SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT
Praziquantel Tablets 600 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each tablet contains 600 mg praziquantel.
For a full list of excipients see section 6.1

3. PHARMACEUTICAL FORM
Tablet.
White to off white, capsule shaped, film coated tablets with breaklines on both sides.
The tablet can be divided into equal halves.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Praziquantel Tablets 600mg is indicated in adults and children over 6 years for large scale preventive chemotherapy interventions for the control of schistosomainfectionsdue to various types of blood fluke worms (*Schistosomamansoni, Schistosomahaematobium, Schistosomajaponicum, Schistosomamekongi, Schistosomaintercalatum*) following the recommendations of the WHO Global Programme to Eliminate Schistosomiasis.

Groups targeted for treatment are:
• school-age children (6-15 years of age) in endemic areas
• adults (> 15 years) considered to be at risk in endemic areas from special groups: pregnant and lactating women and groups with occupations involving contact with infested water, such as fishermen, farmers, irrigation workers, or women whose domestic tasks bring them in contact with infested water

• entire communities living in highly endemic areas.

4.2 Posology and method of administration

Dose recommendations in preventive chemotherapy interventionsin school-age children and adults

Height (cm/inches)	**Number of tablets (mg) of Praziquantel Tablets 600mg**
94-109 cm (37-42 inches)	1 tablet (600 mg)
110-124 cm (43-48 inches)	1 ½ tablets (900 mg)
125-137 cm (49-53 inches)	2 tablets (1200 mg)
138-149 cm (54-58 inches)	2 ½ tablets (1500 mg)
150-159 cm (59-62 inches)	3 tablets (1800 mg)
160-177 cm (63-69 inches)	4 tablets (2400 mg)
≥178 cm (>70 inches)	5 tablets (3000 mg)

Recommended treatment strategy for preventive chemotherapy in school-age children and adults
Intervention frequency is determined by the prevalence of infection in school-age children or visible haematuria. In high-transmission areas, treatment may have to be repeated every year for a number of years. Monitoring is essential to determine the impact of control interventions.

Praziquantel Tablets 600mg should be taken once a year in high-risk communities, once every 2 years in moderate-risk communities, and twice during the period of primary schooling age in low-risk communities (e.g. once at entry and once on exit). In low risk communities adults should be treated only if infection is suspected.
High-risk community is defined as detection of intestinal and urinary schistosomiasis ≥50% by parasitological methods or ≥ 30 % by questionnaire for visible haematuria in 50 children from the upper classes of a selection of schools in areas around water.
Moderate-risk community is defined as detection of intestinal and urinary schistosomiasis ≥10% but < 50% by parasitological methods or < 30% by questionnaire for visible haematuria.
Low-risk community is defined as detection of intestinal and urinary schistosomiasis <10% by parasitological methods.

Method of administration

Oral use.

Praziquantel Tablets 600mg should be swallowed whole with some liquid, preferably during or after meals.

Special populations

Liver Disease
Praziquantel Tablets 600mg should be administered with caution to patients with moderate to severe liver impairment (see section 4.4).

Renal Impairment
No dose adjustments for renal impairment are necessary (see section 4.4.).

Elderly
No special precautions are required in the elderly.

Children < 4 years
There is no documented information on the safety of praziquantel for children under 4 years of age (or under 94 cm height). In principle, these children should therefore be excluded from treatment or mass preventive treatment but can be treated on an individual case by case basis by medical personnel.

4.3 Contraindications

Known hypersensitivity to praziquantel or any of the excipients.
Ocular cysticercosis - parasite destruction within the eye may cause serious ocular damage.
Concomitant administration of strong inducers of Cytochrome P450 such as rifampicin (see section 4.5).

4.4 Special warnings and special precautions for use

Caution should be exercised in administering the usual recommended dose of praziquantel to hepatosplenic schistosomiasis patients with moderate to severe liver impairment (Child Pugh Class B and C). Reduced metabolism of praziquantel in these patients may lead to considerably higher and longer lasting plasma concentrations of unmetabolized praziquantel.

Approximately 80% of a dose of praziquantel is excreted in the kidneys, almost exclusively (>99%) in the form of metabolites. Excretion may be delayed in patients with impaired renal function, but accumulation of unchanged drug would not be expected. Therefore, dose adjustment for renal impairment is not considered necessary. Nephrotoxic effects of praziquantel or its metabolites are not known.

Patients suffering from cardiac arrhythmias or cardiac insufficiency treated with digoxin should be monitored during treatment.

Praziquantel should not be used in patients with a history of or suffering from epilepsy and/or other signs of potential central nervous system involvement due to schistosomiasis, paragonimiasis or Taeniasoliumcysticercosis such as subcutaneous nodules of cysticercosis.
Patients with neurocysticercosis should always be treated in hospital because of the risk of pericysticoedema.

