Professional information for VERMOX® SD suspension

SCHEDULING STATUS

S1

1. NAME OF THE MEDICINE

VERMOX® SD suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each bottle (10 mL suspension) contains 500 mg mebendazole.

Excipients with known effect:

Preservatives:

Methylparaben 0,18 % *m/v*

Propylparaben 0,02 % *m/v*

Contains alcohol: Ethyl alcohol: 0,48 % *v/v*

Contains sugar (150 mg sucrose per mL).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension.

White to off-white suspension with a chocolate flavour.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

VERMOX® SD suspension is indicated for the treatment of single and mixed helminth gastrointestinal infestations caused by:

- **Nematodes such as:**
- *Trichuris trichiura* (whipworm)
- *Ancylostoma duodenale* (hookworm)
- *Necator americanus* (hookworm)
- *Ascaris lumbricoides* (large roundworm)
- *Enterobius vermicularis* (pinworm)

4.2 Posology and method of administration

Whipworm; hookworm; large roundworm; pinworm:

Adults and children older than 1 year: 10 mL given as a single dose.

A single dose of VERMOX® SD suspension may not be sufficient to cure infestations with hookworm and whipworm (*Trichuris*) although a substantial reduction in egg count can be expected.

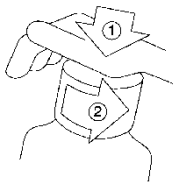
A second course of treatment should be given to those patients who are still infected three to four weeks after the first course.

In worm-eradication campaigns the standard course should be administered every quarter during the first year.

The efficacy of VERMOX® SD suspension is dependent upon the duration of physical contact between the medicine and parasite.

For infants under 1 year of age, see “section 4.3 and 4.4".

Instructions for use of VERMOX® SD suspension:



Shake the bottle before use.

The bottle comes with a child-proof cap, and should be opened as follows:

1. Push the plastic screw cap down
2. While pressing down, turn the cap counterclockwise.

4.3 Contraindications

VERMOX® SD suspension should not be used in children below the age of 1 year.

VERMOX® SD suspension is contraindicated in persons with a known hypersensitivity to mebendazole or to any of the other ingredients in VERMOX® SD suspension (see section 6.1).

VERMOX® SD suspension should not be given during pregnancy, as it is teratogenic in animals (see section 4.6).

Concomitant use of mebendazole and metronidazole should be avoided (see section 4.4 and 4.5).

4.4 Special warnings and precautions for use

Convulsions in children, including in infants below one year of age, have been reported during post-marketing experience with VERMOX® SD suspension (see section 4.8). VERMOX® SD suspension should not be given to children below 1 year of age. VERMOX® SD suspension should only be given to very young children if their worm infections interfere significantly with the nutritional status and the physical development.

There have been reports of reversible liver function disturbances, hepatitis, neutropenia, agranulocytosis and glomerulonephritis described in patients who were treated with dosages substantially
above those recommended for prolonged periods of time (see section 4.9).

Results from a case control study investigating an outbreak of Stevens Johnson syndrome/toxic epidermal necrolysis (SJS/TEN) indicated a possible relationship between SJS/TEN and the concomitant use of VERMOX® SD suspension and metronidazole. Further data on interactions are not available. Therefore, concomitant use of VERMOX® SD suspension and metronidazole should be avoided (see section 4.3 and 4.5).
Patients with high parasitic burdens when treated with VERMOX® SD suspension have manifested diarrhea and abdominal pain.

Sucrose
VERMOX® SD suspension contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take VERMOX® SD suspension.

4.5 Interaction with other medicines and other forms of interaction

Concomitant treatment with cimetidine may inhibit the metabolism of the mebendazole in the liver, resulting in increased plasma concentrations of VERMOX® SD suspension especially during prolonged treatment.
Concomitant use of VERMOX® SD suspension and metronidazole should be avoided (see section 4.3 and 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy

VERMOX® SD suspension is contraindicated during pregnancy (see section 4.3). Mebendazole has shown embryotoxic and teratogenic activity in rats and in mice at single oral doses.

Lactation

Limited date from case reports demonstrate that a small amount of mebendazole is present in human milk following oral administration. VERMOX® SD suspension is therefore not recommended during lactation.

