Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Vermox 100 mg tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 100 mg mebendazole.

Excipients: Each tablet also contains 0.06 mg Sunset Yellow (E110) and 3.8 mg sodium.

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Tablet.
Faintly orange circular, flat, half-scored, bevel-edged tablet with 'ME 100' inscribed on one side and 'Janssen' on the other. The half-score is only to facilitate breaking for ease of swallowing and not to divide into equal halves.

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. Official guidelines should be taken into consideration. Official guidelines will normally include WHO and public health authorities' guidelines.

4.2 Posology and method of administration

Paediatric population
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.

Vermox Oral Suspension should be considered for patients such as young children who are unable to swallow the tablet.

Children under 2 years of age:
Vermox Tablets has not been extensively studies in children below the age of 2 years. Currently available data are described in section 4.4, 4.8 and 5.2, but no recommendations on a posology can be made. Because of the lack of sufficient safety data, Vermox Tablets should not be used in children below the age of 1 year (see section 4.4, 4.8 and 5.2).

<u>For the indication Strongyloidiasis and Taeniasis:</u>

<u>Paediatric population / Children and adolescents (≥2 to 16 years)</u>
Data on efficacy and safety in children and adolescents ≥2 years to 16 years are limited.
Mebendazole should be used only, if there is no therapeutic alternative.

<u>Method of administration:</u>
Oral Use.

<u>Adults and children 2 years or older</u>:

Ascariasis, trichuriasis, ankylostomiasis and mixed infections:	100 mg twice daily for three consecutive days.
Enterobiasis:	100 mg as a single dose repeated after 2 to 4 weeks.

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

Vermox oral suspension should be considered for patients such as young children who are unable to swallow the tablet.

4.3 Contraindications

- Vermox is contraindicated in pregnancy.
- In persons with a known hypersensitivity to the active substance or any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Not recommended in the treatment of children under 2 years.

Convulsions in children, including in infants below one year of age, have been reported very rarely during postmarketing experience with Vermox (see section 4.8). Vermox Tablets are indicated for use in children aged 2 years onwards (see section 4.2). Vermox Tablets has not been extensively studied in children below the age of 2 years. Vermox Tablets should only be given to very young children if their worm infestation interferes significantly with their nutritional status and physical development. Therefore, Vermox Tablets should be used in children aged 1-2 years only if the potential benefit justifies the potential risk. Because of the lack of sufficient safety data, Vermox Tablets should not be used in children below the age of 1 year.

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.

Vermox oral suspension should be considered for patients such as young children who are unable to swallow the tablet.

There have been rare reports of reversible liver function disturbances, hepatitis, and neutropenia described in patients who were treated with mebendazole at standard dosages for indicated conditions (see Section 4.8). These events, along with glomerulonephritis and agranulocytosis, have also been reported with dosages substantially above those recommended and with treatment for prolonged periods of time.

As higher doses and longer treatment is recommended in patients with Trichinellosis and Echinococcosis, careful consideration should be given when treating patients with severe chronic hepatic diseases and/or bone marrow depression. These patients should be closely monitored with hematological, liver and renal function tests.

Consider discontinuing Vermox Tablets if clinically significant laboratory abnormalities are found. Official guidelines should be taken into consideration.

Sunset yellow (E110) may cause allergic reactions.

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, especially during prolonged treatment. Concomitant use of mebendazole and metronidazole should be avoided (see section 4.4).

4.6 Fertility, pregnancy and lactation

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

Lactation: Limited data from case reports demonstrate that a small amount of mebendazole is present in human milk following oral administration. Therefore, this product should only be used during breastfeeding under medical supervision and when the potential benefit of treatment to the mother outweighs the possible risks to the nursing infant. Caution should be exercised when Vermox 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

Vermox may cause dizziness (see section 4.8). It might have a negligible influence on the ability to drive and operate 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 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 mebendazoleare 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)	**Very Rare** (<1/10,000)
Blood and lymphatic system disorders			Neutropoenia [b]	Agranulocytosis [a, c]
Immune system disorders			Hypersensitivity including anaphylactic reaction and anaphylactoid reaction [b]	
Nervous system disorders			Convulsions [b], Dizziness [b]	
Gastro-intestinal disorders	Abdominal pain [a]	Abdominal discomfort [a], Diarrhoea [a], Flatulence [a], Nausea[a],		

		Vomiting[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, Urticaria [b], Alopoecia [b]	
Renal and urinary disorders				Glomerulonephritis [a, c]

[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 HPRA Pharmacovigilance, website: www.hpra.ie.

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).

Sign 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 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. 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 Vermox is effective in the treatment of cysticercosis.

5.2 Pharmacokinetic properties

Paediatric population:
Limited data of the mebendazole concentrations in plasma are available in children and adolescents 1 to 16 years of age. These data do not indicate substantially higher systemic exposure to mebendazole in subjects 3 to 16 years of age compared to adults.
In subjects 1 to <3 years of age, systemic exposure is higher than in adults due to higher mg/kg dose relative to adults.

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 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 glycollate Type A
Talc
Maize starch
Saccharin sodium

Magnesium stearate
Hydrogenated vegetable oil
Orange flavour
Colloidal anhydrous silica
Sodium lauryl sulfate
Sunset Yellow (E110)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25°C.

Keep blister in the outer carton in order to protect from light.

6.5 Nature and contents of container

Blister strips of PVC genotherm glass clear aluminium foil coated on the inside with a heat seal lacquer.

Pack size: 6 tablet pack.

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 requirements.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER

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