

## DATA SHEET

### 1. BILTRICIDE® (600 mg film coated tablet)

Biltricide, 600 mg film coated tablet

### 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 600 mg praziquantel.

For a full list of excipients, see Section 6.1.

### 3. PHARMACEUTICAL FORM

The film-coated tablets are white to pale yellow lacquer-coated oblong shaped tablets with three scores with "Bayer" on one side and "LG" on the reverse.

### 4. CLINICAL PARTICULARS

#### 4.1 Therapeutic indications

Treatment of schistosoma infections due to various types of blood fluke (eg *Schistosoma haematobium*, *S.japonicum*, *S.mekongi*, *S.mansoni*).

#### 4.2 Dose and method of administration

The doctor must prescribe individual doses for individual cases, according to the diagnosis.

<i>Schistosoma haematobium</i>	}	20 mg/kg body weight
<i>Schistosoma mansoni</i>		three times a day
<i>Schistosoma japonicum</i>		at four hourly intervals
<i>Schistosoma mekongi</i>		for one day.

The tablet has 3 score marks, each fragment contains 150 mg active substance, thus allowing a precise dose to be given, corresponding to the patient's body weight.

If 1/4 of a tablet is required, it is convenient to begin by breaking the tablet at one of the outer grooves.

The simplest way to break the tablet is to place the thumbnail in the groove.

**Table 1: Conversion Table**

	BODY WEIGHT IN KG								
	20-25	26-33	34-41	42-48	49-56	57-63	64-70	71-78	79-86
No. of tablets corresponding to 1 x 20 mg/kg	¾	1	1¼	1½	1¾	2	2¼	2½	2¾

Biltricide should be swallowed whole with a little liquid, preferably after meals.

#### 4.2.1 Paediatric population

See Section 4.4.

#### 4.2.2 Hepatic impairment

See Section 4.4.

#### 4.2.3 Renal impairment

See Section 4.4.

### 4.3 Contraindications

Known hypersensitivity to praziquantel or any of the excipients.

Ocular cysticercosis - parasite destruction within the eye may cause irreparable damage.

The concomitant administration of strong inducers of Cytochrome P 450 such as rifampicin must be avoided as therapeutically effective plasma levels may not be achieved.

### 4.4 Special warnings and precautions for use

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.

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 praziquantel 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.

Neurocysticercosis is not an approved indication due to insufficient data. In animals, venous thrombosis and the development of granulomas at the site of worm attachment has been observed following treatment with praziquantel. Patients treated with praziquantel (for neurocysticercosis) have had a high incidence of severe headache and seizures. Some patients also developed intracranial hypertension. Because of the potential for undiagnosed neurocysticercosis to be present in patients originating from endemic areas, extra care is necessary in managing such patients. If cerebral cysticercosis is present and treatment is still considered essential, the patient should be hospitalised under specialist care.

The concomitant administration of praziquantel with efavirenz, a strong inducer of cytochrome P 450 should be avoided as therapeutically effective plasma levels of praziquantel may not be achieved (see Section 4.5 Interaction with other medicines and other forms of interactions).

#### **4.4.1 Renal impairment**

Since 80% of praziquantel and its metabolites are excreted in the kidneys, excretion might be delayed in patients with impaired renal function. Nephrotoxic effects of praziquantel are not known.

#### **4.4.2 Hepatic impairment**

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

#### **4.4.3 Paediatric population**

Safety in children has not been established.

### **4.5 Interaction with other medicines and other forms of interaction**

Praziquantel is believed to be metabolised via the CYP450 enzyme system. Many categories of medicines are known to inhibit or induce CYP450 enzymes causing an increase or decrease in serum concentrations or bioavailability. Care must therefore be exercised when co-administering such medicines.

Concomitant administration of medicines that increase the activity of drug metabolising liver enzymes (CYP450 inducers), e.g. antiepileptic medicines and dexamethasone may reduce plasma levels of praziquantel. Concomitant administration of strong inducers of CYP450 such as rifampicin must be avoided (see Section 4.3 Contraindications). Chloroquine, when taken simultaneously, can lead to lower concentrations of praziquantel in blood.

Concomitant administration with efavirenz should be avoided as therapeutically effective plasma levels of praziquantel may not be achieved (see Section 4.4 Special warnings and precautions for use) and no dosage recommendation for praziquantel can be given due to missing pharmacokinetic and safety data. Therapeutic alternatives to praziquantel should be considered.

Concomitant administration of medicines that decrease the activity of drug metabolising liver enzymes (CYP450 inhibitors) e.g. cimetidine, ketoconazole, itraconazole, erythromycin and ritonavir may increase plasma levels of praziquantel.

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

## 4.6 Fertility, pregnancy and lactation

### 4.6.1 Pregnancy

Reproduction studies performed so far in rats and rabbits have revealed no evidence of impaired fertility or harm to the fetus due to praziquantel. An increase in abortion rate was seen in rats given single doses of 300 mg/kg. There are no adequate and well controlled studies on the use of praziquantel in pregnant women.

Because animal reproduction studies are not always predictive of human response, for safety reasons praziquantel should not be used in pregnancy unless clearly needed.

### 4.6.2 Lactation

Praziquantel has been reported to be excreted in the milk of nursing women. Women should not nurse on the day of Biltricide treatment and during the subsequent 72 hours.

