WHO-PQ RECOMMENDED SUMMARY OF PRODUCT CHARACTERISTICS

This summary of product characteristics focuses on uses of the medicine covered by WHO's Prequalification Team - Medicines. The recommendations for use are based on WHO guidelines and on information from stringent regulatory authorities.[*]

The medicine may be authorised for additional or different uses by national medicines regulatory authorities.

[*]https://extranet.who.int/prequal/sites/default/files/document_files/75%20SRA%20clarification_Feb2017_newtempl.pdf

1. NAME OF THE MEDICINAL PRODUCT

[NT011 trade name]†

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains praziquantel 600 mg

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film coated tablets

[NT011 trade name] is white to orange tinged, oblong, film-coated tablet. They are biconvex (rounded on top and bottom) with a bevelled edge. The tablets are plain on the other side with three break lines on one side with "P8" debossed (stamped into the tablet) and two scores with "H" debossed (stamped into the tablet) on the other side.

The break line can be used to divide [NT011 trade name] into either two or four equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

[NT011 trade name] is used for the following parasitic infections:

- **Schistosomiasis (blood fluke infection)**

  [NT011 trade name] is indicated for the treatment and prevention of infections due to various types of blood flukes (*Schistosoma mansoni, S. haematobium, S. japonicum, S. mekongi, S. intercalatum*).

- **Taeniasis (tapeworm infection)**

  [NT011 trade name] is indicated for treatment and prevention of *Taenia solium* infection.

- **Neurocysticercosis (tapeworm infection affecting the brain)**

  [NT011 trade name] is indicated for treatment *Taenia solium* neurocysticercosis.

- **Foodborne trematodiasis (flatworm infections)**

  [NT011 trade name] is indicated for the treatment and prevention of **clonorchiasis** and **opisthorchiasis** (liver fluke infections).

  [NT011 trade name] can also be used for treating **paragonimiasis** (lung fluke infection).

Treatment and community prevention programmes should follow authoritative guidelines including those issued by WHO.

4.2 Posology and method of administration

Posology

The recommended dose of praziquantel depends on the therapeutic indication.

† Trade names are not prequalified by WHO. This is the national medicines regulatory agency's responsibility.

Schistosomiasis

Treatment and prevention

For treating schistosomiasis (blood flukes) in an individual or for mass drug administration in areas where schistosomiasis is endemic, the dose is:

> 40 mg/kg as a single dose. For mass drug administration, the dose is repeated annually (or at 6-month intervals if response to annual treatment is inadequate)

This dose can also be used for children in communities where both schistosomiasis and taeniasis are endemic.

To facilitate administration, the individual's height can be used to determine the appropriate dose:

Height	**Praziquantel dose**	
	As 600-mg tablet	**In mg of praziquantel**
94–109 cm	1 tablet as a single dose	600 mg as a single dose
110–124 cm	1½ tablets as a single dose	900 mg as a single dose
125–137 cm	2 tablets as a single dose	1200 mg as a single dose
138–149 cm	2½ tablets as a single dose	1500 mg as a single dose
150–159 cm	3 tablets as a single dose	1800 mg as a single dose
160–177 cm	4 tablets as a single dose	2400 mg as a single dose
178 cm or taller	5 tablets as a single dose	3000 mg as a single dose

Taeniasis

Treatment and prevention

For treating taeniasis (tapeworm infection) in an individual or for controlling *Taenia solium* infection in communities where taeniasis is endemic, the dose is:

> 10 mg/kg as a single dose.

In communities where taeniasis as well as soil-transmitted helminths are endemic, preventative treatment with praziquantel and albendazole (also given as a single dose) may be considered.

Neurocysticercosis

Treatment

For treating *Taenia solium* neurocysticercosis, praziquantel is given in combination with albendazole. The dose of praziquantel is:

> 50 mg/kg daily, divided in 2–3 doses for 1–2 weeks in parenchymal disease, or for longer than 1 month for subarachnoid involvement.

Concomitant corticosteroid treatment is usually recommended. However, praziquantel should **not be given** in patients with pronounced inflammation caused by parenchymal cysts (see section 4.4).

Foodborne trematode infections

Treatment

For treating **clonorchiasis, opisthorchiasis** (liver flukes), the dose is:

> 25 mg/kg 3 times daily for 2–3 days

For treating **paragonimiasis** (lung fluke) the dose is:

> 25 mg/kg 3 times daily for 3 days.

Prevention

For preventing **clonorchiasis** and **opisthorchiasis** among all residents in areas where infection appears to be clustered, the dose is:

40 mg/kg as a single dose, repeated every 12 months

This dose can also be used in communities where taeniasis is also endemic.

