Vermox® 500 mg (mebendazole)
Tablets

NAME OF THE MEDICINAL PRODUCT
VERMOX®
DOSAGE FORMS AND STRENGTHS
VERMOX 500mg tablet: white to faintly cream-colored, circular, flat, bevel-edged tablet.
Each tablet contains 500 mg mebendazole.
CLINICAL INFORMATION
Indications-Adults and Children: VERMOX 500 mg is indicated for the mass treatment of single or mixed gastrointestinal infestations by *Enterobius vermicularis* (pinworm); *Trichuris trichiura* (whipworm); *Ascaris lumbricoides* (large roundworm); *Ancylostoma duodenale, Necator americanus* (hookworm).
In patients living in heavily endemic areas, regular treatment with VERMOX 500mg (1-2 times a year) will substantially reduce the overall wormload and keep it well below the level of clinical significance.
VERMOX is indicated for the treatment of Trichinella spiralis or trichinosis (Trichinella infestation).
VERMOX is indicated for the treatment of inoperable or not radically operable Echinococcus granulosus or cystic echinococcosis or hydatid disease (dog tapeworm infestation).
Indications-Adults Only: VERMOX is indicated for the treatment of inoperable or not radically operable Echinococcus multilocularis or alveolar echinococcosis (fox tapeworm infestation) in adults. Use of VERMOX for these indications have not been studied in children.
Dosage and Administration
Enterobiasis, Ascariasis, Trichuriasis, hookworm and mixed infestations
1 single tablet of VERMOX 500 mg.
Trichinella
5 mg/kg/day in two divided doses for 10–15 days.
Echinococcus granulosus
40-60 mg/kg/day in 2-3 divided doses for at least 3-6 months.
Echinococcus multilocularis
40-60 mg/kg/day in 2-3 divided doses continuously, for many years, depending on the response.
Special populations (Pediatrics):
Enterobiasis, Ascariasis, Trichuriasis, hookworm and mixed infestations
VERMOX 500 mg given as a single dose.
Trichinella
5 mg/kg/day in two divided doses for 10-15 days.
Echinococcus granulosus
40-60 mg/kg/day in 2-3 divided doses for at least 3-6 months.
Pediatrics < 2 years of age: Because of the risk of convulsions, VERMOX is contraindicated in children below the age of 1 year for the mass treatment of single or mixed gastrointestinal infestations
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 only if the potential benefit justifies the potential risk.
No special procedures, such as diet or use of laxatives, are required.
Contraindications: VERMOX is contraindicated in children below the age of 1 year for the mass treatment of single or mixed gastrointestinal infestations. In addition, VERMOX 500 mg is contraindicated in persons with a known hypersensitivity to the drug or its excipients.
Warnings and Precautions: Convulsions in children, including in infants below one year of age have been reported very rarely during post-marketing experience with VERMOX. VERMOX should be used in children aged 1-2 years only if the potential benefit justifies the potential risk (e.g. if their worm infestation interferes significantly with their nutritional status and physical development). 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. 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) 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.
Patients with Trichinellosis or Echinococcosis.
As higher doses and longer treatment is recommended in patients with Trichinellosis and Echinoccocosis, 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 if clinically significant laboratory abnormalities are found.
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.
Pregnancy, Breast-feeding and Fertility
Pregnancy: Mebendazole has shown embryotoxic and teratogenic activity in rats and in mice. No harmful effects on reproduction were noted in other animal species tested. The possible risks associated with prescribing VERMOX 500 mg during pregnancy, particularly during the first trimester, should be weighed against the expected therapeutic benefits.
Breast-feeding: Limited data from case reports demonstrate that a small amount of mebendazole is present in human milk following oral administration. Therefore, caution should be exercised when VERMOX 500 mg is administered to breast-feeding women.
Fertility: Results of mebendazole reproduction studies showed no effects on fertility up to and including doses of 10 mg/kg/day (60 mg/m^2).
Effects on Ability to Drive and Use Machines
VERMOX 500mg does not affect the mental alertness or driving ability.
Adverse Reactions: 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.
Clinical Trial Data: 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 occurred in ≥1% of VERMOX-treated subjects. Adverse reactions occurring in <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, Diarrhea, Flatulence
Skin and Subcutaneous Tissue Disorders:	Rash

Post-marketing experience: Adverse reactions first identified during postmarketing experience with VERMOX (mebendazole) are included in Table 2. In the table the frequency categories are provided according to the following

convention:

Very common ≥ 1/10	Common ≥ 1/100 and <1/10	Uncommon ≥ 1/1,000 and <1/100	Rare ≥ 1/10,000 and <1/1,000	Very rare < 1/10,000 including isolated reports

In Table 2, ADRs are presented by frequency category based on spontaneous reporting rates.