## 4.7 Effects on ability to drive and use machines

Patients should be warned not to drive or operate machinery on the day of treatment (and during the subsequent 24 hours), as their ability to do so may be temporarily impaired by the use of praziquantel.

## 4.8 Undesirable effects

### 4.8.1 Summary of the safety profile

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 medical literature.

### 4.8.2 Tabulated list of adverse reactions

Side effects vary according to dose and duration of praziquantel medication; furthermore they are dependent on the parasite species, extent of parasitisation, duration of infection and localisation of the parasites in the body. Side effects occur earlier and are more frequent and pronounced in patients with severe parasitic infestation. Mild increases in liver enzymes have been reported in some patients.

Table 2: Adverse reactions

	Very Common	Common	Uncommon	Rare	Very Rare
<b>Immune System Disorders</b>					Allergic reaction Polyserositis Eosinophilia
<b>Nervous System Disorders</b>	Headache Dizziness	Vertigo Somnolence			Seizures
<b>Cardiac Disorders</b>					Unspecified arrhythmias
<b>Gastrointestinal Disorders</b>	Gastrointestinal and abdominal pains Nausea Vomiting	Anorexia Diarrhoea (very rarely bloody diarrhoea)			

<b>Skin and Subcutaneous Tissue Disorders</b>	Urticaria	Rash			Pruritus
<b>Musculoskeletal, Connective Tissue and Bone Disorders</b>		Myalgia			
<b>General Disorders and Administrative Site Conditions</b>	Fatigue	Feeling unwell (asthenia, malaise) Fever			

It is often not clear whether the complaints reported by patients or the undesirable effects reported by the physician are caused by praziquantel itself (I, direct relation), or may be considered to be an endogenous reaction to the death of the parasites produced by praziquantel (II, indirect relation), or are symptomatic observations of the infestation (III, no relation). It may be difficult to differentiate between the possible variations I, II and III.

#### 4.8.3 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 to <https://nzphvc.otago.ac.nz/reporting/>

#### 4.9 Overdose

Information on overdosage in humans is not available. Treatment should be supportive and provide symptomatic care.

Activated charcoal may reduce absorption of the medicine if given within one to two hours after ingestion. In patients who are not fully conscious or have impaired gag reflex, consideration should be given to administering activated charcoal via a nasogastric tube, once the airway is protected.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764 766).

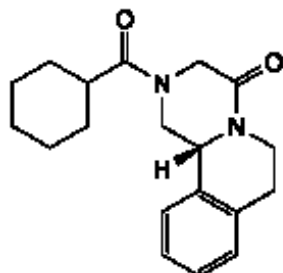
### 5. PHARMACOLOGICAL PROPERTIES

#### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antihelmintics, ATC code: P02BA01

Praziquantel is 2-(cyclohexylcarbonyl)-1,2,3,6,7,11b-hexahydro-4H-pyrazino (2,1a) isoquinolin-4-one. CAS Number: 55268-74-1

Praziquantel is a white crystalline powder of bitter taste. The compound is stable under normal conditions and melts at 136°C-140°C with decomposition. The active substance is hygroscopic. Praziquantel is easily soluble in chloroform and dimethylsulfoxide, soluble in ethanol and very slightly soluble in water. The molecular formula is C<sub>19</sub>H<sub>24</sub>N<sub>2</sub>O<sub>2</sub>. The structural formula is as follows:



### 5.1.1 Pharmacodynamic effects

Animal studies show that praziquantel induces a rapid contraction of schistosomes by a specific effect on the permeability of the cell membrane. The medicine further causes vacuolisation and disintegration of the schistosome tegument. The effect is more marked on the adult than on young worms.

## 5.2 Pharmacokinetic properties

### 5.2.1 Absorption

After oral administration praziquantel is rapidly absorbed (80%). It is, however, subject to first pass effect and extensive metabolism. One hour after administration approximately 6% only of the medicine in serum is in the unmetabolised form. Both the unchanged medicine and the metabolites are excreted primarily by the kidneys. Maximal serum concentration is achieved 1-3 hours after dosing. The half life of praziquantel in serum is 0.8-1.5 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

Hypromellose, macrogol 4000, magnesium stearate, maize starch, microcrystalline cellulose, povidone K25, sodium lauryl sulfate, titanium dioxide (CI77891).

### 6.2 Incompatibilities

Not applicable.

### **6.3 Shelf life**

48 months.

### **6.4 Special precautions for storage**

Not applicable.

### **6.5 Nature and contents of container**

Each brown glass bottle contains 8 tablets.

### **6.6 Special precautions for disposal**

Any unused medicine or waste material should be disposed of in accordance with local requirements.

## **7. MEDICINE SCHEDULE**

Prescription Medicine

## **8. SPONSOR**

Bayer New Zealand Limited

P O Box 2825

Shortland Street

Auckland 1140

New Zealand

Free phone: 0800 233 988

## **9. DATE OF FIRST APPROVAL**

13 September 2012

## **10. DATE OF REVISION OF THE TEXT**

03 July 2023

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### Summary table of changes

<b>Section changed</b>	<b>Summary of new information</b>
4.4, 4.5	Addition of interaction between praziquantel and efavirenz
4.5	Addition of interaction between praziquantel and ritonavir