SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

INTA PRAZIQUANTEL (Praziquantel Tablets USP 600 mg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains:
Praziquantel USP 600 mg

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film coated tablet

White, capsule shaped, film coated tablet with three breaklines on one side and two breaklines and a break mark in-between the breaklines, on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of schistosoma infections due to various types of blood fluke (eg *Schistosoma haematobium, S.japonicum, S.mekongi, S.mansoni*).

4.2 Posology and method of administration

The doctor must prescribe individual doses for individual cases, according to the diagnosis.

Schistosoma haematobium	20 mg/kg body weight three times a day at four hourly intervals for one day.
Schistosoma mansoni	
Schistosoma japonicum	
Schistosoma mekongi	

The tablet has 3 score marks, each fragment contains 150 mg active substance, thus allowing a precise dose to be given, corresponding to the patient's body weight.

If 1/4 of a tablet is required, it is convenient to begin by breaking the tablet at one of the outer grooves.

The simplest way to break the tablet is to place the thumbnail in the groove.

Table 1: Conversion Table

	BODY WEIGHT IN KG								
	20-25	26-33	34-41	42-48	49-56	57-63	64-70	71-78	79-86
No. of tablets corresponding to 1 x 20 mg/kg	¾	1	1¼	1½	1¾	2	2¼	2½	2¾

INTA PRAZIQUANTEL should be swallowed whole with a little liquid, preferably after meals.

4.2.1 Paediatric population

See Section 4.4.

4.2.2 Hepatic impairment

See Section 4.4.

4.2.3 Renal impairment

See Section 4.4.

4.3 Contraindications

Known hypersensitivity to praziquantel or any of the excipients.

Ocular cysticercosis - parasite destruction within the eye may cause irreparable damage.

The concomitant administration of strong inducers of Cytochrome P 450 such as rifampicin must be avoided as therapeutically effective plasma levels may not be achieved.

4.4 Special warnings and special precautions for use

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 praziquantel 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 system involvement such as subcutaneous nodules suggestive of cysticercosis.

Neurocysticercosis is not an approved indication due to insufficient data. In animals, venous thrombosis and the development of granulomas at the site of worm attachment has been observed following treatment with praziquantel. Patients treated with praziquantel (for neurocysticercosis) have had a high incidence of severe headache and seizures. Some patients also developed intracranial hypertension. Because of the potential for undiagnosed neurocysticercosis to be present in patients originating from endemic areas, extra care is necessary in managing such patients. If cerebral cysticercosis is present and treatment is still considered essential, the patient should be hospitalized under specialist care.

4.4.1 Renal impairment

Since 80% of praziquantel and its metabolites are excreted in the kidneys, excretion might be delayed in patients with impaired renal function. Nephrotoxic effects of praziquantel are not known.

4.4.2 Hepatic impairment

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 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.

4.4.3 Paediatric population

Safety in children has not been established.

4.5 Interaction with other medicinal products and other forms of interaction

Praziquantel is believed to be metabolised via the CYP450 enzyme system. Many categories of medicines are known to inhibit or induce CYP450 enzymes causing an increase or decrease in serum concentrations or bioavailability. Care must therefore be exercised when co-administering such medicines.

Concomitant administration of medicines that increase the activity of drug metabolising liver enzymes (CYP450 inducers), e.g. antiepileptic medicines, dexamethasone may reduce plasma levels of praziquantel. Concomitant administration of strong inducers of CYP450 such as rifampicin must be avoided. Chloroquine, when taken simultaneously, can lead to lower

concentrations of praziquantel in blood.

Concomitant administration of medicines that decrease the activity of drug metabolising liver enzymes (CYP450 inhibitors) e.g. cimetidine, ketoconazole, itraconazole, erythromycin, may increase plasma levels of praziquantel.

When administered concomitantly with grapefruit juice, an increase in praziquantel exposure of less than two fold was observed in clinical studies.

4.6 Fertility, Pregnancy and lactation

4.6.1 Pregnancy

Reproduction studies performed so far in rats and rabbits have revealed no evidence of impaired fertility or harm to the fetus due to praziquantel. An increase in abortion rate was seen in rats given single doses of 300 mg/kg. There are no adequate and well controlled studies on the use of praziquantel in pregnant women.

Because animal reproduction studies are not always predictive of human response, for safety reasons praziquantel should not be used in pregnancy unless clearly needed.

