

PRODUCT INFORMATION

BILTRICIDE®

(praziquantel)

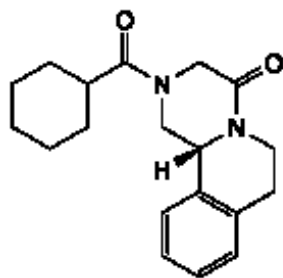
NAME OF THE MEDICINE

praziquantel

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

DESCRIPTION

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 C₁₉H₂₄N₂O₂. The structural formula is as follows:



Biltricide lacquer coated tablets are available as 600 mg of praziquantel.

Besides the active ingredient, Biltricide tablets also contain the following excipients: maize starch, magnesium stearate, microcrystalline cellulose, povidone 25, sodium lauryl sulfate, macrogol 4000, hypromellose, titanium dioxide (C177891).

PHARMACOLOGY

Pharmacodynamic Properties

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

Pharmacokinetic Properties

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 drug in serum is in the unmetabolised form. Both the unchanged drug 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.

INDICATIONS

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

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.

PRECAUTIONS

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.

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.

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 drug 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.

Use in Pregnancy (Category B1)

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.

Use in 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.

Paediatric Use

Safety in children has not been established.

Effects on Ability to Drive or Use Machines

Patients should be warned not to be 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.

INTERACTION WITH OTHER MEDICINES

Praziquantel is believed to be metabolised via the CYP450 enzyme system. Many categories of drugs 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 drugs.

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

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

Co-administration of grapefruit juice and praziquantel is not recommended. Co-administration has been reported to increase praziquantel C_{max} by 1.6 (90% CI 1.05, 2.0)

and AUC by 1.9 (90% CI 1.03, 2.47). The effect of this increase in exposure on efficacy and safety of praziquantel has not been studied.

ADVERSE EFFECTS

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.

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.

	Very Common	Common	Uncommon	Rare	Very Rare
Immune System Disorders					Allergic reaction Polyserositis Eosinophilia
Nervous System Disorders	Headache Dizziness	Vertigo Somnolence			Seizures
Cardiac Disorders					Unspecified arrhythmias
Gastrointestinal Disorders	Gastrointestinal and abdominal pains Nausea Vomiting	Anorexia Diarrhoea (very rarely bloody diarrhoea)			
Skin and Subcutaneous Tissue Disorders	Urticaria	Rash			Pruritus
Musculoskeletal, Connective Tissue and Bone Disorders		Myalgia			
General Disorders and Administrative Site Conditions	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.

DOSAGE AND ADMINISTRATION

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

Schistosoma haematobium
Schistosoma mansoni } 20 mg/kg body weight
three times a day

Schistosoma japonicum at four hourly intervals
Schistosoma mekongi 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.

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.

Children: see PRECAUTIONS

Hepatic impairment: see PRECAUTIONS

Renal impairment: see PRECAUTIONS

OVERDOSAGE

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

Activated charcoal may reduce absorption of the drug 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.

In cases of overdose, it is advisable to contact the Poisons Information Centre (131126) for recommendations on the management and treatment of overdose.

PRESENTATION AND STORAGE CONDITIONS

Biltricide is sold in bottles of 8 tablets.

Biltricide tablets contain 600 mg praziquantel. The tablets are white to pale yellow lacquer-coated oblong shaped tablets with three scores with Bayer on one side and "LG" on the reverse. Store below 25 degrees Celsius.

NAME AND ADDRESS OF THE SPONSOR

BAYER AUSTRALIA LTD
ABN 22 000 138 714

875 Pacific Highway
PYMBLE NSW 2073

POISON SCHEDULE OF THE MEDICINE

Schedule 4 (Prescription Only Medicine)

DATE OF FIRST INCLUSION IN THE ARTG

8 October 1991

DATE OF MOST RECENT AMENDMENT

28 July 2017

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