SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Bermoxel 600 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 600mg praziquantel.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet.
White, capsule shaped tablets, scored on one side and embossed MC on the other.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Parasitic infestations by trematodes, of which:

- Bilharziases: *Schistosoma haematobium, Schistosoma intercalatum, Schistosoma japonicum, Schistosoma mansoni* .
- Distomatoses: *Clonorchis sinensis, Opisthorchis viverrini, Paragonimus westermani*

4.2. Posology and method of administration

Posology

The dosage varies according to the parasite:

Schistosoma haematobium	A single dose of 40 mg per kg of body weight
Schistosoma mansoni, Schistosoma intercalatum	A single dose of 40 mg or 2 doses of 20 mg per kg of body weight administered every 24 hours.
Schistosoma japonicum	A single dose of 60 mg or 2 doses of 30 mg per kg of body weight every 24 hours.
Clonorchis sinensis, Opisthorchis viverrini	3 doses of 25 mg per kg of body weight given in 24 hours
Paragonimus westermani	3 x 25 mg/day per kg of body weight for 2 days

Pediatric population

Safety in children under 1 year of age has not been established. Currently available data is described in section 5.1.

Method of administration

For oral administration.

The tablets should be swallowed whole, with a little liquid, preferably during or after meals.

In order to prevent choking in children under 6 years old, the tablets may be crushed or broken up and mixed with semi-solid food or liquid.

For the once-daily dosing, it is recommended take the tablets in the evening.

If ingestion of tablets several times a day is prescribed, the interval between administration should not be less than 4h and not more than 6h.

The number of tablets needed can be calculated from the following table:

Body weight (kg)	No. of tablets (=20mg/kg)	Body weight (kg)	No. of tablets (=25mg/kg)	Body weight (kg)	No. of tablets (=30mg/kg)
20-25/26	3/4	22-26	1	24-28	1 1/4
26/27-33	1	27-33	1 1/4	29-33	1 1/2
34-41	1 1/4	34-38	1 1/2	34-37	1 3/4
42-48	1 1/2	39-44	1 3/4	38-43	2
49-56	1 3/4	45-50	2	44-48	2 1/4
57-63	2	51-56	2 1/4	49-53	2 1/2
64-70	2 1/4	57-62	2 1/2	54-56	2 3/4
71-78	2 1/2	63-68	2 3/4	58-63	3
79-86	2 3/4	69-75	3	64-67	3 1/4

4.3. Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1

Ocular cysticercosis,

Co-administration of rifampicin: rifampicine is a potent inducers of cytochrome P450, and therefore therapeutically effective plasma concentrations of praziquantel may not be reached (see section 4.5).

4.4. Special warnings and precautions for use

Bilharziases during invasion phase

Praziquantel lacks efficacy against migrant schistosomula in Schistosomiasis (bilharzia). Consequently, praziquantel is not effective when administered during acute schistosomiasis. In addition, the use of praziquantel in the acute phase of schistosomiasis may be associated with paradoxical reactions (Jarisch-Herxheimer-like reactions: sudden inflammatory immune response probably caused by the release of schistosome antigens). This can lead to potentially life-threatening myocarditis, encephalitis and lung involvement.

Central nervous effects

When schistosomiasis or fluke infection is found in patients living in or coming from areas where cysticercosis is endemic, the patient should be taken up in the hospital for the duration of treatment with praziquantel. As a result of the activity on Taenia solium larvae cysticercosis, praziquantel can worsen the potential of the eye or involvement of the central nervous system. Praziquantel can worsen cysticercosis produced by schistosomiasis, Paragonimiasis or Taenia solium due to the pathological effects on the central nervous system. Therefore, this drug should usually not be administered to patients with a history of epilepsy and / or other signs of potential involvement of the central nervous system, such as subcutaneous nodules indicative of cysticercosis.

Heart rhythm disorders

During treatment with praziquantel, patients with heart rhythm disorders or a history of arrhythmias should be monitored.

Renal failure

Considering that 80% of praziquantel and its metabolites are excreted renally , excretion may be delayed in patients with renal impairment.

Liver failure and hepatosplenic schistosomiasis

Praziquantel must be administered with caution in patients with severe hepatic impairment and in patients with hepatosplenic schistosomiasis; in fact, blood levels substantially higher and persistent un-metabolized praziquantel can be observed because of the decreased hepatic metabolism of praziquantel thus resulting in an extension of plasma half - life.

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say it is essentially “sodium-free”.

4.5. Interactions with other medicinal products and other forms of interaction

Contraindicated combinations

Rifampicin: there is a dramatic decrease in plasma concentrations of praziquantel, with the risk of treatment failure by increasing the hepatic metabolism of praziquantel by rifampicin. The effective plasma concentrations of praziquantel may not be achieved (see section 4.3).

Combinations not recommended:
Enzyme inducing anticonvulsants (carbamazepine, phenytoin, Phenobarbital, primidone): due to marked decrease in plasma concentration of praziquantel, with a risk of treatment failure due to increased praziquantel hepatic metabolism.

Concomitant use with efavirenz is not recommended due to significant decrease in plasma concentrations of praziquantel, with risk of treatment failure due to increased hepatic metabolism by efavirenz. In case the combination is needed, an increased dose of praziquantel could be considered.