The intensity and the severity of the undesirable effects that appear after administration of Praziquantel tablets 600mg may be associated with the level of worm burden (see section 4.8).

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant use of rifampicin should be avoided (see section 4.3). Rifampicin should be discontinued 4 weeks before administration of praziquantel. Rifampicin can be restarted one day after praziquantel treatment. Concomitant administration of drugs that increase the activity of drug metabolizing liver enzymes (Cytochrome P450), e.g. antiepileptic drugs (phenytoin, phenobarbital and carbamazepine), dexamethasone may reduce plasma levels of praziquantel and concomitant use is not recommended.

Concomitant administration of drugs that decrease the activity of drug metabolizing liver enzymes (Cytochrome P450), e.g. cimetidine, ketoconazole, itraconazole, or erythromycin may increase plasma levels of praziquantel.

Chloroquine, when taken simultaneously, may lead to lower concentrations of praziquantel in blood. The mechanism of this drug-drug interaction is unclear.

Drug-food interactions
Praziquantel tablets 600mg should be swallowed whole with some liquid, preferably during or after meals.

Glucose and bicarbonate lower praziquantel bioavailability and serum levels.

Patients should be advised not to drink grapefruit juice on the day of administration of Praziquantel tablets 600mg.

4.6 Fertility, pregnancy and breast-feeding

Pregnancy

In areas where schistosomiasis is endemic, risk-benefit analyses have revealed that the health advantages of treating women of reproductive age and pregnant women far outweigh the risk to their health and to their babies. Evidence also shows that women can be treated with praziquantel at any stage of pregnancy or breast-feeding.
Breast-feeding
Praziquantel has been reported to be excretedin the milk of nursing women. Women should not breast-feed on the day of treatment with Praziquantel tablets 600mg and during the subsequent 24 hours.

Fertility
Reproduction studies performed so far in rat and rabbits have revealed no evidence of impaired fertility (see section 5.3)

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive or use machines have been performed. Patients should be warned about the potential for dizziness, somnolence or seizures (see section 4.8) while taking Praziquantel tablets 600mg and should be advised not to drive or operate machines if any of these symptoms occur on the day of treatment.

4.8 Undesirable effects

The following adverse reactions have been observed and reported during treatment with praziquantel with the following frequencies: Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000), not known (cannot be estimated from the available data).

The most frequently (>1/10) reported adverse reactions are headache, dizziness, fatigue, abdominal pain, nausea, vomiting, and urticaria.

System Organ Class	Very common	Common	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		Bloody diarrhoea
Hepatobiliary disorders			Liver function tests increased	
Skin and subcutaneous tissue disorders	Urticaria			
Musculoskeletal and connective tissue disorders		Myalgia		
General disorders and administration site conditions	Fatigue	Feeling unwell (asthenia, malaise)		

* In cysticercosis, death of the cysts results in local inflammation and oedema. Within the brain, this oedema can simulate an acute space-occupying lesion.

Side effects may be more frequent and/or serious in patients with a heavy worm burden. It is often not clear whether the complaints reported by patients or the undesirable effects reported by the health care provider are caused by praziquantel itself, or may be considered to be an endogenous reaction to the death of the parasites produced by praziquantel, or are symptomatic observations of the infestation.

4.9 Overdose

Information on over dosage in humans is not available.

Treatment
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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antihelmintics, ATC code: P02B A01
Mechanism of action
Praziquantel is a chinolin derivative and induces a rapid contraction of schistosomes by a specific effect on the permeability of the cell membrane. The drug further causes vacuolization and disintegration of the schistosome tegument. The effect is more marked on adult than on young worms.

5.2 Pharmacokinetic properties

Absorption and bioavailability
After oral administration praziquantel is rapidly absorbed. It undergoes first-pass metabolism and 80% of the dose is excreted mainly as metabolites in the urine within 24 hours.
Following single dose administration of 2 tablets Praziquantel tablets 600mg in two sequences (full replicate design), used to compare the bioavailability of this product with the same dose of the reference formulation, mean Cmax (± SD) values of praziquantel were 1363 ng/ml (±880) at T1 and 1372 ng/ml (±962) at T2 and the corresponding AUC values were 2938 ng.h/ml (±1607) at T1 and 3098 ng.h/ml (±1936) at T2. The mean (± SD) tmax values were 2.44 (±1.74) hours and 2.55 (±1.36) hours at T1 and T2, respectively.

Distribution
Praziquantel is 80% bound to serum proteins. It passes the blood-brain barrier and liquor concentration is about 14–20% of the concurrent total (free plus protein-bound) plasma concentration. Praziquantel is excreted in the milk of nursing mothers in concentrations about 25% of maternal serum concentrations.

