Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Vermox 100 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 100mg mebendazole.

Excipients: Each tablet also contains sunset yellow (E110)

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet.

Products imported from the UK and Greece:
Faintly-orange, circular, flat, bevel-edged tablet with 'ME/100' and a breakline on one side and 'JANSSEN' on the other.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

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

4.2 Posology and method of administration

Method of administration:
Oral Use.

Adults and children 2 years or older:
Ascariasis, Trichuriasis, Ancylostomiasis and mixed infestations: 100mg twice daily for three consecutive days.

Enterobiasis: 100 mg as a single dose repeated after 2 and 4 weeks.

Taeniasis and Strongyloidiasis:

Adults:
200mg twice daily for three consecutive days.
Children 2 years or older:
100mg twice daily for three consecutive days.

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.

4.3 Contraindications

- Use in pregnancy or lacatation in women breast feeding infants.
  It is not known if mebendazole crosses the placenta or is excreted in human 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.

Sunset yellow (E110) may cause allergic reactions.

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 are 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.

The safety of mebendazole has been 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, <1/10) Uncommon (≥1/1000, <1/100) Rare (≥1/10000, <1/1000) Very rare (<1/10000); 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 b
Gastrointestinal disorders	Abdominal pain a	Abdominal discomfort a; Diarrhoea a; Flatulence a	
Hepato-biliary 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; 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 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*

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. Inhibitors 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 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

Microcrystalline cellulose,
Sodium starch glycolate
Talc
Maize starch
Sodium saccharin

Magnesium stearate
Hydrogenated vegetable oil
Colloidal anhydrous silica
Sodium laurilsulfate
Orange flavour
Sunset yellow (E110).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The shelf life expiry date of this product shall be the date shown on the container and outer package of the product on the market in the country of origin.

6.4 Special precautions for storage

Do not store above 25°C
Store in the original package

6.5 Nature and contents of container

Blister packs of 6 tablets.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirments

7 PARALLEL PRODUCT AUTHORISATION HOLDER

PCO Manufacturing
Unit 10, Ashbourne Business Park
Rath
Ashbourne
Co. Meath

8 PARALLEL PRODUCT AUTHORISATION NUMBER

PPA 0465/076/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 13 July 2006

10 DATE OF REVISION OF THE TEXT

December 2013