

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

Thelmox 500 mg chewable tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each chewable tablet contains 500 mg of mebendazole.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Chewable tablet.

Off-white to pale yellow, round, flat, scored chewable tablets.

The tablet can be divided into equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of *Trichuris trichuria* (whipworm), *Enterobius vermicularis* (pinworm or threadworm), *Ascaris lumbricoides* (roundworm), *Ancylostoma duodenale* (common hookworm), *Necator americanus* (American hookworm) in single or mixed gastrointestinal infestations.

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

4.2 Posology and method of administration

Posology

Adults and children over 2 years:

1) *Enterobius vermicularis* (Threadworm).

One 100 mg tablet in a single dose, repeated if necessary after 2 to 3 weeks. It is recommended that all members of the family be treated simultaneously.

2) *Trichuris trichiura* (Whipworm),

Ascaris lumbricoides (Roundworm),

Ancylostoma duodenale (Hookworm),

Necator americanus (American hookworm).

One 100 mg tablet in the morning and one in the evening for three consecutive days. A single dose of one 500 mg tablet may also be effective.

Elderly:

The dose of Thelmox in elderly patients is the same as for adults.

Thelmox tablets of 100 mg may be chewed or swallowed.

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.

Method of administration

Oral use.

4.3 Contraindications

Thelmox is contraindicated in pregnancy and in patients who have shown hypersensitivity to the product or any components.

4.4 Special warnings and precautions for use

Not recommended in the treatment of children under 2 years.

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.

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 Thelmox is contraindicated in pregnancy, patients who think they are, or may be, pregnant should not take this preparation.

Lactation

As it is not known whether mebendazole is secreted in human milk, it is not advisable to breast feed following administration of Thelmox.

4.7 Effects on ability to drive and use machines

Thelmox has no influence on the ability to drive and use machines.

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 Thelmox based on the comprehensive assessment of the available adverse event information. A causal relationship with Thelmox 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.

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 ($\geq 1/100$ to $< 1/10$); Uncommon ($\geq 1/1000$ to $< 1/100$); Rare ($\geq 1/10,000$ to $< 1/1000$); Very rare ($< 1/10,000$), Not known (cannot be estimated from the available data).

Table 1: Adverse Drug Reactions Reported in Clinical Trials and Post-marketing Experience for Mebendazole

System Organ Class	Adverse Drug Reactions		
	Frequency Category		
	Common ($\geq 1/100$ to $< 1/10$)	Uncommon ($\geq 1/1000$ to $< 1/100$)	Rare ($\geq 1/10,000$ to $< 1/1000$)
Blood and lymphatic system disorders			Neutropenia ^b
Immune system disorders			Hypersensitivity including anaphylactic reaction and anaphylactoid reaction ^b
Nervous system disorders			Convulsions ^b Dizziness ^a
Gastrointestinal disorders	Abdominal pain ^a	Abdominal discomfort ^a ; Diarrhoea ^a ; Flatulence ^a	
Hepatobiliary disorders			Hepatitis ^b ; Abnormal liver function tests ^b
Skin and subcutaneous tissue disorders			Rash ^a Toxic epidermal necrolysis ^b ; Stevens-Johnson syndrome ^b ; Exanthema ^b ; Angioedema ^b ; Urticaria ^b ; Alopecia ^b

^a ADR frequency data derived from Clinical Trials or Epidemiological Studies

^b ADRs not observed in clinical trials and frequency calculated using “Rule of 3”, as detailed in SmPC guideline 2009. 6276 patients exposed in clinical trials and epidemiological studies, divided by 3 (Frequency = $1/2092$). Note: frequencies differ from those reported in the August 2009 CCDS, as these were not calculated using the formula detailed in the SmPC guideline 2009.

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 national reporting system.

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).

Signs and symptoms

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

Treatment

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Anthelmintics; Antinematodal agents
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 ThelmoX is effective in the treatment of cysticercosis.

5.2 Pharmacokinetic properties

Absorption:

Following oral administration, < 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.

Metabolism:

Orally administered mebendazole is extensively metabolised 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

No relevant information additional to that contained elsewhere in the Summary of Product Characteristics.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose
Povidone
Acesulfame potassium
Colloidal silicon dioxide
Magnesium stearate
Talc
Orange Flavour
Sodium starch glycolate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

5 years

6.4 Special precautions for storage

Do not store above 30 °C. Protect from light and moisture.

6.5 Nature and contents of container

Cardboard box containing 1 Aluminium-PVC blister of 1 chewable tablets.
Pack size of 1 chewable tablet.

Polypropylene container with a polyethylene security closure.
Pack size of 100 chewable tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Remedica Ltd
Aharnon Str., Limassol Industrial Estate,
3056 Limassol, Cyprus

8. MARKETING AUTHORITY NUMBER(S)

04735/06692/REN/2018

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 18 August 2014
Date of latest renewal: 07 November 2019

10. DATE OF REVISION OF THE TEXT

06/07/2023