PROFESSIONAL INFORMATION – BILTRICIDE TABLETS

Bayer (Pty) Ltd	**Date of revision of text: 09 December 2021**

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

BILTRICIDE® 600 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 600 mg praziquantel.
Sugar free
For a full list of excipients, refer to section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablets.
Oblong, white, film-coated, marked with LG on the one side and BAYER on the other. The tablet can be divided into four (4) equal segments because of the three score lines.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications:

Infections due to organisms of the following species pathogenic to man:
Schistosoma haematobium; Schistosoma mansoni.

4.2 Posology and method of administration:

Posology
For the treatment of Schistosomiasis, caused by S. haematobium and S. mansoni, the intake of 40 mg/kg body mass once or 20 mg/kg body mass twice, on a single day is recommended.

Special populations

Hepatic impairment
See section 4.4.

Renal impairment
See section 4.4.

Paediatric population

Post-marketing experience indicates that children (1-17 years of age) may experience similar side effects as adults during praziquantel treatment. The safety profile of children younger than 1 year of age has not been established.

Method of Administration

For oral use.
BILTRICIDE film-coated tablets should be swallowed whole with a little liquid, preferably during or after meals.
With single daily doses; it is recommended to take the film-coated tablets in the evening.

If ingestion of tablets several times a day is prescribed, the interval between administrations should not be less than 4 hours and not more than 6 hours.

Special monitoring advice: When broken, each of the four segments of the tablet contains 150 mg of praziquantel, so that the dosage can be easily adjusted to the patient's body weight.

4.3 Contraindications

BILTRICIDE must not be used in cases of known hypersensitivity to praziquantel or to any of the excipients.

BILTRICIDE should not be taken during the first trimester of pregnancy (see section 4.6).

Since parasite destruction within the eye may cause irreversible lesions, ocular cysticercosis must not be treated with this compound.

The concomitant administration of strong inducers of Cytochrome P450 such as rifampicin must be avoided as therapeutically effective plasma levels may not be achieved (see section 4.5).

4.4 Special warnings and precautions for use

In uncompensated liver insufficiency and in patients with hepatosplenic schistosomiasis, caution should be taken, since due to reduced medicine metabolisation in the liver, considerably higher and longer lasting concentrations of unmetabolised BILTRICIDE can occur in vascular and/or collateral circulation, leading to prolonged plasma half-life. If necessary, the patient should be hospitalised for the duration of the treatment.

Published in vitro data have shown a potential lack of efficacy of praziquantel against migrating schistosomulae. Data from two observational cohort studies in patients indicate that treatment with praziquantel in the acute phase of infection may not prevent progression into chronic phase.
In addition, the use of praziquantel in patients with schistosomiasis may be associated with clinical deterioration (paradoxical reactions, serum sickness Jarisch-Herxheimer like reactions: sudden inflammatory immune response suspected to be caused by the release of schistosomal antigens).
These reactions predominantly occur in patients treated during the acute phase of schistosomiasis.

They may lead to potentially life-threatening events, e.g. respiratory failure, encephalopathy, and/or cerebral vasculitis.

Since 80% of BILTRICIDE and its metabolites are excreted in the kidneys, excretion might be delayed in patients with impaired renal function.

Patients suffering from cardiac irregularities should be monitored during treatment.

When schistosomiasis or fluke infection is found in patients living in or coming from areas with endemic human cysticercosis, it is advised to hospitalise the patient for the duration of treatment.

As BILTRICIDE can exacerbate central nervous system pathology due to schistosomiasis, paragonimiasis or Taenia solium cysticercosis, as a general rule this medicine should not be administered to individuals reporting a history of epilepsy and/or other signs of potential central nervous system involvement such as subcutaneous nodules suggestive of cysticercosis.

The patient's ability to drive or to operate machinery may be temporarily impaired. (See section 4.7)

Caution should be exercised where there is a possibility of a simultaneous occurrence of both Schistosomiasis and CNS-cysticercosis infection, as cerebral cysticercosis requires hospital-based treatment by a specialist.

4.5 Interactions with other medicines and other forms of interactions

Effects of other medicines on praziquantel

Concomitant administration of medicines decreasing the activity of drug metabolising liver enzymes (cytochrome P450) e.g. cimetidine, ketoconazole, itraconazole, and erythromycin may increase plasma levels of BILTRICIDE.

When administered concomitantly with grapefruit juice, an increase in praziquantel exposure of less than twofold was observed in clinical studies.

Concomitant administration of medicines increasing the activity of drug metabolising liver enzymes (cytochrome P450), e.g. antiepileptic medicines, dexamethasone may reduce plasma levels of BILTRICIDE.

Concomitant administration of strong inducers of cytochrome P450 such as rifampicin must be avoided. (see section 4.3).

4.6 Fertility, pregnancy and lactation

Pregnancy
Safety in pregnancy has not been established.

Breastfeeding
BILTRICIDE appears in the milk of breastfeeding women at a concentration of 20 - 25 % of maternal serum. It is not known whether a pharmacological effect is likely to occur in children. For short-term therapy breastfeeding should be discontinued for the day(s) of treatment and for the following 24 hours.