Metabolism
Praziquantel is subject to first pass effect and extensive metabolism in the liver, mainly via the cytochrome P450 isoenzymes CYP2B1 and CYP3A4. One hour after administration only approximately 6% of the medicine in serum is in the unmetabolised form.

Elimination
Approximately 80% of a dose of praziquantel is excreted in the kidneys within four days, almost exclusively (>99%) in the form of metabolites. Excretion might be delayed in patients with impaired renal function, but accumulation of unchanged drug would not be expected.

Pharmacokinetics in hepatic impairment
The pharmacokinetics of praziquantel were studied in 40 patients with Schistosomamansoni infections with varying degrees of hepatic dysfunction. In patients with schistosomiasis, the pharmacokinetic parameters did not differ significantly between those with normal hepatic function (Group 1) and those with mild (Child-Pugh B) hepatic impairment. However, in patients with moderate-to-severe hepatic dysfunction (Child-Pugh Class B and C), praziquantel half-life, Cmax, and AUC increased progressively with the degree of hepatic impairment. In Child-Pugh class B, the increases in mean half-life, Cmax, and AUC relative to Group 1 were 1.58-fold, 1.76-fold, and 3.55-fold, respectively. The corresponding increases in Child-Pugh class C patients were 2.82-fold, 4.29-fold, and 15-fold for half-life, Cmax, and AUC.

5.3 Preclinical safety data

Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the human exposure indicating little relevance to clinical use.

Carcinogenesis
Mutagenic effects in Salmonella tests found by one laboratory have not been confirmed in the same tested strain by other laboratories. Long term carcinogenicity studies in rats and golden hamsters did not reveal any carcinogenic effect.

Reproductive toxicity
Reproduction studies have been performed in rats and rabbits at doses up to 40 times the human dose and have revealed no evidence of impaired fertility or harm to the foetus due to praziquantel.
An increase of the abortion rate was found in rats at three times the single human therapeutic dose.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients

Core tablet: Microcrystalline cellulose, pregelatinized starch, sodium lauryl sulfate, povidone, magnesium stearate.

Tablet coating: Hypromellose, polyethylene glycol, titanium dioxide

6.2 Incompatibilities
Not applicable.

6.3 Shelf life

48 months
For 100 count bottle pack: Should be used within 28 days after opening.
For 500 count bottle pack: Should be used within 85 days, once opened

Blister Pack - Keep blisters in the provided outer carton to protect from light

6.4 Special precautions for storage

Store below 30°C in a dry place. Protect from light.
Keep blisters in the provided outer carton to protect from light.

6.5 Nature and contents of container

The tablets are supplied in:
Blister packs of clear film PVC/PVdC 250/60 with 60 GSM PVdC - plain 25-micron aluminium foil. Each Blister pack consists of 10 tablets; 9 and 10 such blisters are packed in a box.

HDPE containers: 200cc or 850cc round, white, containers with 38 mm or 53 mm polypropylene child resistant/continuous thread closure with pulp, HS 123 white printed liner, polyester coil 12g/yard. (Pack sizes: 100 and 500 tablets).

6.6 . Instructions for use and handling and disposal

No special requirements.
Any unused product or waste material should be disposed of in accordance with local requirements.

7. SUPPLIER
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January 2018
Section 6 updated in March 2019

Detailed information on this medicine is available on the World Health Organization (WHO) web site:
https://extranet.who.int/prequal/

Reference list

General reference:

This text is primarily based on:
WHO model prescribing information; Drugs used in parasitic diseases, Second edition, WHO Geneva, 1995
at:http://apps.who.int/medicinedocs/en/d/Jh2922e/3.8.1.html

Preventive chemotherapy in human helminthiasis available at:
http://apps.who//iris/bitsream/10665/43545/1/924154703_eng.pdf

Prevention and control of schistosomiasis and soil-transmitted helminthiasis. Report of a WHO Expert Committee. Geneva, World Health Organization, 2002 (WHO Technical Report Series, No. 912).
Preventive chemotherapy in human helminthiasis, ISBN 92 4 154710 3
Dollery Colin: Therapeutic Drugs 2nd edition, Edinburgh, London, New York, Philadelphia, San Francisco, Sidney, Toronto; Churchill Livingstone 1999: Praziquantel, p 184-189
Martindale. The Complete Drug reference, 38th edition, 2014, Vol A p164-165; ISBN 9780857111395
Bayer. Biltricide (praziquantel) tablets prescribing information. 2011 Bayer healthcare Pharmaceuticals Inc.

http://www.drugs.com/monograph/praziquantel.html

Product Monograph, Biltricide, Bayer , May 9 2017 available at http://omr.bayer.ca/omr/online/biltricide-pm-en.pdf