

FINAL PACKAGE INSERT

VERMOX® SD Suspension

SCHEDULING STATUS

Schedule 1

PROPRIETARY NAME (and dosage form)

VERMOX® SD suspension

COMPOSITION

Each bottle (10 ml suspension) contains 500 mg of the active substance, mebendazole polymorph

C. Preservatives: methylparaben 0,18 % m/v and propylparaben 0,02 % m/v

Ethyl alcohol content: 0,48 % v/v

PHARMACOLOGICAL CLASSIFICATION

A.12 Anthelmintics, Bilharzia medicines, Filaricides, etc.

PHARMACOLOGICAL ACTION

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 an extent that an autolytic process occurs.

INDICATIONS

VERMOX® 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)

CONTRA-INDICATIONS

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

VERMOX® is contraindicated in persons with a known hypersensitivity to the medicine or its components.

VERMOX® should not be given during pregnancy, as it is teratogenic in animals (SEE PREGNANCY AND LACTATION)

Concomitant use of mebendazole and metronidazole should be avoided.

WARNINGS

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

See “Known Symptoms of Overdosage and Particulars of Its Treatment”.

INTERACTIONS

Concomitant treatment with cimetidine may inhibit the metabolism of the mebendazole in the liver, resulting in increased plasma concentrations of VERMOX® especially during prolonged treatment.

Concomitant use of VERMOX® and metronidazole should be avoided.

PREGNANCY AND LACTATION

VERMOX® is contra-indicated during pregnancy and lactation. (See Contra-Indications).

Mebendazole has shown embryotoxic and teratogenic activity in rats and in mice at single oral doses. It is not known whether mebendazole is excreted in human breast milk.

DOSAGE AND DIRECTIONS FOR USE

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 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.

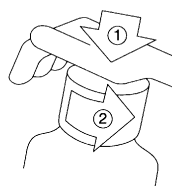
In worm-eradication campaigns the standard course should be administered every quarter during the first year.

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

For infants under 1 year of age, see “Contra-indications and “Special Precautions”.

Instructions for use of VERMOX®:

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



SIDE-EFFECTS AND SPECIAL PRECAUTIONS

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

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® 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® have manifested diarrhea and abdominal pain.

Clinical Trial Data

The safety of VERMOX® 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 $\geq 1\%$ of VERMOX®-treated subjects. ADRs occurring in $\leq 1\%$ of VERMOX®-treated subjects are shown in Table 1.

Table 1. Adverse Drug Reactions Reported by $< 1\%$ of VERMOX®-Treated Subjects in 39 Clinical Trials

System/Organ Class

Adverse Reaction

Gastrointestinal Disorders

Abdominal Discomfort

Diarrhoea

Flatulence

Skin and Subcutaneous Tissue Disorders

Rash

Postmarketing Experience

Adverse drug reactions first identified during post-marketing experience with VERMOX® (mebendazole) are included below.

System/Organ Class

Adverse Reaction

Blood and lymphatic system disorders

Neutropenia

Immune System Disorders

Hypersensitivity including anaphylactic reaction and anaphylactoid reaction

Nervous System Disorders

Convulsions

Gastrointestinal Disorders

Abdominal pain

Hepatobiliary Disorders

Hepatitis, Abnormal liver function tests

Skin and subcutaneous Tissue Disorders

Toxic epidermal necrolysis, Stevens Johnson syndrome, Exanthema, Angioedema, Urticaria, Alopecia

Special Precautions

Convulsions in children, including in infants below one year of age, have been reported during post-marketing experience with VERMOX®. VERMOX® should not be given to children below 1 year of age. VERMOX® 500 mg or VERMOX® SD should not be used and VERMOX® 100 mg Tablets or VERMOX® 20mg/ml should only be given to very young children if their worm infections interfere significantly with the nutritional status and the physical development.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

In patients treated at dosages substantially higher than recommended or for prolonged periods of time, the following adverse reactions have been reported; liver function disturbances, hepatitis, neutropenia, and glomerulonephritis. With the exception of glomerulonephritis, these also have been reported in patients who were treated with mebendazole at standard dosages.

In the event of accidental overdose, abdominal cramps, nausea, vomiting and diarrhoea may occur. If poisoning or excessive overdose is suspected it is recommended, on general principles, that vomiting be induced or gastric lavage be performed, and such symptomatic supportive therapy be administered as appears indicated. Activated charcoal may be given.

IDENTIFICATION

White to off-white suspension with a chocolate flavour.

PRESENTATION

15 ml amber glass bottles containing 10 ml VERMOX® SD suspension

STORAGE INSTRUCTIONS

Store below 25°C.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

34/12/0058

**NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF
REGISTRATION**

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RETREAT

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South Africa

DATE OF PUBLICATION OF THIS PACKAGE INSERT

TBA

REFERENCES:

Reference 1 (Available upon request)

- European Guideline on Summary of Product Characteristics, December 1999
- Van Cauteren H et al. Expert Report on the Toxicological, Pharmacokinetic and Pharmacodynamic Documentation Related to Mebendazole. Pharmacotoxicological Expert Report on R017635, Second Revision, April 1992. (LMD183575)
- Clinical Expert Statement on the Efficacy of Mebendazole in Taeniasis. EDMS-PSDB-2959435:2.0 (LMD186958)

Reference 2 (Available upon request)

- European Guideline on Summary of Product Characteristics, October 2005

Reference 3

- Module 2.5 - Clinical Overview - August 2009 Modification of the Company Core Data Sheet for VERMOX (500 mg) R017635 (mebendazole). 10 September 2009. EDMS-PSDB-10550534:2.0

Reference 4

- Sanderson-Bongiovanni D. Clinical Overview Supporting the Post-Marketing Safety-Related Changes in the August 2009 Modification of the Company Core Data Sheet for VERMOX® (mebendazole). 16 September 2009. EDMS-PSDB-10504851

Reference 5 (Available upon request)

- Kung'U A. Glomerulonephritis Following Chemotherapy of Hydatid Disease With Mebendazole. East African Medical Journal 59 (6), P.404-409, 1982. (LMD34917)