

1.4 Product Information

1.4.1 Prescribing Information

Summary of Product Characteristics

1. Name of the medicinal product

Praziquantel Tablets USP 600mg

2. Qualitative and quantitative composition

Each film-coated tablet contains 600 mg of Praziquantel USP

For the full list of excipients, see section 6.1

3. Pharmaceutical form

Film Coated Tablet

White to orange tinged, oblong, film-coated tablets with three scores on one side and two scores on the other side. The tablet is de-bossed with “P8” on one side and “H” on the other side.

The tablet can be divided into equal halves.

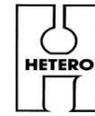
4. Clinical Particulars

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 schistosoma infections due to various types of blood fluke worms (*Schistosomamansoni*, *Schistosomahaematobium*, *Schistosomajaponicum*, *Schistosomamekongi* and *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 interventions in school-age children and adults

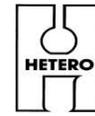
| Height (cm/inches) | Number of tablets (mg) of Praziquantel Tablets USP 600mg |
|---------------------------|---|
| 94-109 cm (37-42 inches) | 1 tablet (600 mg) |
| 110-124 cm (43-48 inches) | 1 ½ tablets (900 mg) |
| 125-137 cm (49-53 inches) | 2 tablets (1200 mg) |
| 138-149 cm (54-58 inches) | 2 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 $\geq 50\%$ by parasitological methods or $\geq 30\%$ 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 \geq 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.

Renal Impairment

No dose adjustments for renal impairment are necessary.

Elderly

No special precautions are required in the elderly.

Children $<$ 4 years

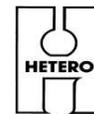
There is no documented information on the safety of praziquantel for children under 4 years of age (or under 94 cm height). In principle, these children should therefore be excluded from treatment or mass preventive treatment but can be treated on an individual case by case basis by medical personnel.

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.

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 Taeniasolium cysticercosis 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.

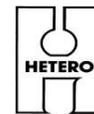
4.5 Interaction with other medicinal products and other forms of interactions

Concomitant use of rifampicin should be avoided. 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 lactation

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 excreted in 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

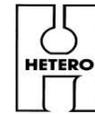
Reproduction studies performed so far in rat and rabbits have revealed no evidence of impaired fertility.

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 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 ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1,000$ to $< 1/100$); rare ($\geq 1/10,000$ to $< 1/1,000$); very rare ($< 1/10,000$), not known (cannot be estimated from the available data).

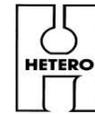
ZIQUANTA (Praziquantel Tablets USP 600mg)**Module 1-Administrative Information And Product Information**

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

| System Class | Organ | 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 | | Fatigue | Feeling unwell | | |

ZIQUANTA (Praziquantel Tablets USP 600mg)

Module 1-Administrative Information And Product Information



| | | | | |
|--|--|-----------------------------|--|--|
| disorders and administration site conditions | | (asthenia,malaise) Fever | | |
|--|--|-----------------------------|--|--|

* 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: Anti-Helminthics, ATC code: P02BA01

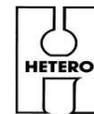
Mechanism of action

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 C_{max} (\pm SD) values of praziquantel were 1363 ng/ml (\pm 880) at T1 and 1372 ng/ml (\pm 962) at T2 and the corresponding AUC values were 2938 ng.h/ml (\pm 1607) at T1 and 3098 ng.h/ml (\pm 1936) at T2. The mean (\pm SD) t_{max} values were 2.44 (\pm 1.74) hours and 2.55 (\pm 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

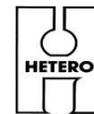
Praziquantel is subject to first pass effect and extensive metabolism in the liver, mainly via the cytochrome P450 isoenzymes CYP2B1 and CYP3A4. One hour after administration only approximately 6% of the medicine in serum is in the unmetabolised form.

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, C_{max}, and AUC increased progressively with the degree of hepatic impairment. In Child-Pugh class B, the increases in mean half-life, C_{max}, 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, C_{max}, 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

Pre gelatinized starch, Povidone, Sodium lauryl sulphate, Purified water, Magnesium stearate, Microcrystalline cellulose, Opadry white 03F580079.

Film coating Opadry white 03F580079 ingredients are: Hypromellose, Titanium dioxide, Macrogol

6.2 Incompatibilities

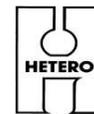
Not applicable.

6.3 Shelf life

24 Months

6.4 Special precautions for storage

Store below 30°C.



6.5 Nature and contents of container

Container pack:

6's Count: 40cc H.W HDPE container with 33mm CR closure with purified cotton.

100's Count: 200cc H.W HDPE container with 38mm CR closure with purified cotton.

500's Count: 750cc H.W HDPE container with 53mm CT closure with purified cotton.

1000's Count: 1500cc H.W HDPE container with 53mm CT closure with purified cotton.

Blister pack:

1 x 6's and 10 x 10's Alu-Alu Blister pack: Cold Form foil (60 μ PVC/45 μ aluminium/25 OPA) - 25 μ plain aluminium foil.

6.6 Special precautions for disposal and other handling

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

7. SUPPLIER

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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).