ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Arpraziquantel 150 mg dispersible tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dispersible tablet contains 150 mg of arpraziquantel.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Dispersible tablet (tablet).

White to off-white, round, biconvex tablet.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Arpraziquantel is indicated for the treatment of schistosomiasis caused by *Schistosoma mansoni* or *Schistosoma haematobium* in children aged 3 months to 6 years.

4.2 Posology and method of administration

Posology

S. mansoni infection: The recommended target dose for Arpraziquantel is a single dose of 50 mg/kg body weight.

S. haematobium infection: The recommended target dose for Arpraziquantel is a single dose of 60 mg/kg body weight.

There is no information on the use of multiple dosing with arpraziquantel.

The recommended dose of Arpraziquantel based on body weight in children aged 3 months to 6 years and weighing at least 5 kg is provided in tables 1 and 2.

Table 1: Dosing for *S. mansoni* infection (target dose 50 mg/kg)

***S. mansoni* infection, target dose 50 mg/kg**	
Body weight in kg	**Number of tablets**
5.0 - 6.9	2
7.0 - 9.9	3
10.0 - 12.9	4
13.0 - 16.9	5
17.0 - 22.9	7
23.0 - 30.0	9

Table 2: Dosing for *S. haematobium* infection (target dose 60 mg/kg)

***S. haematobium* infection, target dose 60 mg/kg**	
Body weight in kg	**Number of tablets**
5.0 - 5.9	2
6.0 - 7.9	3
8.0 - 10.9	4
11.0 - 13.9	5
14.0 - 18.9	7
19.0 - 23.9	9
24.0 - 30.0	11

The use of Arpraziquantel in children with mixed infection (*S. mansoni* and *S. haematobium*) has not been evaluated. However, the recommended dose for *S. haematobium* (60 mg/kg) is expected to be efficacious in these cases.

The safety and efficacy of Arpraziquantel in children younger than 3 months or weighing less than 5 kg have not been established. No data are available.

Special populations

Renal impairment
No clinical data on patients with renal impairment are available for arpraziquantel. Therefore, no dosage recommendation can be made (see section 5.2).

Hepatic impairment
Arpraziquantel should be used with caution in patients with severe hepatic insufficiency and patients with hepatosplenic schistosomiasis (see sections 4.4 and 5.2).

Method of administration

For oral use. The tablets should be taken after a meal.

Arpraziquantel tablets should be administered under the supervision of an adult.

Arpraziquantel tablets should be fully dispersed in water and gently stirred until a white homogeneous dispersion is obtained. A minimum volume of 10 mL water is recommended for 1-5 tablets and a minimum of 20 mL is recommended for 6-11 tablets. The resulting dispersion should be administered immediately using a cup or a syringe.

Mixing with food or drinks other than water has not been studied.

4.3 Contraindications

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

Known or suspected cysticercosis (see section 4.4).

Known or suspected acute schistosomiasis (see section 4.4).

Concomitant administration of strong cytochrome P450 inducers (e.g. rifampicin, carbamazepine and phenytoin) (see section 4.5).

4.4 Special warnings and precautions for use

Co-existing cysticercosis

Arpraziquantel is contraindicated in children with known or suspected cysticercosis (see section 4.3).

Seizures have occurred during racemic praziquantel treatment in patients with co-existing cysticercosis. The increased intracranial pressure caused by neurocysticercosis may be temporarily intensified during treatment with racemic praziquantel due to the host inflammatory response to destruction of *Taenia solium* cysticerci. In patients with a history of seizures and with other central nervous system symptoms, cysticercosis should be ruled out first before commencing the treatment with Arpraziquantel.

Another manifestation of cysticercosis is intraocular cysticercosis presenting with visual impairment and ocular inflammation depending on the location of the cyst. The intraocular cyst must be removed by surgery before antihelminthic treatment is started as lysis and degeneration of the cyst may induce further intraocular inflammatory reactions and result in loss of vision.

Central nervous system disorders

There may be a risk of exacerbation of central nervous system disorders (e.g. seizures) by racemic praziquantel in patients with other parasitoses with cerebral localisation.

Acute schistosomiasis (Katayama syndrome)

Arpraziquantel is contraindicated in patients with known or suspected acute schistosomiasis (see section 4.3).

