SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

VERMOX 100 mg tablets
VERMOX 20 mg/mL oral suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

- One tablet contains:
  Active substance: mebendazole 100 mg
  Excipients with known effects: This medicine contains sunset yellow and sodium

- 1 mL of oral suspension contains:
  Active substance: mebendazole 20 mg
  Excipients with known effects: sucrose, methylparaben, propylparaben

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

100 mg tablets
20 mg/mL oral suspension

4. CLINICAL PARTICULARS

VERMOX (mebendazole) is a synthetic benzimidazole derivative with potent anthelmintic activity against nematodes and cestodes.
VERMOX is particularly active in humans against:

- Enterobius vermicularis (pinworm)
- Ascaris lumbricoides (large roundworm)
- Trichuris trichiura (whipworm)
- Ancylostoma duodenale (hookworm)
- Necator Americanus (hookworm)
- Strongyloides stercolaris (threadworm)
- Taenia spp. (tapeworm)

The correct dose for each indication allows complete elimination of the worms in over 90% of patients, even in the presence of heavy or mixed infestations.

4.1 Therapeutic indications

This medicinal product is for infestations by pinworms, large roundworms, whipworms, hookworms, threadworms, tapeworms.

4.2 Posology and method of administration

1. Enterobiasis: single dose of 100 mg (one tablet or one 5 mL measuring cup of suspension).
   Enterobius, the cause of enterobiasis, has a very short life cycle. Therefore the risks of reinfection are extremely high, especially in large social groups. For this reason, it is advisable to repeat the treatment after 2 and 4 weeks.

2. Ascariasis, trichuriasis, hookworm and mixed infestations: one 100 mg dose (one tablet or one 5 mL measuring cup of suspension) twice a day (in the morning and the evening), for three consecutive days, regardless of the patient's age and weight.

3. Taeniasis and strongyloidiasis:
   Adults: although favorable results have been obtained with lower dosages, a dose of 200 mg (two tablets or two 5 mL measuring cups of suspension) twice a day (in the morning and the evening), for three consecutive days is recommended.
   Children: one 100 mg dose (one tablet or one 5 mL measuring cup of suspension) twice a day (in the morning and the evening), for three consecutive days.

Paediatric population / Children and adolescents (≥2 to 16 years)
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.

Children under 2 years of age:
VERMOX has not been extensively studied 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).

The tablets can be swallowed with a small amount of water or chewed during a meal. The treatment does not require a particular diet, nor the use of laxatives. Shake the suspension before use.

Paediatric population
VERMOX 20 mg/mL oral suspension should be considered for patients such as young children who have difficulty swallowing tablets.
If needed, the tablet must be crushed before it is given to a young child. A child must always be supervised while they are taking VERMOX.

4.3 Contraindications
Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use
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 has not been extensively studied in children below the age of 2 years. Therefore, VERMOX should be used in children aged 1-2 years of age only if the potential benefit justifies the potential risk
Because of the lack of sufficient safety data, VERMOX should not be used in children below the age of 1 year.

Glomerulonephritis and agranulocytosis have been reported very rarely with dosages substantially higher than those recommended and for prolonged treatment periods.

Results from a case-control study investigating an acute case 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 on this type of interaction are not available. Therefore, concomitant use of mebendazole and metronidazole must be avoided.

Important information about some excipientsVERMOX 20 mg/mL oral suspension contains methylparaben and propylparaben. These may cause allergic reactions (possibly delayed).

VERMOX 20 mg/mL oral suspension contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase deficiency must not take this medicine.

VERMOX 20 mg/mL oral suspension contains sodium. This medicine contains less than 1 mmol sodium (23 mg) per mL, that is to say essentially 'sodium-free'.

VERMOX 100 mg tablets contains Sunset Yellow. Sunset Yellow is a an azo dye that may cause allergic reactions.
VERMOX 100 mg tablets contains sodium. This medicine contains 3.8 mg sodium per tablet, equivalent to 0.19% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

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 must be avoided (see section 4.4).

4.6 Fertility, pregnancy and lactation
Mebendazole has shown embryotoxic and teratogenic activity in rats and mice. No harmful effects on reproduction have been observed in other animal species tested.

The possible risks associated with prescribing VERMOX in pregnancy, particularly during the first trimester, must be weighed against the expected therapeutic benefits.

Breastfeeding
Limited data from case reports show that a small amount of mebendazole is present in breast milk after oral administration. Therefore, caution should be exercised when VERMOX is administered to breastfeeding women.

4.7 Effects on ability to drive and use machines
No studies have been conducted on the ability to drive and use machines.

4.8 Undesirable effects
In this section, adverse reactions are presented. Adverse reactions are adverse events that were considered to be reasonably associated with the use of VERMOX based on the comprehensive assessment of the available adverse event information. A causal relationship with VERMOX 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 cannot reflect the rates observed in clinical practice.
The safety of VERMOX was 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 reactions (adverse drug reactions, ADRs) were reported in $\geq$1% of VERMOX-treated

subjects. The adverse reactions (ADRs) reported in clinical trials and during postmarketing experience with VERMOX are shown in Table 1. Frequencies are stated according to the following convention:

Very common (≥1/10)
Common (≥1/100, <1/10)
Uncommon (≥1/1 000, <1/100)
Rare (≥1/10 000, <1/1 000)
Very rare (<1/10 000),
Not known (the frequency cannot be defined on the basis of the available data).

