

# Vermox® (mebendazole)

Tablets / Suspension

## NAME OF MEDICINAL PRODUCT

Vermox®

## QUALITATIVE AND QUANTITATIVE COMPOSITION

Vermox 100mg tablets  
Each tablet contains:  
Mebendazole.....100mg  
Vermox 100mg/5ml Suspension:  
Each 5 ml contains:  
Mebendazole.....100mg

## PHARMACEUTICAL FORM

Vermox (Mebendazole) 100 mg tablet: slightly orange, circular, flat, bevel-edged, half-scored tablet.  
Vermox (Mebendazole) 100mg/5ml oral suspension: white homogeneous suspension.

## CLINICAL PARTICULARS

### Indications – Adults and Children

Vermox (Mebendazole) is indicated for the treatment of single or mixed gastrointestinal infestations by *Enterobius vermicularis* (pinworm); *Trichuris trichiura* (whipworm); *Ascaris lumbricoides* (large roundworm); *Ancylostoma duodenale*, *Necator americanus* (hookworm); *Strongyloides stercoralis* (threadworm); *Taenia spp.* (tapeworm).

Vermox (Mebendazole) is indicated for the treatment of *Trichinella spiralis* or trichinosis (*Trichinella* infestation).

Vermox (Mebendazole) 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 (Mebendazole) is indicated for the treatment of inoperable or not radically operable *Echinococcus multilocularis* or alveolar echinococcosis (fox tapeworm infestation) in adults. Use of Vermox (Mebendazole) for these indications have not been studied in children.

## Dosage and administration

### Dosage (100 mg tablets and 20 mg/ml oral suspension):

1) **Enterobiasis: Adults and children:** Take 1 tablet or 5 ml oral suspension given as a single dose. Since reinfections by *Enterobius vermicularis* are known to be very frequent, it is recommended that the treatment be repeated after 2 and 4 weeks, particularly in eradication programmes.

2) **Ascariasis, trichuriasis, hookworm and mixed infestations: Adults and children:** Take 1 tablet or 5 ml oral suspension two times a day, in the morning and in the evening for 3 consecutive days.

### 3) Taeniasis and strongyloidiasis:

**Adults:** Although favorable results have been obtained with lower dosages, it is suggested that 2 tablets or 10 ml oral suspension two times a day, be prescribed in the morning and the evening for 3 consecutive days, to obtain complete cure.

**Children:** Take 1 tablet or 5 ml oral suspension two times a day, in the morning and in the evening for 3 consecutive days. No special procedures, such as diet or use of laxatives, are required.

### 4) Trichinella

5 mg/kg/day in two divided doses for 10–15 days.

### 5) Echinococcus granulosus

40–60 mg/kg/day in 2–3 divided doses for at least 3–6 months.

### 6) Echinococcus multilocularis (Adults only)

40–60 mg/kg/day in 2–3 divided doses continuously, for years, depending on the response.

**Pediatrics:** Vermox (Mebendazole) 100 mg tablets should not be

used in children below the age of 1 year. Vermox (Mebendazole) suspension should be considered for patients such as young children who are unable to swallow the tablet.

## Contraindications

Mebendazole 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 Mebendazole (see Adverse Reactions). Mebendazole 100 mg should only be given to very young children if their worm infestation interferes significantly with their nutritional status and physical development.

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 and agranulocytosis, 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 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 Mebendazole if clinically significant laboratory abnormalities are found.

**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 Warnings and Precautions).

## Pregnancy, Breast-feeding and Fertility:

Mebendazole has shown embryotoxic and teratogenic activity in rats and in mice. No harmful effects on reproduction were noted in other animal species tested. (see Non-Clinical Information - Reproductive Toxicology). The possible risks associated with prescribing Mebendazole during pregnancy, particularly during the first trimester, should be weighed against the expected therapeutic benefits.

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 Mebendazole is administered to breast feeding women. Results of mebendazole reproduction studies showed no effects on fertility up to and including doses of 10 mg/kg/day (60 mg/m<sup>2</sup>) (see Non-clinical information - Fertility).

## Effects on ability to drive and use machines

Mebendazole does not affect the mental alertness or driving ability.

## Adverse Reactions

Throughout this section adverse reactions are presented. 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 Trial Data**

The safety of Mebendazole 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 reactions occurred in  $\geq 1\%$  of Mebendazole-treated subjects. Adverse reactions occurring in  $< 1\%$  of Mebendazole-treated subjects are shown in Table 1.

Table-1: Adverse Drug Reactions Reported by $< 1\%$ of Mebendazole-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 drug reactions first identified during post-marketing experience with Mebendazole are included in Table 2. In the table the frequency categories are provided according to the following convention:

Very Common $\geq 1/10$	Common $\geq 1/100$ and $< 1/10$	Uncommon $\geq 1/1,000$ and $< 1/100$	Rare $\geq 1/10,000$ and $< 1/1,000$	Very Rare $< 1/10,000$ Including isolated reports
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In Table 2, ADRs are presented by frequency category based on spontaneous reporting rates.

Table 2: Adverse Drug Reactions Identified During Post Marketing Experience with Mebendazole by Frequency Category Estimated from Spontaneous Reporting Rates / Clinical Trials or Epidemiology		
System/Organ Class:	Frequency Category	Adverse Reaction
Blood and lymphatic system disorders	Very Rare	Agranulocytosis, Neutropenia
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, Glomerulonephritis
Renal and Urinary Disorders	Very Rare	

**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, neutropoemia, and glomerulonephritis. With the exception of agranulocytosis and glomerulonephritis, these also have been reported in patients who were treated with mebendazole at standard dosages.

**Sign & 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:** 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. There is no evidence that Mebendazole is effective in the treatment of cysticercosis

**Pharmacokinetic properties:**

**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).

The majority of an orally administered dose remains in the gastrointestinal tract. Maximum plasma concentrations are generally seen 2 to 4 hours after administration. Dosing with a high fat meal increases the bioavailability of mebendazole, although the overall effect of food on the amount of drug remaining in the gastrointestinal tract is not expected to be substantial.

**Distribution:** The plasma protein binding of mebendazole is 90 to 95%. The volume of distribution is 1 to 2 L/kg, indicating that

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 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 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.

**Preclinical Safety data:** 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 (240mg/m<sup>2</sup>) 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 (60mg/m<sup>2</sup>) 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 (240mg/m<sup>2</sup>) 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<sup>2</sup>) 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 100mg (Mebendazole) is supplied in blister pack of 6x10 tablets.

Vermox 100mg/5ml (Mebendazole) drinkable suspension is supplied in bottle of 30 ml with a measuring cup of 5 ml.

**Instructions for use/handling:**

The suspension should be shaken before use.

Manufactured by:

**Aspin Pharma (Pvt) Ltd.,**

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Vermox, TM of JANSSEN PHARMACEUTICA,

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