Racemic praziquantel is not effective during acute schistosomiasis due to lack of activity against migrating schistosomulae. The most common clinical manifestations of acute schistosomiasis are skin lesions (pruritus, skin eruption), fever, cough, abdominal pain and diarrhoea.

The use of racemic praziquantel in the acute phase of schistosomiasis may be associated with clinical deterioration (paradoxical reactions, serum sickness, Jarisch-Herxheimer-like reactions). These reactions may lead to potentially life-threatening events (e.g. respiratory failure, encephalopathy, myocarditis and/or cerebral vasculitis). The risk for these reactions may be higher in non-immune patients. As the first infection event in most endemic areas occurs early at the preschool age, theoretically, the risk of Katayama syndrome could be higher in preschool-aged children however, there are no data to confirm or reject this.

Severe allergic reactions

Severe allergic reactions were reported in patients receiving racemic praziquantel. Therefore, they may occur in patients treated with arpraziquantel. The risk for the development of allergic reactions may be higher in preschool-aged children compared to other age groups.

Hepatic impairment

Due to reduced drug metabolism in the liver, considerably higher plasma concentrations of arpraziquantel and a prolonged plasma half-life may occur in patients with severe hepatic insufficiency or with hepatosplenic schistosomiasis. Caution is recommended when using Arpraziquantel in these patients (see sections 4.2 and 5.2).

Use in children below 1 year of age

Data for children below 1 year of age are limited. Therefore, caution is required when Arpraziquantel is administered to these patients.

Sodium

This medicinal product contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

No clinical drug-drug interaction studies have been performed with arpraziquantel.

Arpraziquantel is a component of racemic praziquantel. Therefore, drug-drug interactions that are known or expected to occur with use of the racemate are applicable to the use of arpraziquantel.

Effects of other medicinal products on arpraziquantel

Concomitant administration of arpraziquantel with strong cytochrome P450 inducers (e.g. rifampicin, carbamazepine and phenytoin), is contraindicated due to the resulting sub-therapeutic exposures to arpraziquantel leading to treatment failure (see section 4.3).

Concomitant administration of arpraziquantel with moderate cytochrome P450 inducers (e.g. efavirenz and dexamethasone) is not recommended due to the risk of sub-therapeutic exposures to arpraziquantel leading to treatment failure.

Concomitant administration of arpraziquantel with chloroquine or with systemic corticosteroids may potentially lead to sub-therapeutic exposures, with a risk of treatment failure.

Concomitant administration of arpraziquantel with inhibitors of CYP1A2, 2C9, 2C19 or 3A4/5 (e.g. cimetidine, ketoconazole, itraconazole, erythromycin and grapefruit juice) is not recommended due to the expected increase in arpraziquantel plasma exposures, which may lead to an increased risk of adverse reactions.

When racemic praziquantel was administered concomitantly with albendazole, an increase of the plasma concentration of arpraziquantel by approximately 65% was observed. Concomitant use of arpraziquantel with albendazole may increase plasma concentrations of the active metabolite of albendazole by approximately 2.5-fold. An increase in adverse reactions cannot be ruled out.

Effects of arpraziquantel on other medicinal products

In-vitro data indicate that arpraziquantel is unlikely to cause clinically important drug-drug interactions by inhibition or induction of CYP isoenzymes.

In-vitro, arpraziquantel weakly inhibits the transporter proteins P-glycoprotein (P-gp), breast cancer resistance protein (BCRP), organic anion transporting polypeptide (OATP) 1B1 and 1B3, and organic cation transporter (OCT) 1 at clinically relevant concentrations. Consequently, the plasma concentrations of medicinal products (e.g. sulfasalazine, erythromycin, methotrexate and digoxin) whose disposition is dependent on these transporter proteins may be increased by co-administration of arpraziquantel and caution is advised.

4.6 Fertility, pregnancy and lactation

Pregnancy

Not applicable. Arpraziquantel is intended for use in children aged 3 months to 6 years.

Breast-feeding

Not applicable. Arpraziquantel is intended for use in children aged 3 months to 6 years.

Fertility

No clinical data on fertility are available for arpraziquantel or racemic praziquantel. In animal studies, racemic praziquantel revealed no impact on fertility.

4.7 Effects on ability to drive and use machines

Not applicable. Arpraziquantel is intended for use in children aged 3 months to 6 years.

4.8 Undesirable effects

Summary of the safety profile

The safety of arpraziquantel has been evaluated in two clinical studies including 442 children aged 3 months to 6 years infected with *S. mansoni* or *S. haematobium* with 43 children below 2 years of age.

