

VERMOX®

Mebendazole tablets and suspension

name of the MEDICINE

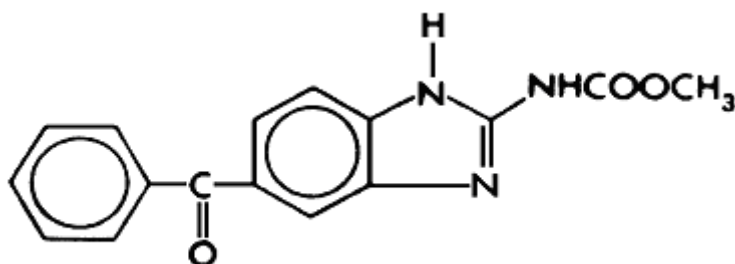
Mebendazole

DESCRIPTION

Mebendazole is methyl 5-benzoyl-2-benzimidazole carbamate a synthetic benzimidazole derivative and is an off white to yellowish powder, insoluble in water and common organic solvents but freely soluble in formic acid.

VERMOX tablets contain mebendazole 100 mg - slightly orange, circular, flat, bevel-edged, half-scored tablet with orange flavour.

VERMOX suspension contains mebendazole 2% w/v - a white banana flavoured suspension. Each spoonful contains mebendazole 100 mg.



$C_{16}H_{13}N_3O_3$

M.W. 295.30

USES:

Action

Therapeutic Classification: Anthelmintic

Parasitology

In vitro and *in vivo* studies indicate that mebendazole inhibits *Trichuris trichiura* and hookworms (*Ancylostoma duodenale* and *Necator americanus*). *In vivo* efficacy has been demonstrated against *Trichuris*, *Ascaris*, hookworm, and *Enterobius*. The mechanism of action is probably a result of an inhibitory effect on the ability of the organism to utilise exogenous glucose. This interferes with the generation of phosphate bonds (ATP), ultimately leading to the death of the parasite.

Pharmacology

Mebendazole at 40 mg/kg in mice and 160 mg/kg in rats is devoid of parasympatholytic, parasympathomimetic CNS-stimulating, CNS-depressing, hypnotic, morphine-like, aspirin-like, anti-convulsive, and toxic effects. Mebendazole has also been tested in rats for its anti-inflammatory effects in the *Mycobacterium butyricum* arthritis test and was found devoid of effect.

Pharmacokinetics

Little information is available concerning the metabolism of mebendazole in man. In rats and dogs, the drug is mainly excreted in the faeces (about 90%) in its unchanged form. Only 1% (dogs) and 5 - 10% (rats) of the dose was eliminated in the urine up to 4 days after drug administration. The urine samples of these treated animals contained mainly metabolic breakdown products. Blood and tissue levels were low and the main metabolite was the decarboxylated form. In the liver, they never exceeded 4% of the administered dose.

In a human study, where 3 male subjects were administered 0.1 mg/kg of ¹⁴C mebendazole, plasma levels were low, peaking 2 to 4 hours after treatment. Approximately 10% of the administered dose was excreted in the urine in less than 8 hours. The major metabolite detected in the urine was 2-amino-5-benzimidazolyl phenyl ketone.

In summary, human studies indicate that mebendazole is poorly absorbed. Tissue levels are low and are probably due to metabolites. Mebendazole is excreted mainly in the faeces as unchanged drug with small amounts appearing in the urine.

Toxicology

Acute oral toxicity has been investigated in twelve animal species. Results reveal that mebendazole was well tolerated by all species. The only side effects were softening of the faeces and diarrhoea with weight loss in pigs, and in one study, diarrhoea occurred in horses. The oral LD₅₀ exceeds 1280 mg/kg in mice and rats; 1000 mg/kg in cats; 640 mg/kg in rabbits and dogs; 400 mg/kg in horses; 320 mg/kg in sheep; 80 mg/kg in cattle, and 20 mg/kg in pigs.

Subacute and chronic oral toxicity has been investigated in four animal species and the chronic oral toxicity in rats, dogs and horses.

In these studies, the oral administration of mebendazole to rats and dogs at doses up to 40 mg/kg once daily for 6 weeks, to horses at doses up to 6 g/250 lb (53 mg/kg) once daily for 15 days, did not cause any significant abnormality as observed

by clinical examination, clinical pathology, gross pathology, or histopathology. In rats and not in other species, testicular atrophy, degeneration of tubules, desquamation of germinal cells in the epididymis and inhibition of spermatogenesis at doses of 40 mg/kg and above.

Reproduction and teratology studies

The effect of mebendazole on reproduction was determined in various animal species. Included in these studies were determinations on potential embryotoxicity and teratogenicity in rats, rabbits, dogs, sheep and horses and on male and female fertility in rats.

