PROFESSIONAL INFORMATION FOR PRAZIBIL 600

SCHEDULING STATUS

S4

1 NAME OF THE MEDICINE

PRAZIBIL 600 film coated tablet

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains praziquantel 600 mg.

PRAZIBIL 600 is sugar free.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

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

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

Patients with renal impairment:

See **section 4.4**.

Patients with hepatic 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

The tablets should be swallowed whole with a little liquid, preferably during or after meals. With single daily doses it is recommended to take the 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 contains 150 mg of active ingredient, so that the dosage can be easily adjusted to the patient's bodyweight.

4.3 Contraindications

- Known hypersensitivity to praziquantel or to any of the excipients of **PRAZIBIL 600** (see **section 6.1**).
- **PRAZIBIL 600** 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

Since 80 % of **PRAZIBIL 600** and its metabolites are excreted in the kidneys, excretion might be delayed in patients with impaired renal function.

In uncompensated liver insufficiency and in patients with hepatosplenic schistosomiasis, caution should be taken, since due to reduced drug metabolisation in the liver, considerably higher and longer lasting concentrations of unmetabolised **PRAZIBIL 600** 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 **PRAZIBIL 600** can exacerbate central nervous system pathology due to schistosomiasis, paragonimiasis or Taenia sodium 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 systems involvement such as subcutaneous nodules suggestive of cysticercosis.

The patient ability to drive or to operate machinery may be temporarily impaired.

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 Interaction with other medicine and other forms of interaction

Concomitant administration of medicines increasing the activity of drug metabolising liver enzymes (Cytochrome P450), e.g. antiepileptic medicines, dexamethasone may reduce plasma levels of PRAZIBIL 600

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

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 **PRAZIBIL 600.**

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

Pregnancy

Safety in pregnancy has not been established.

Breastfeeding

PRAZIBIL 600 appears in the milk or breastfeeding women at a concentration of 20 – 25 % or 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 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 **PRAZIBIL 600**; furthermore, they are dependent on the parasite species, extent of parasitisation, duration of infection and localisation of the parasites in the body.

b) Tabulated summary of adverse reactions

Immune system disorders
Less frequent: Allergic reaction polyserositis, eosinophilia
Nervous system disorders
Frequent: Headache, dizziness, vertigo, somnolence (including drowsiness)
Less frequent: Seizures

Cardiac disorders
Less frequent: Unspecific dysrhythmias
Gastrointestinal disorders
Frequent: Gastrointestinal and abdominal pains, nausea, vomiting, anorexia, diarrhoea
Less frequently: Bloody diarrhoea
Skin and subcutaneous tissue disorders

Frequent: Urticaria, rash
Less frequent: Pruritus
Musculoskeletal and connective tissue disorders
Frequent: Myalgia
General disorders and administration site conditions
Frequent: Asthenia, Fatigue, feeling unwell

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. Health care providers are asked to report any suspected adverse reactions via the "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za and to the Holder of certificate of registration through the mail: pvg.cdma@heterogroups.com

4.9 Overdose

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 PROPERTIES

5.1 Pharmacodynamic properties

Category and Class: A.12. Anthelmintics, Bilharzia medicines, Filaricides, etc.

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.

Biotransformation:

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

Elimination:

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.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Magnesium stearate
- Microcrystalline cellulose
- Povidone
- Pregelatinized starch
- Sodium lauryl sulphate
- Purified water
- Opadry white 03F580079 (consists of HPMC 2910/hypromellose, titanium dioxide, macrogol/PEG)

6.2 Incompatibilities

- Not applicable.

6.3 Shelf life

- 24 months.

6.4 Special precautions for storage

- Store at or below 25 °C.
- Keep the tablets in the original container until required for use.
- This medicine does not require any special storage conditions.

6.5 Nature and contents of container

- **HDPE bottle:**

  Tablets are pack in a white opaque high density polyethylene container (HDPE) container with white opaque polypropylene, ribbed, child resistant plastic cap with pulp liner.

  Pack size: 6's, 100's, 500's and 1000's.

- **Bulk pack:**

  Tablets are pack in a clear transparent polyethylene (poly bag), plain triple laminated bag with open mouth and heat-sealed bottom containing 5 grams of silica gel sachet.

  Pack size: 500's.

- **Blister strips:**

  Blister strips of PVC/Aluminium/OPA forming film and plain aluminium lidding foil, containing 10 tablets per blister.

  Pack sizes: 10 tablets per blister. 10's x 10 blisters packed in a box.

  HDPE bottle and blister strips are enclosed in an outer carton box.

  Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

- No special requirements

7 HOLDER OF CERTIFICATE OF REGISTRATION

Hetero Drugs South Africa (Pty) Ltd

Waterfall Corporate Campus

Building No. 2, First floor

74 Waterfall Drive

Midrand

2066

8 REGISTRATION NUMBER(S)

57/12/0056

9 DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

10 JUNE 2025

10 DATE OF REVISION OF THE TEXT

TBA