The most commonly reported adverse reactions during treatment in clinical studies with arpraziquantel were abdominal pain (9.7%), diarrhoea (6.6%), vomiting (4.5%) and somnolence (4.1%).

Tabulated list of adverse reactions

The adverse reactions in Table 3 are listed below by system organ class and frequency. Frequencies are defined as follows: Very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1 000 to < 1/100); rare (≥ 1/10 000 to < 1/1 000); not known (frequency cannot be estimated from the available data).

Table 3: Adverse reactions in children treated with arpraziquantel

System Organ Class/Frequency	**Adverse reactions**
Nervous system disorders	
Common	Somnolence
Uncommon	Headache
Gastrointestinal disorders	
Common	Abdominal pain, diarrhoea, vomiting
Uncommon	Nausea
Skin and subcutaneous tissue disorders	
Uncommon	Urticaria, pruritus
General disorders and administration site conditions	
Uncommon	Pyrexia

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 is limited experience with overdose for arpraziquantel.

In case of overdose, patients should be closely monitored for signs or symptoms of adverse reactions. There is no specific treatment that can be recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: anthelmintics, antitrematodals, ATC code: P02BA03

Mechanism of action

Arpraziquantel is the biologically active enantiomer of praziquantel, which is a racemic mixture composed of the R-(-)-praziquantel (arpraziquantel) and S-(+)-praziquantel enantiomers in a 1:1 ratio. The activity of praziquantel against Schistosoma worms resides in the R-(-)-praziquantel enantiomer (arpraziquantel).

Praziquantel is taken up by susceptible trematode and nematode helminths and induces tegumental disruption and muscular paralysis.

Clinical efficacy

In an open-label Phase 3 clinical study in Schistosoma-infected children aged 4.4 months to 6.9 years with a body weight from 6.9 to 33.8 kg, Arpraziquantel 150 mg tablets were dosed at 50 mg/kg for *S. mansoni* or 60 mg/kg for *S. haematobium*.

The cure rate and egg reduction rate results are summarised in table 4. The cure rate is the proportion of children with clinical cure defined as no parasite eggs in any of the stool samples analysed by the Kato-Katz method (*S. mansoni*) or in urine samples analysed by the urine filtration method (*S. haematobium*).

Table 4: Clinical cure rate and egg reduction rate results from the Phase 3 study

	S. mansoni*				***S. haematobium***	
Group	ar-PZQ 50 mg/kg (n=98)	ar-PZQ 50 mg/kg (n=29)	ar-PZQ 50 mg/kg (n=18)	rac-PZQ 40 mg/kg (n=48)	ar-PZQ 60 mg/kg* (n=58)	ar-PZQ 60 mg/kg** (n=58)
Age	4 – 6 years	2 – 3 years	3 – 24 months	4 – 6 years	3 months – 6 years	3 months – 6 years
BW range	13.0-24.3 kg	9.4-17.0 kg	6.9-11.8 kg	12.7-24.2 kg	8.0-33.8 kg	8.0-33.8 kg
Efficacy endpoints						
Cure Rate (95% CI)	87.8% (79.6, 93.5)	93.1% (77.2, 99.2)	94.4% (72.7, 99.9)	81.3% (67.4, 91.1)	86.2% (74.6, 93.9)	94.8% (85.6, 98.9)
Egg reduction rate (95% CI)	99.7% (99.5, 99.9)	99.6% (98.5, 100.0)	99.3% (96.6, 100.0)	99.5% (98.9, 99.8)	98.8% (97.5, 99.7)	99.4% (98.2, 100.0)

ar-PZQ=arpraziquantel, rac-PZQ=racemic praziquantel, BW=body weight, CI=confidence interval
* measured 3 weeks after treatment
** measured 5 weeks after treatment

Children (3 months to 6 years) infected with *S. haematobium* who were dosed at 50 mg/kg (n=29) achieved lower cure rate (58.6%) measured at week 3 compared to 60 mg/kg (86.2%), while the egg reduction rate was 99.1%, similarly high as for 60 mg/kg dosing (98.8%).

Lower cure rates were observed in moderate/heavy-infections than in light-infections (see table 5).

