Professional Information

SCHEDULING STATUS

S1

1. NAME OF THE MEDICINE

WORMSTOP ® 500 (TABLETS)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Mebendazole 500 mg

Sugar free, Artificially sweetened: Sodium saccharin 10 mg / tablet

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Tablet

Light orange coloured, orange flavoured, smooth, capsule shaped

biconvex uncoated tablets.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

WORMSTOP® 500 is indicated for the treatment of single and mixed helminth gastrointestinal infestations caused by:

- nematodes such as:

Ascaris lumbricoides (large roundworm)

Trichuris trichiura (whipworm)

Ancylostoma duodenale	(hookworm)
Necator americanus	(hookworm)
Enterobius vermicularis	(pinworm)

4.2 Posology and method of administration

Whipworm; Hookworm; Large Roundworm; Pinworm:

Adults and children older than 1 year: One tablet (500 mg) given as a single dose. The tablets may be crushed and given with some liquid for children.

A single dose of **WORMSTOP® 500** 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 **WORMSTOP® 500** is dependent upon the duration of physical contact between drug and parasite.

For infants under 1 year of age, see section 4.3 and 4.4.

4.3 Contraindications

Hypersensitivity to mebendazole or to any of the excipients of **WORMSTOP® 500** (see section 6.1).

WORMSTOP® 500 should not be used in children below the age of 1 year.

WORMSTOP® 500 should not be given during pregnancy, as it is teratogenic in animals. (see section 4.6)

Concomitant use of mebendazole and metronidazole should be avoided.

4.4 Special warnings and precautions for use

There have been reports of reversible liver function disturbances, hepatitis, neutropenia and glomerulonephritis described in patients treated with massive doses for prolonged periods of time. Therefore, haematological parameters and liver function tests should be monitored in patients receiving **WORMSTOP® 500** for prolonged periods of time. (see section 4.9).

Convulsions in children, including in infants below one year of age, have been reported **WORMSTOP® 500** should not be given to children below 1 year of age. **WORMSTOP® 500** should only be given to very young children if their worm infections interfere significantly with the nutritional status and the physical development.

4.5 Interaction with other medicines and other forms of interaction

Concomitant treatment with cimetidine may inhibit the metabolism of the mebendazole in the liver, resulting in increased plasma concentrations of the medicine especially during prolonged treatment. In the latter case, determination of plasma concentrations is recommended in order to allow dose adjustments.

Concomitant use of **WORMSTOP® 500** and metronidazole should be avoided.

4.6 Fertility, pregnancy and lactation

WORMSTOP® 500 is contra-indicated during pregnancy and lactation. (see section 4.3). 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.

4.7 Effects on ability to drive and use machines

WORMSTOP® 500 has no influence on the ability to drive and use machines.

4.8 Undesirable effects

System Organ Class	Frequent	Less frequent
Blood and Lymphatic		Neutropenia,

System Disorders		Agranulocytosis*
Immune System Disorders		Hypersensitivity including anaphylactic reaction and anaphylactoid reaction
Nervous System Disorders		Convulsions, Dizziness
Gastrointestinal Disorders	Abdominal pain	Abdominal discomfort, Diarrhoea, Flatulence, Nausea, Vomiting
Hepatobiliary Disorders		Hepatitis Abnormal liver function tests
Skin and Subcutaneous Tissue Disorders		Rash, Toxic epidermal necrolysis, Stevens-Johnson syndrome, Exanthema' Angioedema, Urticaria, Alopecia
Renal and Urinary Disorders		Glomerulonephritis*

* Reported in higher and prolonged doses

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. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

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; 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 overdosage, abdominal cramps, nausea, vomiting and diarrhoea may occur.

If poisoning or excessive overdosage 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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A.12 Anthelmintics, Bilharzia medicines, Filaricides, etc.

Pharmacotherapeutic group: anthelmintic for oral administration, benzimidazole derivatives; ATC code: P02CA01.

Mebendazole is a broad-spectrum anthelmintic.

It appears to affect the cytoplasmic microtubules of the tegumental or intestinal cells of parasitic worms resulting in a transport blocking of secretory vesicles. This may lead to impaired coating of the membranes followed by a decreased digestion and absorption of nutrients, eg. glucose, thereby depleting the energy level until it is inadequate for survival.

5.2 Pharmacokinetic properties

Absorption

Following oral administration, < 10 % of the dose reaches the systemic circulation, due to incomplete absorption and 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. Administration with a high fat meal increases the bioavailability of mebendazole, but 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 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 3-21 months) that show drug levels in tissue.

Metabolism

Orally administered mebendazole is extensively metabolised primarily by the liver. Plasma concentrations of its major metabolites (hydrolysed 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 entero hepatic 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., 40 mg/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.

Paediatric population

Limited data of the mebendazole concentrations in plasma are available in children and adolescents 1 to 16 years of age. These data do not indicate substantially higher systemic exposure to mebendazole in subjects 3 to 16 years of age compared to adults.

In subjects 1 to <3 years of age, systemic exposure is higher than in adults due to higher mg/kg dose relative to adults.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Calcium hydrogen phosphate
- Colour sunset yellow FCF (C.I.15985)
- Flavour orange DC-116 PH
- Gelatin
- Magnesium stearate
- Maize starch
- Purified talc
- Sodium carboxy methyl cellulose
- Sodium lauryl sulphate
- Sodium saccharin
- Vanillin

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

48 months

6.4 Special precautions for storage

Store in a cool place, at or below 25 ºC. Keep well closed.

6.5 Nature and contents of container

Cartons containing one strip pack of 1 tablet, 20 strip packs of 1 tablet.

6.6 Special precautions for disposal

No special requirements

7 HOLDER OF CERTIFICATE OF REGISTRATION

RANBAXY PHARMACEUTICALS (PTY) LTD

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Stormill, Ext.1,

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South Africa

8 REGISTRATION NUMBER(S)

31 / 12 / 0527 (S.A.)

S2	Bot 0500777 (Botswana)
NS2	04/12/1633 (Namibia)

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

22 January 1998

10 DATE OF REVISON OF THE TEXT

30 October 2021