Special populations

Liver disease

[NT011 trade name] should be administered with caution in patients with moderate to severe liver impairment (see section 4.4).

Renal impairment

No dose adjustment is necessary for patients with renal impairment.

Elderly

No special precautions are required in the elderly.

Children

The safety of praziquantel has not been established for children under 1 year of age. The decision to use praziquantel in children aged under 1 year should be based on testing and clinical judgement.

Method of administration

Oral administration.

[NT011 trade name] should be taken with a meal for the prevention and treatment of schistosomiasis, including co-endemicity with taeniasis, of neurocysticercosis, or of foodborne trematode infections. Taking praziquantel with a meal improves its bioavailability and leads to higher blood levels (see section 5.2).

For treatment of taeniasis infection only, [NT011 trade name] should be taken at least 2 hours after a meal and 30 minutes before the next meal. This leads to higher intestinal and lower systemic praziquantel levels, which is desirable for this condition.

The medicine should be swallowed without chewing.

4.3 Contraindications

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

[NT011 trade name] must not be used in patients with:

- ocular cysticercosis – parasite destruction within the eye may cause serious ocular damage.
- concomitant administration of strong inducers of cytochrome P450 (see section 4.5).

4.4 Special warnings and precautions for use

Liver impairment

Patients with moderate to severe liver impairment (Child Pugh Class B and C) should be monitored for adverse effects since reduced metabolism of praziquantel may lead to considerably higher and longer lasting praziquantel plasma concentrations.

Caution should be exercised with the usual recommended dose of praziquantel for hepatosplenic schistosomiasis in patients with moderate to severe liver impairment (Child Pugh Class B and C).

Cardiac impairment

Patients with bradycardia, ectopic rhythms, ventricular fibrillation, and AV block should be monitored during treatment.

Neurological effects

Since praziquantel can exacerbate central nervous system disorders caused by schistosomiasis, it should not be used in patients with epilepsy or a history of epilepsy or other signs of central nervous system involvement due to schistosomiasis, paragonimiasis or *Taenia solium* cysticercosis such as subcutaneous nodules suggestive of cysticercosis.

Patients with neurocysticercosis should always be treated in hospital because of the risk of pericystic oedema. Praziquantel should **not be given** to patients with pronounced inflammation caused by degenerating parenchymal cysts.

Possible lack of effect in schistosomiasis

Praziquantel treatment in the acute phase of infection may not prevent progression from asymptomatic infection to acute schistosomiasis or from asymptomatic infection or acute schistosomiasis to chronic phase.

Inflammatory reactions

The use of praziquantel in patients with schistosomiasis may be associated with sudden inflammatory immune response suspected to be caused by the release of schistosomal antigens (paradoxical reactions, serum sickness, Jarisch-Herxheimer like reactions). These reactions may lead to potentially life-threatening events, for example, respiratory failure, encephalopathy, and cerebral vasculitis. The reactions occur mainly during the acute phase of schistosomiasis.

4.5 Interaction with other medicinal products and other forms of interaction

Praziquantel is metabolised by the CYP450 enzyme system.

Strong cytochrome P450 inducers: e.g. rifampicin

Concomitant use of rifampicin (a strong cytochrome P450 inducer) is contraindicated as therapeutically effective plasma levels of praziquantel may not be achieved. In patients receiving rifampicin who need immediate treatment for schistosomiasis, alternative medicines for schistosomiasis should be considered.

Moderate cytochrome P450 inducers: e.g. efavirenz, phenytoin, phenobarbital, carbamazepine, dexamethasone

Concomitant administration of medicines that induce cytochrome P450 enzymes), e.g. efavirenz, antiepileptic drugs (phenytoin, phenobarbital, and carbamazepine) and dexamethasone, may reduce plasma levels of praziquantel; concomitant use is not recommended.

Cytochrome P450 inhibitors: cimetidine, ketoconazole, itraconazole, erythromycin, ritonavir

Concomitant administration of drugs that decrease cytochrome P450 activity, e.g. cimetidine, ketoconazole, itraconazole, erythromycin, and ritonavir may increase plasma levels of praziquantel.

Grapefruit juice

Grapefruit juice may increase praziquantel levels. Patients should be advised not to drink grapefruit juice on the day they take [NT011 trade name].

Chloroquine

Concomitant administration of chloroquine may lead to lower concentrations of praziquantel in blood. The mechanism of this drug-drug interaction is unclear.

4.6 Fertility, pregnancy and breastfeeding

Pregnancy

Published studies have not identified an association with praziquantel use during pregnancy and major birth defects, miscarriage or adverse maternal or fetal outcomes.