Table 1: Adverse drug reactions identified during post marketing experience with VERMOX, reported by frequency category estimated from clinical studies.

Classification by systems and organs	**Adverse drug reactions**				
	Frequency				
	Very common (≥1/10)	**Common** (≥1/100, <1/10)	**Uncommon** (≥1/1 000, <1/100)	**Rare** (≥1/10 000, <1/1 000)	**Very rare** (<1/10 000),
Blood and lymphatic system disorders				Neutropenia	Agranulocitosys*
Immune system disorders				Hypersensitivity reactions such as anaphylactic and anaphylactoid reactions	
Nervous system disorders				Convulsions, Vertigo	
Gastrointestinal disorders		Abdominal pain	Abdominal disorders, diarrhea, flatulence, Nausea, vomiting		
Hepatobiliary disorders				Hepatitis, abnormal liver function tests	
Skin and subcutaneous tissue disorders				Rash, toxic epidermal necrolysis, Stevens-Johnson syndrome, exanthema, angioedema, urticaria, alopecia	

Renal and urinary disorders					Glomerulonephritis*

* Observe at higher and longer doses

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization 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 at the address http://www.agenziafarmaco.gov.it/content/come-segnalare-una-sospetta-reazione-avversa.

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 adverse reactions have also been reported in patients who were treated at standard dosages (see section 4.8).

Symptoms
In the event of accidental overdose, abdominal cramps, nausea, vomiting and diarrhea may occur.

Treatment
There is no specific antidote. Activated charcoal may be given if appropriate.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Anthelmintics for oral administration, benzimidazole derivatives.

ATC code: P02CA01

In therapeutic indications (see section 4.1), mebendazole acts locally in the lumen of the stomach by interfering with cellular tubulin formation in the intestines of parasites. Mebendazole binds specifically to tubulin and causes ultrastructural degenerative changes in the intestine. As a result of this process, glucose absorption by the parasites is blocked, and their digestive functions are disrupted, leading to an autolytic process.

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

5.2 Pharmacokinetic properties
Following oral administration of 0.1 mg/kg body weight of radiolabeled mebendazole, minimal absorption by the gastrointestinal tract was observed. At normal therapeutic dosages bioavailability is low, because the drug is subject to an extensive first pass metabolism and because of its low solubility. About 90% of the absorbed portion is bound to plasma proteins.
It is eliminated in the stools within 24-48 hours.
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.

5.3 Preclinical safety data

- **Acute administration:**
  LD50 (albino rat, oral route): 1500 mg/kg; lung
  LD50 (albino mouse, oral route): 1500 mg/kg

- **Prolonged administration:**
  Albino rat oral route (28 days): maximum dose not causing alterations: 200 mg/kg/day
  Albino rat oral route (180 days): maximum dose not causing alterations: 40 mg/kg/day
  Dog oral route (180 days): maximum dose not causing alterations: 40 mg/kg/day
  No suspected carcinogenic histological manifestations.

- **Fetal toxicity:**
  Albino female rat, oral route: increase in resorptions (30 mg/kg/day)
  Female rabbit, oral route: maximum dose not causing alterations: 30 mg/kg/day.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

One tablet contains:
Excipients: corn starch, sodium saccharin, **sodium** lauryl sulfate, **Sunset Yellow**, orange flavor, microcrystalline cellulose, colloidal silica, magnesium stearate, **sodium** starch glycolate, talc, hydrogenated cottonseed oil.

1 mL of oral suspension contains:
Excipients: microcrystalline cellulose and sodium carmellose, sodium lauryl sulfate, **methylparaben, propylparaben**, citric acid monohydrate, methylcellulose, banana flavor, **sucrose**, purified water.

6.2 Incompatibilities

VERMOX 100 mg tablets: not applicable.
VERMOX 20 mg/mL oral suspension: in the absence of compatibility studies, this medicinal product should not be mixed with other products.

6.3 Shelf life

100 mg tablets: 3 years
20 mg/mL oral suspension: 3 years

6.4 Special precautions for storage

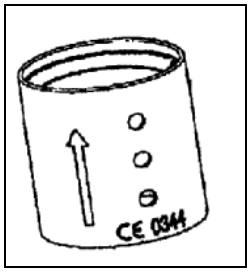
Tablets: this medicinal product does not require any special storage conditions.
Suspension: do not store above 25°C.

6.5 Nature and contents of container

Six 100 mg tablets in opaque blisters
One 30 mL bottle of oral suspension

6.6 Special precautions for disposal
Shake the solution before use.

Using the measuring cup: POUR THE SUSPENSION INTO THE HOLLOW INDICATED BY THE ARROW ON THE MEASURING CUP (as shown in the drawing)



The holes on the measuring cup allow leakage of the suspension if it is poured from the side opposite to that indicated by the arrow by mistake

7. MARKETING AUTHORIZATION HOLDER
Janssen-Cilag SpA
Viale Fulvio Testi, 280/6
20126 Milano MI

8. MARKETING AUTHORIZATION NUMBER(S)
100 mg tablets 6 tablets: MA n. 023821010
20 mg/mL oral suspension 30 mL bottle: MA n. 023821022

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION
Date of first authorisation: June 2000
Date of latest renewal: June 2005

10. DATE OF REVISION OF THE TEXT
November 2023