PROFESSIONAL INFORMATION

SCHEDULING STATUS: S4

1. NAME OF THE MEDICINE

QUANTIMAK 600 (Film-coated tablet)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains Praziquantel 600 mg

Sugar free

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Film coated tablet

White to off-white, capsule shaped, film coated tablets with breakline on both side. The breakline is included for dosage adjustment.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

QUANTIMAK 600 is indicated for the treatment of:

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

Renal and Hepatic impairment:

Refer to 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.

QUANTIMAK 600 should be swallowed whole with a little liquid, preferably during or after meals. With single daily doses it is recommended to take **QUANTIMAK 600** in the evening. If ingestion of **QUANTIMAK 600** several times a day is prescribed, the interval between administrations should not be less than 4 hours and not more than 6 hours.

When broken each of the segments of the tablet contains 300 mg of praziquantel, so that the dosage can be easily adjusted to the patient's body weight.

4.3 Contraindications

QUANTIMAK 600 is contraindicated:

- in patients with a known hypersensitivity to praziquantel or to any of the excipients listed in section 6.1.
- 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 **QUANTIMAK 600**
- with concomitant administration of strong inducers of Cytochrome P 450 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 praziquantel as in **QUANTIMAK 600** and its metabolites are excreted in the kidneys, excretion might be delayed in patients with impaired renal function, but accumulation of unchanged drug would not be expected. Therefore, dosage adjustment for renal impairment is not considered necessary. Nephrotoxic effects of praziquantel or its metabolites 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 unmetabolized 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.

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 **QUANTIMAK 600** 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 systems involvement such as subcutaneous nodules suggestive of cysticercosis.

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 medicines 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 **QUANTIMAK 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 P 450) e.g. cimetidine, ketoconazole, itraconazole, erythromycin, may increase plasma levels of **QUANTIMAK 600**

Chloroquine, when taken simultaneously, can lead to lower concentrations of **QUANTIMAK 600** in blood. The mechanism of this drug-drug interaction in unclear.

Grapefruit juice was reported to produce a 1, 6 fold increase in the C_{max} and a 1, 9 fold increase in the AUC of praziquantel. However, the effect of this exposure increase on the therapeutic effect and safety of praziquantel has not been systemically evaluated.

4.6 Fertility, pregnancy and lactation

Pregnancy

Safety in pregnancy has not been established. (see section 4.3)

Breast feeding

Praziquantel appears in the milk of breastfeeding women at a concentration of 20-25 % of 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.

Fertility

There is no data currently available.

4.7 Effects on ability to drive and use machines

The patient's ability to drive or to operate, machinery may be temporarily impaired. Dizziness, vertigo and drowsiness may occur with **QUANTIMAK 600**, and this may affect the patient’s ability to drive and operate machinery (see section 4.8)

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

Summary of the safety profile

Side effects vary according to dose and duration of **QUANTIMAK 600**; furthermore, they are dependent on the parasite species, extent of parasitisation, duration of infection and localisation of the parasites in the body.

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.

Tabulated summary of adverse reactions

System organ class	**Frequent**	**Less frequent**	**Frequency unknown**
Immune system disorders	-	Allergic reactions, Polyserositis, Eosinophilia	-
Nervous system disorders	Headache, Dizziness Vertigo, Somnolence (including drowsiness)	Seizures	-
Cardiac disorders	-	Unspecified dysrhythmias (bradycardia, ectopic rhythms, ventricular fibrillation, AV blocks).	-
Gastrointestinal disorders	Gastro-intestinal and abdominal pains, Nausea, Vomiting	bloody diarrhoea	-

	Anorexia, Diarrhoea		
Skin and subcutaneous tissue disorders	Urticaria	Pruritis	-
Musculoskeletal connective tissue and bone disorders	Myalgia	-	-
General disorders and administration site conditions	Asthenia, Feeling unwell, Rise in temperature	-	-

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 to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website or to Macleods Pharmaceuticals SA (Pty) Ltd. at safety@macleodspharma.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

Pharmacotherapeutic group – Quinoline derivatives and related substances;

ATC code: P02BA01

Mechanism of action

Praziquantel is a treamtodicide.

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 0,6µM/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

Tablet core contains:

Magnesium stearate, microcrystalline cellulose, povidone, pregelatinized starch, sodium lauryl sulphate.

Coating material contains:

Hypromellose, polyethylene glycol, titanium dioxide.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

48 months for container pack from manufacturing date.

36 months for blister pack from manufacturing date.

6.4 Special precautions for storage

Store below 30 °C in a dry place.

Protect from light.

Keep the HDPE container tightly closed.

Keep the blister in the outer carton until required for use.

KEEP OUT OF REACH OF CHILDREN

6.5 Nature and contents of container

HDPE container pack

Tablets are packed in a round white opaque HDPE container closed with continuous thread closure with pulp and heat seal liner.

Pack size include 500 tablets.

Blister pack

Tablets are packed in PVC/PVdC as forming material and aluminium foil as lidding material.

Pack size include 4 tablets or 10 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

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

7. HOLDER OF CERTIFICATE OF REGISTRATION

MACLEODS PHARMACEUTICALS SA (PTY) LTD

GROUND FLOOR, BLOCK 1,

BASSONIA ESTATE OFFICE PARK (EAST),

1 CUSSONIA DRIVE,

BASSONIA ROCK EXT 12

ALBERTON

GAUTENG

8. REGISTRATION NUMBERS

QUANTIMAK 600: 56/12/1162

9. DATE OF FIRST AUTHORISATION

QUANTIMAK 600: 17 September 2024

10. DATE OF REVISION OF THE TEXT

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PM0237