Table 5: Clinical cure rate stratified by baseline infection intensity in the Phase 3 study

Cure Rate [95% CI]	***S. mansoni****				***S. haematobium***	
Group	ar-PZQ 50 mg/kg 4 - 6 years	ar-PZQ 50 mg/kg 2 - 3 years	ar-PZQ 50 mg/kg 3 - 24 months	rac-PZQ 40 mg/kg 4 - 6 years	ar-PZQ 60 mg/kg* 3 months - 6 years	ar-PZQ 60 mg/kg** 3 months - 6 years
Light infection	n=59	n=12	n=14	n=27	n=52	n=52
	94.9% (85.9, 98.9)	100% (73.5, 100)	92.9% (66.1, 99.8)	85.2% (66.3, 95.8)	86.5% (74.2, 94.4)	94.2% (84.1, 98.8)
Moderate/ heavy infection	n=39	n=17	n=4	n=21	n=6	n=6
	76.9% (60.7, 88.9)	88.2% (63.6, 98.5)	100% (39.8, 100)	76.2% (52.8, 91.8)	83.3% (35.9, 99.6)	100% (54.1, 100)

ar-PZQ=arpraziquantel, rac-PZQ=racemic praziquantel, CI=confidence interval
* measured 3 weeks after treatment
** measured 5 weeks after treatment

Similar high egg reduction rates (about 99%) were observed in moderate/heavy-infected children and light-infected children regardless of age.

5.2 Pharmacokinetic properties

Absorption

After oral administration, maximum plasma concentrations of arpraziquantel are reached within 2-3 hours. The absolute bioavailability of arpraziquantel in human is unknown but is expected to be low due to extensive first pass metabolism.

In adults, a positive food effect is observed with a higher arpraziquantel C_{max} and AUC (296% and 167%, respectively) after dosing in the fed state compared to the fasting state.

Distribution

Arpraziquantel is approximately 80% bound to plasma proteins in animals and humans. The apparent volume of distribution after oral administration of arpraziquantel is 1.73 L/kg for the 50 mg/kg dose and 2.6 L/kg for the 60 mg/kg dose. Unchanged racemic praziquantel penetrates the blood-brain barrier; racemic praziquantel concentration in human cerebrospinal fluid is about 24% of the serum level.

Biotransformation

Arpraziquantel is rapidly metabolised and undergoes extensive first pass metabolism in the liver by CYP1A2, 2C9, 2C19 and 3A4/5. The major metabolite of arpraziquantel in human plasma is trans-4-hydroxy-arpraziquantel. *In vitro* data suggests that trans-4-hydroxy-arpraziquantel is formed by rapid conversion of cis-4-hydroxy-arpraziquantel which itself is formed via oxidation by CYP1A1, 1A2, 2C9, 2C19, and 2D6. Trans-4-hydroxy-arpraziquantel has weak *in vitro* activity against *S. mansoni* and *S. haematobium* and may contribute to clinical activity.

Elimination

More than 80% of administered racemic praziquantel and its metabolites are excreted in urine within 4 days and more than 90% of total renal excretion occurs within the first 24 hours.

Based on a population pharmacokinetic (PK) analysis, the estimated apparent systemic clearance of arpraziquantel is 33.8 L/h/kg and the elimination half-life of unchanged arpraziquantel is approximately 3 hours.

Linearity/Nonlinearity

No clinically relevant difference in systemic exposure of arpraziquantel at 50 mg/kg or 60 mg/kg is observed.

Renal impairment

Based on data obtained with racemic praziquantel, delayed excretion of arpraziquantel and its metabolites is expected in patients with impaired renal function (see section 4.2).

Hepatic impairment

In patients with moderate (Child-Pugh Class B) and severe hepatic impairment (Child-Pugh Class C), higher serum concentrations of racemic praziquantel are observed compared to patients with normal hepatic function or mild (Child-Pugh Class A) hepatic impairment (3.5- and 15-fold increases in AUC, for the moderate and severe hepatic dysfunction groups respectively, when compared to the normal hepatic function group) (see sections 4.2 and 4.4).

5.3 Preclinical safety data

Nonclinical data on racemic praziquantel reveal no special hazard for humans based on studies of acute and repeat-dose toxicity, genotoxicity, carcinogenicity and toxicity to fertility, reproduction and embryofetal development.