Table 2. Adverse Reactions Identified During Postmarketing Experience with VERMOX by Frequency Category Estimated from Spontaneous Reporting Rates

System Organ Class	Frequency Category	Adverse Reaction
Blood and lymphatic system disorders	Very Rare	Agranulocytosis, Neutropoenia
Immune System Disorders	Very Rare	Hypersensitivity including anaphylactic reaction and anaphylactoid reaction
Nervous System Disorders	Very Rare	Convulsions, Dizziness
Gastrointestinal Disorders	Very Rare	Abdominal pain, Nausea, Vomiting
Hepatobiliary Disorders	Very Rare	Hepatitis, Abnormal liver function tests
Skin and Subcutaneous Tissue Disorders	Very Rare	Toxic epidermal necrolysis, Stevens-Johnson syndrome, Exanthema, Angioedema, Urticaria, Alopecia
Renal and Urinary Disorders	Very Rare	Glomerulonephritis

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.

Signs and 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 considered appropriate.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic Properties

Mechanism of action: In therapeutic indications 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.

Pharmacokinetic Properties

Absorption: Following oral administration, approximately <10% of the dose reaches the systemic circulation, due to incomplete absorption and to extensive pre-systemic metabolism (first-pass effect). The majority of an orally administered dose remains in the gastrointestinal tract. Maximum plasma concentrations are generally seen 2 to 4 hours after administration.

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., 40mg/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 (hydrolyzed 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., 40mg/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.

Specific populations

Pediatric

Based on a limited number of blood samples, the pharmacokinetic results following single-dose administration of a 500 mg mebendazole tablet to pediatric patients (age 1 to 16 years) with single or mixed infections of T. trichiura and/or A. lumbricoides indicated that children aged 1 to 3 years have higher systemic exposure than adults.

NON CLINICAL INFORMATION

The single-dose toxicity evaluations in multiple species revealed that mebendazole was well tolerated and has a large margin of safety. Repeated-dose, oral, chronic toxicity results in rats, at toxic dose levels of 40 mg/kg (240 mg/m^2) and above, showed altered liver weights with some slight centrilobular swelling and hepatocellular vacuolation, and altered testicular weights with some tubular degeneration, desquamation and marked inhibition of spermatogenic activity.

Carcinogenicity and Mutagenicity: No carcinogenic effects were observed in the mouse or rat. No mutagenic activity was shown in in-vitro gene-mutagenicity studies. In vivo tests revealed no structural chromosome damaging activity. Micronucleus test results have shown aneugenic effects in mammalian somatic cells above a threshold plasma concentration of 115 ng/mL.

Reproductive Toxicology: At maternal toxic doses, embryotoxic and teratogenic activity has been shown in pregnant rats at a single dose of 10 mg/kg and above. Teratogenic and fetotoxic effects have also been observed in mice at maternally toxic doses of 10 mg/kg (60 mg/m^2) and higher. No harmful effects on reproduction were noted in other animal species tested.

Fertility: Male rat fertility was not affected with doses up to 40 mg/kg (240 mg/m^2) for 60 days. When female rats were dosed at up to 10 mg/kg body weight for 14 days before gestation and during pregnancy, no significant effect upon fetuses and offspring were observed. However, when female rats were dosed at 40 mg/kg (240 mg/m^2) a reduction in the pregnancy rate was observed.

PHARMACEUTICAL PARTICULARS

Shelf Life

Observe expiry date on the outer pack.

Special Precautions for Storage

Do not store above 30°C.
Keep all medicines out of reach of children.
Protect from light and moisture.

Nature and Contents of Container

Vermox 500mg (mebendazole) is supplied in blister pack of 4x3 tablets.

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
۳۰ ڈگری سینٹی گریڈ سے زیادہ درجہ حرارت پر نہ رکھیں۔
بچوں کی پہنچ سے دور رکھیں۔
دوا کو روشنی اور نمی سے بچائیں۔

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