NEW ZEALAND DATA SHEET

VERMOX®

1. PRODUCT NAME

Vermox 100 mg Tablets

Vermox Choc Chews 100 mg Chewable Tablets

Vermox Suspension 2% w/v

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 100 mg mebendazole

Excipients: Each tablet also contains 0.06 mg of sunset yellow (E110).

Each chewable tablet contains 100 mg mebendazole

Each 5 mL of suspension contains 100 mg mebendazole

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet: slightly orange, circular, flat, bevel-edged, half-scored tablet with orange flavour.

Chewable tablet: lightly speckled chocolate brown, circular, flat, bevel-edged, half-scored tablet with chocolate flavour.

Suspension: white banana flavoured.

4. CLINICAL PARTICULARS

4.1 Therapeutic 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.

4.2 Dose and method of administration

Method of Administration

Oral use.

Vermox orange flavoured tablets may be swallowed whole, chewed or crushed into a teaspoon of food.

Vermox Choc Chews chewable tablets may be chewed or crushed into a teaspoon of food.

Shake the Vermox suspension well before use.

For control of *enterobiasis*

Adults and children 2-12 years: 1 Vermox tablet (100 mg) or 5 mL 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

Adults and children 2-12 years: 1 Vermox tablet (100 mg) or 5 mL of suspension (100mg) is administered in the morning and evening for three consecutive days.

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.

4.3 Contraindications

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

Paediatric Use

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

Convulsions in children, including infants below one year of age have been reported very rarely during post-marketing experience with Vermox.

4.4 Special warnings and precautions for use

Precautions risk/ benefit analysis should be considered for the following:

Crohn's ileitis or ulcerative colitis: May increase absorption and toxicity of mebendazole, especially in high dose therapy.

Use in Patients with Hepatic Function Impairment

Caution is advised for use in patients with hepatic impairment since this condition may prolong half-life and drug accumulation.

4.5 Interaction with other medicines and other forms of interaction

Concurrent administration of cimetidine may inhibit the metabolism of mebendazole in the liver, producing increased plasma concentrations of the drug, especially during prolonged treatment. In the latter case, determination of plasma concentrations is recommended in order to allow dose adjustments.

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.

4.6 Fertility, pregnancy and lactation

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.

Lactation

It is not known whether mebendazole passes into maternal milk and, thus, whether it is harmful to the newborn infant. The use of Vermox in breastfeeding 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.

4.7 Effects on ability to drive and use machines

Vermox has no influence on the ability to drive or use machines.

4.8 Undesirable effects

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 reactions (ADRS) occurred in ≥1% of Vermox-treated subjects.

ADRs identified from Vermox clinical trials and post-marketing experience are included in Table 1.

The displayed frequency categories use the following convention: Very common (≥1/10); Common (≥1/100 to <1/10); Uncommon (≥1/1000 to <1/100); Rare (≥1/10,000 to <1/1000); Very rare (<1/10,000 including isolated reports).

Table 1: Adverse Drug Reactions Reported in Clinical Trials and Post-marketing Experience for Vermox

System Organ Class	**Adverse Drug Reactions**		
	Frequency Category		
	Common (≥1/100 to <1/10)	**Uncommon** (≥1/1000 to <1/100)	**Rare** (≥1/10,000 to <1/1000)
Blood and Lymphatic System Disorders			Neutropenia
Immune System Disorders			Hypersensitivity including anaphylactic reaction and anaphylactoid reaction
Nervous System Disorders			Convulsions Dizziness
Gastrointestinal Disorders	Abdominal pain	Abdominal discomfort Diarrhoea Flatulence	
Hepatobiliary Disorders			Hepatitis Abnormal liver function tests
Skin and Subcutaneous Tissue Disorders			Rash Toxic epidermal necrolysis Stevens-Johnson syndrome Exanthema Angioedema Urticaria Alopecia

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/

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 rarely: reversible liver function disturbances, hepatitis, neutropenia, and glomerulonephritis. With the exception of glomerulonephritis, these also have been reported in patients who treated with mebendazole at standard dosages.

Respiratory arrest and tachyarrhythmia associated with continuous convulsions have been reported in an 8-week old infant following accidental poisoning with mebendazole. Treatment by exchange transfusion and anticonvulsants was successful.

Symptoms: In the event of accidental overdosage, abdominal cramps, nausea, vomiting and diarrhoea may occur.

There is no specific antidote. Supportive and symptomatic therapy should be initiated in cases of overdosage. Activated charcoal may be given if considered appropriate

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES
5.1 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 Vermox is effective in the treatment of cysticercosis.

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 leads to a modest increase in 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 to 21 months) that show drug levels in tissue.

Metabolism

Orally administered mebendazole is extensively metabolised primarily by the liver. Plasma concentrations of its major metabolites (amino and hydroxylated amino 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.

Excretion

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. Approximately 95% of mebendazole is excreted in the faeces unchanged or as the primary metabolite (2-amino derivatives). Approximately 2 to 5% of mebendazole is excreted in the urine unchanged or as the primary metabolite.

Steady-State Pharmacokinetics

During chronic dosing (e.g. 40 mg/kg/day for 3 to 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.

5.3 Preclinical safety data

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 of 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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablets: Colloidal silicon dioxide, Cottonseed oil, hydrogenated, Magnesium stearate, Maize starch, Microcrystalline cellulose, Orange flavour 173126, Purified talc, Purified water, Saccharin sodium, Sodium lauryl sulfate, Sodium starch glycolate, Sunset yellow FCF (E110).

Choc Chews Chewable Tablets: Chocolate Flavour EI 31536, Fructose, Macrogol 6000, Magnesium Stearate, Maize Starch, Cocoa powder, Purified Talc, Sucralose.

Suspension: Banana flavour 54330 A, Citric acid monohydrate, Cellulose- microcrystalline, Carmellose sodium (carboxymethylcellulose sodium), Methyl hydroxybenzoate, Methylcellulose, Propyl hydroxybenzoate, Purified water, Sodium lauryl sulfate, Sucrose.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life
Tablets: 5 years (Blister pack, PVC/Al); 3 years (Bottle)*; 3 years (Blister pack, Aluminium)*
Choc Chews Chewable Tablets: 2 years
Suspension: 5 years

6.4 Special precautions for storage
Store below 30 degrees Celsius.

Keep out of reach of children.

6.5 Nature and contents of container
Tablets: Blister pack, PVC/Aluminium: 2's, 4's, 6's
Tablets: Bottle: 100's*
Tablets: Blister Pack, Aluminium: 2's*
Choc Chews Chewable Tablets: Blister pack, PVC/Aluminium: 2's*, 4's, 6's, 12's*
Suspension: Bottle, glass: 15 mL

6.6 Special precautions for disposal
No special requirements.

7. MEDICINE SCHEDULE
Pharmacy Medicine

8. SPONSOR
iNova Pharmaceuticals (New Zealand) Limited
c/- Simpson Grierson
88 Shortland Street,
Auckland 1141

Toll-free number: 0508 375 394

9. DATE OF FIRST APPROVAL
Vermox Tablets: 1 July 1976

Vermox Suspension: 2 February 1981

Vermox Choc Chews Chewable tablets: 22 December 2011

10. DATE OF REVISION OF THE TEXT
19 January 2018

*Not marketed

SUMMARY TABLE OF CHANGES

Date	**Changes**
31 May 2017	Reformatted to new DS format; Choc Chews: Chocolate flavour Proprietary ingredient changed from Chocolate Flavour AP07773 to Chocolate Flavour EI 31536
19 January 2018	Change in sponsor name and address to iNova Pharmaceuticals (New Zealand) Limited