Observations on women exposed to praziquantel during the first trimester of pregnancy, case reports of treatment during the first trimester, and results of over 30 years of post-marketing surveillance involving many millions of doses (usually of 40 mg/kg for schistosomiasis) indicate that praziquantel is probably safe during the first trimester of pregnancy.

Although the safety of praziquantel is not likely to be different in pregnant and non-pregnant women, preventative chemotherapy (e.g. mass administration for preventing taeniasis) may not be justified in the first trimester of pregnancy.

Animal studies have not revealed teratogenic effects with praziquantel.

Breast feeding

There is no information on the effects of praziquantel in breast-fed infants or effects on milk production. A breast-feeding mother treated with a recommended single dose of praziquantel would result in her infant ingesting a maximum of 0.1% of the weight-adjusted maternal dose.

The developmental and health benefits of breast-feeding should be considered along with the mother's clinical need for praziquantel and any potential adverse effects on the breast-fed infant from praziquantel or from the underlying maternal condition. However, praziquantel may be regarded as safe for the treatment of schistosomiasis during breast-feeding.

Fertility

Reproduction studies in rats and rabbits have revealed no evidence of impaired fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

[NT011 trade name] may cause dizziness, somnolence, or, rarely, seizures (see section 4.8). Patients taking [NT011 trade name] should be advised not to drive or operate machines on the day of treatment and for 24 hours after treatment.

4.8 Undesirable effects

The most serious adverse reactions of [NT011 trade name] include neurological side effects resulting from the exacerbation of neurological effects due to schistosomiasis, paragonimiasis or Taenia solium cysticercosis (see section 4.4). The most frequently reported adverse reactions are headache, dizziness, fatigue, abdominal pain, nausea, vomiting, and urticaria.

The undesirable effects of [NT011 trade name] are listed below. Frequencies are defined as very common (at least 1 in 10), common (1 in 100 to 1 in 10), uncommon (1 in 1000 to 1 in 100), rare (1 in 10 000 to 1 in 1000), very rare (less than 1 in 10 000) or not known (frequency cannot be estimated from available data).

Immune system disorders

Very rare	Jarisch-Herxheimer reaction, allergic reaction, polyserositis, eosinophilia

Nervous system disorders

Very common	headache, dizziness
Common	somnolence
Very rare	seizures

Cardiac disorders

Very rare	arrhythmias

Ear and labyrinth disorders

Common	vertigo

Gastrointestinal disorders

Very common	gastrointestinal and abdominal pains, nausea, vomiting
Common	anorexia, diarrhoea
Very rare	bloody diarrhoea

Skin and subcutaneous tissue disorders

Very common	urticaria
Common	rash
Very rare	pruritis

Musculoskeletal and connective tissue disorders

Common	myalgia

General disorders and administration site conditions

Very common	fatigue
Common	feeling unwell (asthenia, malaise), fever

Description of selected adverse reactions

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

Side effects may be more frequent or serious in patients with a heavy worm burden. It is often not clear whether undesirable effects are caused by praziquantel, an endogenous reaction to the death of the parasites produced by praziquantel, or are symptomatic of the infestation.

See also section 4.4 for further information on neurological effects, possible lack of effect in schistosomiasis and inflammatory reactions.

Reporting of suspected adverse reactions

Health care providers are asked to report adverse reactions that may be linked to a medicine, to the marketing authorisation holder, or, if available, to the national reporting system. Reports of suspected adverse reactions to a medicine are important for the monitoring of the medicine's benefits and risks.

4.9 Overdose

Symptoms

Information on overdosage 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 1–2 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 after ensuring the airway is protected.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anthelmintics, ATC code: P02B A01

Mechanism of action

Praziquantel induces a rapid contraction of schistosomes by a specific effect on the permeability of the cell membrane. It further causes vacuolization and disintegration of the schistosome tegument (outer 'skin'). The effect is more marked on adult than on young worms.

Secondary effects of praziquantel include 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, such as tapeworms; nematodes (including filariae) are not affected.

