Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Vermox 100mg/5ml Oral Suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5ml of suspension contains 100mg of mebendazole.

Also contains sucrose, methylparabenzoate (E218) and propylparabenzoate (E216).

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Oral suspension.

Product imported from Greece:
A banana flavoured opaque white oral suspension.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

As an anthelmintic against gastrointestinal infestations caused by nematodes and cestodes, including enterobiasis, ascariasis, trichuriasis, ankylostomiasis, strongyloidiasis and taeniasis.

4.2 Posology and method of administration

Method of administration:
Oral Use.

Adults and children 2 years or older

Ascariasis, trichuriasis, ankylostomiasis and mixed infections:	100 mg twice daily for 3 consecutive days.
Enterobiasis:	100 mg as a single dose repeated after 2 to 4 weeks.
Taeniasis and strongyloidiasis:	
Adults:	200 mg twice daily for 3 consecutive days.
Children 2 years or older:	100 mg twice daily for 3 consecutive days.

4.3 Contraindications

- Use in pregnancy or lactation in women breast feeding infants. It is not known if mebendazole crosses the placenta or is excreted in breast milk.
- In persons with a known hypersensitivity to the drug or its components.

4.4 Special warnings and precautions for use

Not recommended in the treatment of children under 2 years.

Results from a case-control study investigating an outbreak of Stevens-Johnson syndrome /toxic epidermal necrolysis (SJS/TEN) suggested a possible relationship between SJS/TEN and the concomitant use of mebendazole and metronidazole. Further data suggesting such a drug-drug interaction are not available. Therefore, concomitant use of mebendazole and metronidazole should be avoided.

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take this medicine.

Methyl (E218) and propyl (E216) parahydroxybenzoate may cause allergic reactions which could possibly be delayed.

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, especially during prolonged treatment. In the latter case, determination of plasma concentrations is recommended in order to allow dose adjustments.
Concomitant use of mebendazole and metronidazole should be avoided (see section 4.4).

4.6 Fertility, pregnancy and lactation

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

Lactation: Mebendazole is only absorbed to a small extent. As it is not known whether mebendazole is excreted in human milk, it is not advisable to breast feed following administration of Vermox.

4.7 Effects on ability to drive and use machines

None known.

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, Vermox is generally well tolerated. However, patients with high parasitic burdens when treated with Vermox have manifested diarrhoea and abdominal pain.

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 and < 1/10); Uncommon (≥ 1/1000 and < 1/100); Rare (≥ 1/10,000 and < 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 and < 1/1000)

Blood and lymphatic system disorders			Neutropoenia [b]
Immune system disorders			Hypersensitivity including anaphylactic reaction and anaphylactoid reaction [b]
Nervous system disorders			Convulsions [b], Dizziness [a]
Gastro-intestinal disorders	Abdominal pain [a]	Abdominal discomfort [a]; Diarrhoea [a]; Flatulence [a]	
Hepato-biliary disorders			Hepatitis [b]; Abnormal liver function tests [b]
Skin and sub-cutaneous tissue disorders			Rash [a] , Toxic epidermal necrolysis [b]; Stevens-Johnson syndrome [b]; Exanthema [b]; Angioedema [b]; Urticaria [b]; Alopoecia [b]

[a] ADR frequency data derived from Clinical Trials or Epidemiological Studies

[b] ADRs not observed in Clinical Trials and frequency calculated using “Rule 3”, as detailed in SmPC guideline 2009. 6279 patients exposed in clinical trials and epidemiological studies, divided by 3 (frequency = 1/2092). Note: frequencies differ from those reported in august 20019 CCDS, as these were not calculated using the formula detailed in SmPC guideline 2009.

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.

Treatment
There is no specific antidote. Within the first hour after ingestion, gastric lavage may be performed. Activated charcoal may be given, if considered appropriate.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic classification: Anthelmintic for oral administration, benzimidazole derivatives
ATC code: P02CA01

Vermox is a broad spectrum anthelmintic. Vermox interferes with the cellular tubulin formation in the worm thus disturbing the glucose uptake and the normal digestive functions of the worm to such an extent that an autolytic process occurs.

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

5.2 Pharmacokinetic properties

Absorption
Following oral administration, approximately 20% 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 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

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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose
Microcrystalline cellulose
Carmellose sodium
Methylparabenzoate (E218)
Propylparabenzoate (E216)
Sodium laurilsulfate
Banana flavour
Citric acid monohydrate
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The shelf life, expiry date of this product is the date shown on the bottle and outer package of the product as marketed in the country of origin.

6.4 Special precautions for storage

Store below 25°C.
Keep bottle in the outer carton to protect from light.

6.5 Nature and contents of container

Amber glass bottle with child resistant polypropylene screw cap lined inside with a LDPE insert. A 5ml polypropylene dosing spoon graduated for 2.5ml and 5ml is provided.

Pack size of 30ml.

6.6 Special precautions for disposal and other handling

No special requirements.

7 PARALLEL PRODUCT AUTHORISATION HOLDER

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8 PARALLEL PRODUCT AUTHORISATION NUMBER

PPA1328/180/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 1st February 2013

10 DATE OF REVISION OF THE TEXT