Bridging studies in rats on repeat-dose toxicity showed that the safety profile of arpraziquantel is comparable to the profile of racemic praziquantel.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Mannitol
Starch pregelatinized
Sodium starch glycolate type A
Maize starch
Sucralose
Sodium stearyl fumarate
Silica colloidal anhydrous
Vitamin E polyethylene glycol succinate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years.

In-use shelf life after first opening: 60 days.

6.4 Special precautions for storage

Do not store above 30°C.

6.5 Nature and contents of container

High-density polyethylene (HDPE) bottle with polyethylene (PE) closure.
Each bottle contains 150 dispersible tablets.

6.6 Special precautions for disposal and other handling

No special requirements.

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

7. SCIENTIFIC OPINION HOLDER

Merck Europe B.V.
Gustav Mahlerplein 102
Ito Toren
1082 MA Amsterdam
Netherlands

8. SCIENTIFIC OPINION NUMBER

EMEA/H/W/004252/001

9. DATE OF FIRST SCIENTIFIC OPINION

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE SCIENTIFIC OPINION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

Fundação Oswaldo Cruz – Instituto de Tecnologia em Fármacos
Av. Comandante Guaranys, No 447, Jacarepagua
22775-903 Rio de Janeiro
Brazil

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE SCIENTIFIC OPINION

- **Periodic safety update reports (PSURs)**

The scientific opinion holder shall submit the first periodic safety update report for this product within 6 months after the scientific opinion. Subsequently, the scientific opinion holder shall submit periodic safety update reports for this product every 6 months until otherwise agreed by the CHMP.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The scientific opinion holder shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the scientific opinion and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:
- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING (OUTER PACKAGING)

BOTTLE LABEL

1. NAME OF THE MEDICINAL PRODUCT

Arpraziquantel 150 mg dispersible tablets
arpraziquantel

2. STATEMENT OF ACTIVE SUBSTANCE

Each tablet contains 150 mg arpraziquantel.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Dispersible tablet.
150 dispersible tablets.

5. METHOD AND ROUTE OF ADMINISTRATION

Oral use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

After first opening, use within 60 days.

Open date:

9. SPECIAL STORAGE CONDITIONS

Do not store above 30°C.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE SCIENTIFIC OPINION HOLDER

Merck Europe B.V.
Gustav Mahlerplein 102
Ito Toren
1082 MA Amsterdam
Netherlands

12. SCIENTIFIC OPINION NUMBER

EMEA/H/W/004252/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Arpraziquantel 150 mg dispersible tablets
arpraziquantel

Read all of this leaflet carefully before your child starts taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for your child only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as your child's.
- If your child gets any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Arpraziquantel is and what it is used for

Arpraziquantel contains the active substance arpraziquantel and is used to treat parasitic infections caused by blood flukes (worms).

Arpraziquantel is used to treat schistosomiasis caused by *Schistosoma mansoni* or *Schistosoma haematobium* in children aged 3 months to 6 years.

2. What you need to know before your child takes Arpraziquantel

Do not give Arpraziquantel
- if your child is allergic to arpraziquantel or any of the other ingredients of this medicine (listed in section 6).
- if your child has or shows symptoms of a parasitic worm infection (cysticercosis), which could include seizures, lumps under the skin or eye problems.
- if your child has or shows symptoms of schistosomiasis in the acute phase (where the worms begin to produce eggs), which could include skin problems, fever, cough, abdominal pain or diarrhoea.
- if your child is taking certain other medicines that can reduce the efficacy of Arpraziquantel, including rifampicin (an antibiotic used to treat tuberculosis), carbamazepine or phenytoin (used in the treatment of epilepsy).

Warnings and precautions
Talk to your doctor or pharmacist before you give Arpraziquantel if your child:
- has a parasitic infection affecting the brain.
- has liver problems.

The use of Arpraziquantel in the acute phase of schistosomiasis (where the worms begin to produce eggs) may be associated with deterioration of the child's medical condition with symptoms similar to an allergic reaction. This can lead to potentially life-threatening events such as lung failure,

encephalopathy (brain disease), myocarditis (inflammation of the heart muscle) and/or cerebral vasculitis (inflammation of blood vessels in the brain). The risk for these events may be higher if you are coming from a region where schistosomiasis is not present.

The use of Arpraziquantel may be associated with severe allergic reactions. The risk for the development of allergic reactions may be higher in preschool-aged children compared to other age groups.

