SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

Thelmox 100 mg chewable tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each chewable tablet contains 100 mg mebendazole.

Excipient(s) with known effect:
This product contains 54.35 mg lactose.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Chewable tablet.

Orange, round, chewable, flat, flavored tablets.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of Trichuris trichiuria (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 are effective in the treatment of cysticercosis.

4.2 Posology and method of administration

Posology

Adults and children over 2 years
For the control of trichuriasis, ascariasis and hookworm infections, one tablet twice a day for three consecutive days.

For the control of enterobiasis a single tablet is administered. It is highly recommended that a second tablet is taken after two weeks, if re-infection is suspected.

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 for use in children under 2 years old.

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 contra-indicated 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 ≥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 (≥1/10); Common (≥1/100 to <1/10); Uncommon (≥1/1000 to <1/100); Rare (≥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 (≥ 1/100 to < 1/10)	**Uncommon** (≥ 1/1000 to < 1/100)	**Rare** (≥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

Mannitol
Sodium cyclamate
Lactose
Maize starch
Povidone
Microcrystalline cellulose
Colloidal silicon dioxide
Magnesium stearate
Sodium starch glycolate
Talc
Sunset yellow E110
Lemon flavour
Apricot flavour

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

5 years.

6.4 Special precautions for storage

Store below 25 °C. Protect from light and moisture.

6.5 Nature and contents of container

PVC/Aluminium blisters. Pack size of 240 chewable tablets.

6.6 Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

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

8. MARKETING AUTHORISATION NUMBER(S)

04638/06908/REN/2018

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Date of first authorization: 07 September 2004
Date of latest renewal: 24 September 2019

10. DATE OF REVISION OF THE TEXT

06/07/2023