These studies showed that mebendazole is embryotoxic and teratogenic in rats at doses 10 mg/kg and above but not in rabbits up to 40 mg/kg, or dogs and sheep up to 20 mg/kg. There was no significant effect on rat fertility when up to 40 mg/kg was given to males for 60 days before mating and to females at 20 mg/kg for 14 days before exposure to males.

Miscellaneous Studies

Mebendazole was tested for possible cardiovascular effects in dogs. It is concluded that single oral doses up to 160 mg/kg are devoid of electrocardiographic effects in dogs.

INDICATIONS

VERMOX tablets and suspension are indicated for the treatment of single or mixed helminthic infestations. Clinical studies have shown mebendazole to be effective in the treatment of *Enterobius vermicularis* (threadworm), *Ascaris lumbricoides* (roundworm), *Trichuris trichiura* (whipworm) and of *Ancylostoma duodenale* and *Necator americanus* (hookworm).

Efficacy varies as a function of such factors as pre-existing diarrhoea, gastrointestinal transit time, degree of infection, and helminth strain.

CONTRAINDICATIONS

Mebendazole is contraindicated in persons who have shown hypersensitivity to the drug or other benzimidazole derivatives.

PRECAUTIONS

Paediatric Use

Mebendazole has not been studied in children under one years. Therefore, VERMOX cannot be recommended in this age group pending the results of studies.

Use in Pregnancy

Category (B3)

The safety of use in pregnant women has not been established, although animal trials conducted in a wide range of species revealed an embryotoxic and teratogenic effect in the rat. Therefore, VERMOX should not be administered during pregnancy, particularly in the first trimester, unless the potential benefit to the patient outweighs the possible risk to the foetus.

Use in lactation

It is not known whether mebendazole passes into maternal milk and thus whether it is harmful to the newborn. The use of VERMOX in nursing mothers requires that anticipated benefits be weighed against possible risks. If use in the lactating mother is deemed essential by the treating clinician, alternative arrangements to feed the infant should be made.

Interactions with other medicines

Concurrent treatment with cimetidine may inhibit the metabolism of mebendazole in the liver, resulting in increased plasma concentrations, particularly during prolonged treatment. During prolonged treatment, measurement of plasma concentrations is recommended, to allow dosage adjustment if necessary.

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.

Adverse Reactions

At the recommended dose, VERMOX is generally well tolerated. However, patients with high parasitic burdens when treated with VERMOX have manifested diarrhoea, vomiting, and/or abdominal pain. Other adverse reactions reported were drowsiness, itching, headache, and dizziness. Reports from clinical trials also mentioned increased AST, ALT, alkaline phosphatase, and BUN. Eosinophilia and decreased haemoglobin and/or white cell count, haematuria and cylindruria have been reported.

Hypersensitivity reactions such as anaphylactic and anaphylactoid reactions, exanthema, rash, urticaria, , angio-oedema, Stevens-Johnson syndrome and toxic epidermal necrolysis have also been observed, although rarely.

Dosage and Administration

VERMOX is administered orally.

For control of enterobiasis:

One tablet (100 mg) or 5 mL spoonful of suspension (100 mg) is given. Since reinfections by *Enterobius* are known to be very frequent, it is recommended that treatment be repeated after 2 to 4 weeks, especially in eradication programmes.

For control of *trichuriasis*, *ascariasis*, *ancylostomiasis*, and mixed infections:

One VERMOX tablet (100 mg) or 5 mL spoonful of suspension (100 mg) is administered in the morning and evening for three consecutive days.

Paediatric:

The same dosage may be given to children (1 to 12 years) as to adults. As safety and efficacy has not been established in children under 1 year its use is not recommended for this age group (See **PRECAUTIONS**).

If the patient is not cured three weeks after treatment, a second course of treatment is advised.

No special procedures such as fasting or the use of laxative are required.

Overdosage

In the event of accidental overdosage, abdominal cramps, nausea, vomiting and diarrhoea may occur. If this is the case, contact the Poisons Information Centre on 0800 POISON or 0800 764 766.

Although the maximum duration of therapy with VERMOX is 3 days, there have been rare reports of reversible liver function disturbances, hepatitis and neutropenia described in patients who were treated for hydatid disease with large doses over prolonged periods.

MEDICINE CLASSIFICATION

Pharmacy Only Medicine.

PACKAGE QUANTITIES

Tablets, 100 mg, 2s and 6s.

New Zealand Data Sheet

Suspension, 100 mg/5ml, 25ml.

Combination, tablets, 2s and suspension, 15ml.

NAME AND ADDRESS

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DATE OF PREPARATION

12 September 2011.