeneration, desquamation and marked inhibition of spermatogenic activity.

In genotoxicity studies mebendazole was aneugenic in mammalian somatic cells above a threshold plasma concentration of 115 ng/mL, but had no mutagenic or clastogenic activity. In limited long term studies in mice and rats no carcinogenic effects were seen.

Mebendazole has shown embryotoxic and teratogenic activity in pregnant rats and mice at oral doses of 10 mg/kg/day and above and in rats at a single dose of 10 mg/kg, approximately equivalent to the human dose of 100 mg on a body surface area (mg/m<sup>2</sup>) basis.

## **6 PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Lactose, pregelatinized maize starch, sunset yellow (E110), sodium saccharin, sodium lauryl sulphate, natural orange flavour, sodium starch glycollate,

microcrystalline cellulose and magnesium stearate.

**6.2 Incompatibilities**

Not applicable.

**6.3 Shelf life**

2 years

**6.4 Special precautions for storage**

Do not store above 25°C.

**6.5 Nature and contents of container**

Blister packs

Pack size: 1, 2, 4, 6 and 8 tablets.

## **6.6 Special precautions for disposal**

None stated.

Any unused product or waste material should be disposed of in accordance with local requirements

## **7 MARKETING AUTHORISATION HOLDER**

Ennogen IP Ltd,  
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## **8 MARKETING AUTHORISATION NUMBER(S)**

PL 55612/0071

## **9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

6<sup>th</sup> August 1999

**10 DATE OF REVISION OF THE TEXT**

22/05/2024