Children under 3 months of age or weighing less than 5 kg
Do not give this medicine to children below the age of 3 months or below 5 kg in weight as it has not been tested in this population.

Children under 1 year of age
Use Arpraziquantel with caution in children below the age of 1 year as available data are limited.

Other medicines and Arpraziquantel
Tell your doctor or pharmacist if your child is taking, has recently taken or might take any other medicines.

The effects of Arpraziquantel may be reduced by medicines such as:
- efavirenz (used in the treatment of HIV/AIDS)
- chloroquine (used in the treatment of malaria)
- dexamethasone (used to treat inflammatory diseases)

The side effects of Arpraziquantel may be intensified by medicines such as:
- cimetidine (used in the treatment of stomach problems such as ulcers)
- ketoconazole, itraconazole (used in the treament of fungal infections)
- erythromycin (an antibiotic used to treat bacterial infections)
- albendazole (used in the treatment of tapeworm infections)

Concomitant use of Arpraziquantel may affect how well the following medicines work:
- sulfasalazine (used to treat severe bowel and rheumatic joint inflammation)
- erythromycin (an antibiotic to treat bacterial infections)
- methotrexate (used to treat inflammatory diseases or cancer)
- digoxin (used to treat irregular heart beat or other heart problems

Arpraziquantel with food and drink
Do not let your child drink grapefruit juice while taking Arpraziquantel. It can intensify the usual side effects of the medicine.

Pregnancy and breast-feeding
Not applicable. This medicine is intended for children aged 3 months to 6 years.

Driving and using machines
Not applicable. This medicine is intended for children aged 3 months to 6 years.

Arpraziquantel contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially ‘sodium-free’.

3. How to give Arpraziquantel

Always give this medicine to your child exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Your doctor will decide on the right dose of Arpraziquantel based on your child's body weight.

The following tables give the number of tablets to give to your child according to the dose prescribed by your doctor.

Table 1: *S. mansoni* infection (single dose 50 mg/kg)

***S. mansoni* infection, target dose 50 mg/kg**	
Body weight in kg	**Number of tablets**
5.0 - 6.9	2
7.0 - 9.9	3
10.0 - 12.9	4
13.0 – 16.9	5
17.0 - 22.9	7
23.0 – 30.0	9

Table 2: *S. haematobium* infection (single dose 60 mg/kg)

***S. haematobium* infection, target dose 60 mg/kg**	
Body weight in kg	**Number of tablets**
5.0 - 5.9	2
6.0 - 7.9	3
8.0 - 10.9	4
11.0 - 13.9	5
14.0 - 18.9	7
19.0 - 23.9	9
24.0 - 30.0	11

How to give this medicine
Arpraziquantel is for oral use and is to be given as a single dose after a meal.

Always supervise your child while this medicine is taken.

It is recommended to fully disperse the required number of tablets in water and stir gently until a white homogeneous dispersion is obtained. A minimum volume of 10 mL water (approximately 1 tablespoon) is recommended for 1-5 tablets and a minimum of 20 mL (approximately 2 tablespoons) is recommended for 6-11 tablets. Give the resulting dispersion immediately to your child using a cup or a syringe.

Mixing with food or drinks other than water has not been studied.

If you give more Arpraziquantel than you should
If you have given your child more Arpraziquantel than you should, talk to your doctor as soon as possible.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Common side effects (may affect up to 1 in 10 people)
- Sleepiness

- Abdominal pain, diarrhoea, being sick (vomiting)

Uncommon side effects (may affect up to 1 in 100 people)
- Headache
- Feeling sick (nausea)
- Skin rash, itching
- Fever

Reporting of side effects
If your child gets any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Arpraziquantel

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the bottle after EXP. The expiry date refers to the last day of that month.

Do not store above 30°C.

After first opening, the medicine should be used within 60 days.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Arpraziquantel contains
- The active substance is arpraziquantel. Each dispersible tablet contains 150 mg.
- The other ingredients are: mannitol, starch pregelatinized, sodium starch glycolate type A, maize starch, sucralose, silica colloidal anhydrous, sodium stearyl fumarate, vitamin E polyethylene glycol succinate.

What Arpraziquantel looks like and contents of the pack
Arpraziquantel dispersible tablets are white to off-white, round, biconvex tablets.
Each pack contains 150 dispersible tablets in high-density polyethylene plastic bottles with polyethylene closures.

Scientific Opinion Holder
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Other sources of information
Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.