Fertility

The effect on human fertility has not been evaluated.

4.7 Effects on ability to drive and use machines

VERMOX® SD suspension can cause side effects such as dizziness. Caution is advised before driving a vehicle or operating machinery until the effects of VERMOX® SD suspension are known.

4.8 Undesirable effects

Results from a case control study investigating an outbreak of Stevens Johnson syndrome/toxic epidermal necrolysis (SJS/TEN) indicated a possible relationship between SJS/TEN and the concomitant use of VERMOX® SD suspension and metronidazole. Further data on interactions are not available.

Therefore, concomitant use of VERMOX® and metronidazole should be avoided.

Patients with high parasitic burdens when treated with VERMOX® SD suspension have manifested diarrhea and abdominal pain.

Clinical trial data

The safety of VERMOX® SD suspension was 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 VERMOX® SD suspension-treated subjects. ADRs occurring in ≤ 1 % of VERMOX®-treated subjects are shown below.

Blood and the lymphatic system disorders

Less frequent: agranulocytosis (higher and prolonged doses)

Nervous system disorders

Less frequent: dizziness

Gastrointestinal disorders

Frequent: abdominal pain

Less frequent: abdominal discomfort, diarrhoea, flatulence

Skin and subcutaneous tissue disorders

Less frequent: rash

Post-marketing

Blood and the lymphatic system disorders

Less frequent: neutropenia, agranulocytosis (higher and prolonged doses)

Immune system disorders

Less frequent: hypersensitivity including anaphylactic reaction and anaphylactoid reaction

Nervous system disorders

Less frequent: convulsions

Gastrointestinal disorders

Less frequent: nausea, vomiting

Hepato-biliary disorders

Less frequent: hepatitis, abnormal liver function tests

Skin and subcutaneous tissue disorders

Less frequent: toxic epidermal necrolysis, Stevens Johnson syndrome, exanthema, angioedema, urticaria, alopecia

Renal and urinary disorders

Less frequent: glomerulonephritis (higher and prolonged doses)

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of VERMOX® SD suspension is important. It allows continued monitoring of the benefit/risk balance of VERMOX® SD suspension. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications:
https://www.sahpra.org.za/Publications/Index/8.

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: 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.

Symptoms

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

Treatment

There is no specific antidote. If poisoning or excessive overdosage is suspected it is recommended, on general principles, that vomiting be induced and such symptomatic supportive therapy be administered as appears indicated. Activated charcoal may be given.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A.12 Anthelmintics, bilharzia medicines, filaricides, etc.

Pharmacotherapeutic group: Anthelmintic for oral administration, benzimidazole derivatives.

ATC code: P02 CA01.

Mebendazole is a broad-spectrum anthelmintic.

Mebendazole acts locally in the lumen of the gut by interfering with cellular tubulin formation in the intestines of worms. Mebendazole binds specifically to tubulin and causes ultrastructural degenerative changes in the intestine. As a result, the glucose uptake and the digestive functions of the worm are disrupted to such as extent that an autolytic process occurs.

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 increases 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 medicine levels in tissue.

Biotransformation

Orally administered mebendazole is extensively metabolised primarily by the liver. Plasma concentrations of its major metabolites (hydrolysed and reduced forms of mebendazole) are 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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Chocolate flavour

Citric acid (E330)

Ethanol 96 %

Methylcellulose (E461)

Methylparaben (E218)

Microcrystalline cellulose (E460(i)),

Polysorbate 20 (E432)

Propylparaben (E216)

Purified water

Sodium carmellose

Tetrarome orange flavour

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

Store at or below 25 ˚C.

6.4 Special precautions for storage

KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container

15 mL amber glass bottles containing 10 mL VERMOX® SD suspension.

6.6 Special precautions for disposal and other handling

None.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Johnson & Johnson (Pty) Ltd.

241 Main Road

Retreat

7945

South Africa

8. REGISTRATION NUMBER

34/12/0058

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

12/02/2001

10. DATE OF REVISION OF THE TEXT

To be allocated by SAHPRA.

EXPORT REGISTRATION DETAILS:

Namibia: 04/12/0264 NS1

Tanzania: TAN06, 178PO2XJAN