4.7 Effects on ability to drive and use machines

Because of possible effects on vigilance, patients should be warned not to drive a car and not to operate machinery on the day of treatment (and during the subsequent 24 hours).

4.8 Undesirable effects

Side effects vary according to dose and duration of BILTRICIDE; furthermore, they are dependent on the parasite species, extent of parasitisation, duration of infection and localisation of the parasites in the body. Adverse Reactions are based on publications and on spontaneous reports sorted by CIOMS III categories of frequency and MedDRA System Organ Classes (in internationally agreed order). Frequencies of Adverse Reactions are mainly based on data from the medical literature. Status: 2004 (publication year of last literature source used).

Very Common ≥10%	**Common** ≥1% to 10%	**Uncommon** ≥0.1% to <1%	**Rare** ≥0.01% to <0.1%	**Very Rare** <0.01%
Immune System Disorders				
				Allergic reaction Polyserositis Eosinophilia
Nervous System Disorders				
Headache Dizziness	Vertigo Somnolence			Seizures
Cardiac Disorders				
				Unspecific dyshythmias
Gastrointestinal Disorders				
Gastrointestinal and abdominal pains Nausea Vomiting	Anorexia Diarrhoea			Bloody diarrhoea
Skin and Subcutaneous Tissue Disorders				
Urticaria	Rash			Pruritus
Musculoskeletal, Connective Tissue and Bone Disorders				
	Myalgia			
General Disorders and Administration Site Conditions				
Fatigue	Asthenia			

Very Common ≥10%	**Common** ≥1% to 10%	**Uncommon** ≥0.1% to <1%	**Rare** ≥0.01% to <0.1%	**Very Rare** <0.01%
	Feeling unwell			

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 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 Overdosage

Pronounced dizziness, "hang-over" feelings. There is no specific antidote and symptomatic measures should be applied.
No data are available in humans. In the event of overdose, a fast-acting laxative should be given.

5. PHARMACOLOGICAL ACTION

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anthelmintics
ATC code: P02BA01

Praziquantel is a trematodicide.
In vitro studies on trematodes and cestodes (tapeworms) have shown that praziquantel induces a rapid contraction of schistosomes by a specific effect on the permeability of the cell membranes. The medicine further causes vacuolisation and disintegration of the schistosome tegument. An increased Ca^{2+} - influx may play an important role. Secondary effects are inhibition of glucose uptake, lowering of glycogen levels and stimulation of lactate release.
The action of praziquantel is limited very specifically to trematodes and cestodes; nematodes (including filariae) are not affected.

5.2 Pharmacokinetic properties

Absorption

After oral administration, praziquantel is rapidly absorbed. Maximal plasma concentrations are achieved within 1-2 hours.

The medicine's concentration is 0,05 to 5,0 mg/L in peripheral blood after administration of 5 to 50 mg/kg; the concentration in the mesenteric vein is 3 to 4 times higher compared to peripheral blood. The half-life of unchanged praziquantel is 1-2,5 hours.

The half-life of total radioactivity (praziquantel plus metabolites) after administration of 14C-praziquantel is 4 hours.

For attaining a therapeutic effect plasma levels of 0,6 μM/L (0,19 mg/L) have to be maintained for 4-6 (up to 10) hours.

Distribution

Unchanged praziquantel passes the blood brain barrier; its concentration in cerebrospinal fluid is estimated to be 10% to 20% of the plasma concentration.

Metabolism

Praziquantel is rapidly and extensively metabolised by a first pass effect. Main metabolites are hydroxylated degradation products of praziquantel.

Excretion

Praziquantel is eliminated predominantly via the kidneys as metabolites. More than 80% of the dose administered is eliminated renally within 4 days, 90% of this amount within the first 24 hours.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on studies of systemic toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Corn starch
Magnesium stearate
Microcrystalline cellulose
Polyvidone 25
Sodium lauryl sulphate
Polyethyleneglycol 4000
Methylhydroxypropylcellulose
Titanium dioxide (E171/C.I. 77891)

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

60 months (5 years)

6.4 Special precautions for storage

Store at or below 25°C. Keep out of reach of children.

6.5 Nature and contents of container

Brown 20 mℓ wide-necked glass bottle closed with a PE white opaque olive stopper and tamper proof closure or
Polyethylene (PE) colourless transparent monolayer bag in a gold tin can with inner lacquer.

Each bottle contains 4 or 10 tablets
Each tin contains 1000 film-coated tablets
Pack sizes of 4's or 10's or 1000's film-coated tablets
Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicine or waste derived from such medicine and other handling of the product.

BILTRICIDE should not be used after the expiry date.

7. NAME AND BUSINESS ADDRESS OF THE APPLICANT

Bayer (Pty) Ltd
(Reg No: 1968/011192/07)
27 Wrench Road
Isando
1609

8. REGISTRATION NUMBER

P/12/23

9. DATE OF FIRST AUTHORISATION

16 February 1982

10. DATE OF REVISION OF TEXT

09 December 2021