Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Vermox 100mg/5ml Oral Suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml of suspension contains 100 mg of mebendazole.

Excipient(s) with known effect:
Each 5ml also contains 500 mg of sucrose, 9 mg of methyl parahydroxybenzoate (E218), 1 mg of propyl parahydroxybenzoate and 0.819 mg of propylene glycol (E1520).

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Oral suspension
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. 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

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 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 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:	5ml (100 mg) twice daily for 3 consecutive days.
Enterobiasis:	5ml (100 mg) as a single dose repeated after 2 to 4 weeks.
Taeniasis and strongyloidiasis: *Adults:*	2x 5ml (200 mg) twice daily for 3 consecutive days.

Children 2 years or older:	5ml (100 mg) twice daily for 3 consecutive days.

4.3 Contraindications

- Vermox is contraindicated in pregnancy.
- Hypersensitivity to the active ingredient or to 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 Oral Suspension is indicated for use in children aged 2 years onwards (see section 4.2). Vermox Oral Suspension has not been extensively studied in children below the age of 2 years. Vermox Oral Suspension should only be given to very young children if their worm infestation interferes significantly with their nutritional status and physical development. Therefore, Vermox Oral Suspension 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 Oral Suspension 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.

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 Oral Suspension if clinically significant laboratory abnormalities are found. Official guidelines should be taken into consideration.

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

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

This medicine contains less than 1 mmol sodium (23 mg) per 5ml, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interactions

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 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 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 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 [a]	
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				Glomerulonephritis [a, c]

disorders				

[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*).

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 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

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 Pharmacokinetic
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 and sodium carboxymethyl cellulose
Methylcellulose 15 mPa.s.
Methyl parahydroxybenzoate (E218)
Propyl parahydroxybenzoate
Sodium laurilsulfate
Banana flavour (containing propylene glycol (E1520))
Citric acid, monohydrate
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25°C.

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

6.5 Nature and contents of container

Amber glass (Type III) flask with:

1. Pilfer proof screw cap. Cork insert in cap is coated on both sides with polyvinylchloride.

or

2. Child resistant polypropylene screw cap lined inside with a LDPE insert.

A 5ml polypropylene dosing cup graduated for 2.5ml and 5ml is provided.

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

Shake well before use.

No special requirements for disposal.

Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Johnson & Johnson (Ireland) Limited
Airton Road
Tallaght
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0330/046/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 1st April 2008

10 DATE OF REVISION OF THE TEXT

March 2021