Combinations subject to precautions for use
Dexamethasone: Decrease in plasma concentrations of praziquantel, with a risk of treatment failure, due to its hepatic metabolism increased by dexamethasone. Treatment with dexamethasone should be discontinued at least one week prior to administration of praziquantel.
When co-administered with grapefruit juice, increases in exposure to praziquantel less than twice the usual concentrations have been observed in a clinical study.
Concomitant administration of cytochrome P450 inhibitors medications, such as cimetidine, ketoconazole and itraconazole may increase plasma concentrations of praziquantel by decreasing hepatic metabolism.

4.6. Fertility, pregnancy and lactation

Pregnancy
Animal studies have found no embryotoxic or teratogenic effects.
A large number of women treated without damaging effects has been reported in the literature.
In accordance with WHO publication on praziquantel risk-benefit analysis, it has been shown that the benefits of treating fertile and pregnant women are much greater than the risks to their health and the health of their babies, where schistosomiasis and soil helminthiasis are endemically transmitted. The benefit of praziquantel treatment in pregnant women consists of less anemia in the mothers and improvement of birth weight and survival of the baby. Consequently, praziquantel can be used during pregnancy, as clinically necessary.

Breast-feeding
Praziquantel is excreted 0.0008% in milk.

It is not known if can cause a pharmacological effect in infants.
For a short duration treatment, breast- feeding should be discontinued during treatment and for the subsequent 24 hours.

Fertility
There are no clinical data on fertility.
Praziquantel has shown no effect on fertility in animal studies.

4.7. Effects on ability to drive and use machines

Praziquantel has moderate influence on the ability to drive and use machines. Patients should be aware that side effects such as dizziness, lightheadedness, or drowsiness may occur after taking praziquantel. Therefore it is recommended to avoid driving or operating machinery during the treatment period and for 24 hours after treatment discontinuation (see section 4.8)

4.8. Undesirable effects

Side effects are depending on dosage and duration of treatment, the type of parasite, severity of infection, length of infection and location of the parasites in the body.

The side effects are only observed during post-marketing surveillance and they are based on publications and spontaneous reports.
For the side effects a frequency cannot be determined, they are listed under ' Not known' (*cannot be estimated from the available data)*.

System / Organ Class	***Not known***
Blood and lymphatic system disorders	Eosinophilia
Immune system disorders	Allergic reaction
Nervous system disorders	Headache Dizziness Vertigo Drowsiness Seizures
Cardiac disorders	Arrhythmia
Gastrointestinal disorders	Gastrointestinal pain Abdominal pain

	Nausea Vomiting Anorexia Diarrhea Bloody diarrhea
Skin and subcutaneous tissue disorders	Urticaria Pruritus Rash
Musculoskeletal and connective tissue disorders	Myalgia
General disorders and administration site conditions	Fatigue Malaise Fever

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

4.9. Overdose

There are no available data on human overdose.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: anthelmintic, ATC code: P02BA01.

Praziquantel is effective against most trematodes pathogenic for humans, such as:

- *Schistosoma haematobium, Schistosoma mansoni, Schistosoma japonicum, Schistosoma intercalatum;*
- Other species of trematodes such as liver flukes like: *Clonorchis sinensis, Opistorchis viverrini;*
- Lung flukes such as *Paragonimus westermani.*

In vitro experiments enabled to define the mode of action of praziquantel: from 0.4µg/ml, an immediate contraction is observed, followed by an immobilization of the parasite as soon as it is in contact with the product solution. An intense vacuolization of the schistosome tegument occurs.

Paediatric population

Post-marketing experience indicates that children (aged 1 to 17 years) are likely to experience side effects similar to those seen in adults when taking praziquantel.

A review of treatment programs in endemic areas was conducted by WHO which analyzed data on more than 3,000 preschool children (up to 7 years) who received praziquantel for the treatment of schistosomiasis (due to *S. haematobium* and *S. mansoni*). The reported side effects were mild and transient and it was concluded that praziquantel was well tolerated in preschool children.

5.2. Pharmacokinetic properties

Praziquantel is rapidly absorbed after oral administration. Maximum serum concentration is achieved 1 - 3 hours after intake.. The active principle is rapidly and completely metabolized, the elimination half-life of unchanged praziquantel in serum being from 1 – 1,5 hours. Over 80% of the dose administered is eliminated by the kidneys within 4 days, 90% of this amount within the first 24 hours.

In breastfeeding women, the plasma concentrations of praziquantel are on average 4 times higher than those found in milk. Only 0.0008% of the dose administered is eliminated in milk.

The excretion of praziquantel (approximately 80% is excreted by the kidney) may be delayed in patients with impaired renal function.

In case of hepatocellular insufficiency, reduced metabolism of praziquantel may lead to an increase in its plasma half-life.

5.3. Preclinical safety data

Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Povidone, Croscarmellose sodium, Sodium lauryl sulphate, Microcrystalline cellulose, Colloidal anhydrous silica, and Magnesium stearate.

6.2. Incompatibilities

None known.

6.3. Shelf life

5 years

6.4. Special precautions for storage

Store below 25ºC in the original package, in order to protect from light.

6.5. Nature and contents of container

Blisters of polyvinylchloride (PVC) and aluminium, in packs with 6 and 20 tablets are available. Plastic securitainers with 100 and 500 loose tablets, are also available.

Not all pack sizes may be marketed.

6.6. Special precautions for disposal

None.

7. MARKETING AUTHORISATION HOLDER

MEDOCHEMIE LTD, 1-10 Constantinoupoleos street, 3011 Limassol, Cyprus.

8. MARKETING AUTHORISATION NUMBER

07268/08298/REN/2021

9. DATE OF FIRST AUTHORISATION /RENEWAL OF THE AUTHORISATION

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