5.2 Pharmacokinetic properties

The absorption characteristics of [NT011 trade name] have been determined after administration of single dose tablets in healthy volunteers in the fed state as follows:

Pharmacokinetic variable	**Mean value* (± standard deviation)**
Maximum concentration (C_{max})	773 ± 641 ng/mL (527)
Area under the curve (AUC_{0-t}), a measure of the extent of absorption	1328 ± 1082 ng·h/mL (892)
Time to attain maximum concentration (tmax)	2.40 ± 1.04 h

* arithmetic mean

Absorption	
Absorption	t_{max} 1–3 hours
Absolute bioavailability	Not available
Oral bioavailability	80%
Food effect	AUC is increased approximately 2- to 4-fold; glucose and bicarbonate lower praziquantel bioavailability
Distribution	
Volume of distribution (Vd/F)	Not available
Plasma protein binding in vitro	80%, almost exclusively to albumin
Tissue distribution	Extensively distributed. Crosses the blood-brain barrier with approximately 14–20% of the total (free plus protein-bound) plasma concentration. Present in breast milk in concentrations of approximately 25% of the maternal serum concentration.
Elimination	
Elimination half life	1.5–3 hours
Mean systemic clearance (Cl/F)	7.0 L/kg/hour
% of dose excreted in urine	Approximately 80% (> 99% as metabolites)
% of dose excreted in faeces	Not available
Drug interactions (in vitro)	Co-administration with inducers or inhibitors of P450 enzymes can decrease and increase, respectively, the exposure to praziquantel.
Metabolising enzymes	Extensive first pass hepatic metabolism mainly via CYP2B1 and CYP3A4. Approximately 6% of the dose is unmetabolised after 1 hour.
Special populations	
Renal impairment	Accumulation of unchanged drug is not expected with renal impairment due to extensive hepatic metabolism
Hepatic impairment	No significant effect on pharmacokinetics were seen with mild (Child-Pugh A) hepatic impairment.

	C_{max} and AUC increase progressively with moderate to severe hepatic impairment (for Child-Pugh B the increases are 1.8- and 3.6-fold, respectively and for Child-Pugh C 4.3- and 15-fold, respectively)

5.3 Preclinical safety data

Harmful effects in non-clinical studies occurred only at exposures considered sufficiently in excess of the human exposure, indicating little relevance to clinical use.

Carcinogenesis

Long-term carcinogenicity studies were conducted in Sprague-Dawley rats and golden hamsters. Praziquantel was not considered to be carcinogenic in rats. In hamsters, praziquantel might be considered a weak carcinogen based on a slight increase in malignant tumours in female hamsters.

Mutagenesis

Extensive studies in various test systems (both in vitro and in vivo) have yielded no evidence of mutagenicity. Mutagenic effects in Salmonella tests in one laboratory have not been confirmed in the same tested strain by other laboratories.

Reproductive toxicity

Reproduction studies 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 fetus due to praziquantel.

Abortion rate was increased in rats at 3 times the single human therapeutic dose.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core tablet: Pregelatinized starch
Povidone
Sodium lauryl sulfate
Microcrystalline cellulose
Magnesium stearate

Film coat: Hydroxypropyl methylcellulose
Titanium dioxide
Macrogol/ PEG
Sodium lauryl sulfate

This medicine is essentially ‘sodium-free’. It contains less than 1 mmol sodium (23 mg) per *tablet*.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

HDPE bottle pack of 6 tablets and Blister pack of 1 x 6's tablets and 10 x 10's tablets

Do not store above 30ºC. Avoid excursions above 30ºC. Store in the original container.

HDPE bottle pack of 100, 500 and 1000 tablets

Do not store above 30ºC. Avoid excursions above 30ºC. Store in the original container.

Discard the product 180 days after initial opening.

6.5 Nature and contents of container

[NT011 trade name] is white to orange tinged, oblong, film-coated tablet. They are biconvex (rounded on top and bottom) with a bevelled edge. The tablets are plain on the other side with three break lines on one side with "P8" debossed (stamped into the tablet) and two scores with "H" debossed (stamped into the tablet) on the other side.

The break line can be used to divide [NT011 trade name] into either two or four equal doses.

HDPE bottle

[NT011 trade name] is provided in a white opaque, HDPE bottle containing 6,100,500 or 1000 tablets. The bottle also contains purified cotton as a space filler. The bottle has a white opaque, polypropylene ribbed child resistant plastic cap closure with a pulp liner.

Blister

[NT011 trade name] is provided in a cold form PVC/Alu/OPA-Alu blister, each blister card containing 6 or 10 tablets. Available in packs of 1 x 6 or10 x 10's tablets.

6.6 Special precautions for disposal and other handling

No special requirements.

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

7. SUPPLIER

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8. WHO REFERENCE NUMBER (WHO Prequalification Programme)

NT011

9. DATE OF PREQUALIFICATION

23 August 2022

10. DATE OF REVISION OF THE TEXT

September 2024

References

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Detailed information on this medicine is available on the World Health Organization (WHO) website: https://extranet.who.int/prequal/medicines/prequalified/finished-pharmaceutical-products