4.6.2 Lactation

Praziquantel has been reported to be excreted in the milk of nursing women. Women should not nurse on the day of praziquantel treatment and during the subsequent 72 hours.

4.7 Effects on ability to drive and use machines

Patients should be warned not to drive or operate machinery on the day of treatment (and during the subsequent 24 hours), as their ability to do so may be temporarily impaired by the use of praziquantel.

4.8 Undesirable effects

4.8.1 Summary of the safety profile

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.

4.8.2 Tabulated list of adverse reactions

Side effects vary according to dose and duration of praziquantel medication; furthermore they are dependent on the parasite species, extent of parasitisation, duration of infection and localisation of the parasites in the body. Side effects occur earlier and are more frequent and pronounced in patients with severe parasitic infestation. Mild increases in liver enzymes have been reported in some patients.

Table 2: Adverse reactions

	Very Common	Common	Uncommon	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 (very rarely bloody diarrhoea)			
Skin and Subcutaneous Tissue Disorders	Urticaria	Rash			Pruritus
Musculoskeletal, Connective Tissue and Bone Disorders		Myalgia			
General Disorders and Administrative Site Conditions	Fatigue	Feeling unwell (asthenia, malaise) Fever			

It is often not clear whether the complaints reported by patients or the undesirable effects reported by the physician are caused by praziquantel itself (I, direct relation), or may be considered to be an endogenous reaction to the death of the parasites produced by praziquantel (II, indirect relation), or are symptomatic observations of the infestation (III, no relation). It may be difficult to differentiate between the possible variations I, II and III.

4.9 Overdosage

Information on overdosage in humans is not available. 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.

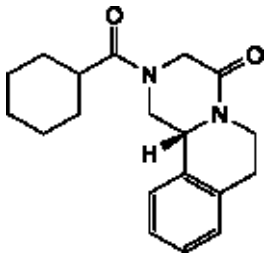
5.0 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antihelmintics, ATC code: P02BA01

Praziquantel is 2-(cyclohexylcarbonyl)-1,2,3,6,7,11b-hexahydro-4H-pyrazino
(2,1a) isoquinolin-4-one. CAS Number: 55268-74-1

Praziquantel is a white crystalline powder of bitter taste. The compound is stable under normal conditions and melts at 136°C-140°C with decomposition. The active substance is hygroscopic. Praziquantel is easily soluble in chloroform and dimethylsulfoxide, soluble in ethanol and very slightly soluble in water. The molecular formula is $C_{19}H_{24}N_2O_2$. The structural formula is as follows:



5.1.1 Pharmacodynamic effects

Animal studies show that praziquantel induces a rapid contraction of schistosomes by a specific effect on the permeability of the cell membrane. The medicine further causes vacuolisation and disintegration of the schistosome tegument. The effect is more marked on the adult than on young worms.

5.2

Pharmacokinetic properties

5.2.1 Absorption

After oral administration praziquantel is rapidly absorbed (80%). It is, however, subject to first pass effect and extensive metabolism. One hour after administration approximately 6% only of the medicine in serum is in the unmetabolised form. Both the unchanged medicine and the metabolites are excreted primarily by the kidneys. Maximal serum concentration is achieved 1-3 hours after dosing. The half life of praziquantel in serum is 0.8-1.5 hours.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on studies of systemic toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction.

6.0 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline Cellulose (PH 102)
Maize Starch
Croscarmellose Sodium
Colloidal Anhydrous Silica
Povidone K-30
Isopropyl Alcohol
Sodium Lauryl Sulphate
Purified Water
Magnesium Stearate
Talc
Opadry OYLS 58900 White

6.2 Incompatibilities
Not Applicable

6.3 Shelf life
36 Months

6.4 Special precautions for storage
Do not store above 30°C.
Keep the container tightly closed.

6.5 Nature and contents of container
INTA PRAZIQUANTEL is available in pack of 10 and 100 Tablets.

6.6 Special precautions for disposal and other handling
Any unused medicine or waste material should be disposed of in accordance with local requirements.

7.0 MARKETING AUTHORISATION HOLDER

Intas Pharmaceuticals Limited
Corporate House, Near Sola Bridge,
S.G. Highway, Thaltej,
Ahmedabad, Gujarat,
India

8.0 MARKETING AUTHORISATION NUMBER

09283/07992/NMR/2019

9.0 DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Dec 16, 2023

10.0 DATE OF REVISION OF THE TEXT

Not Applicable.