Stability. A decrease in the content of piperazine [as citrate] in syrups on storage was attributed to interaction with fructose and glucose formed by hydrolysis of sucrose.[1] A syrup prepared with sorbitol lost no potency when stored at 25° for 14 months.

1. Nielsen A, Reimer P. The stability of piperazine in syrup. *Arch Pharm Chemi (Sci)* 1975; **3:** 73–8.

Piperazine Hydrate

Piperatsiinihydraatti; Piperazin Heksahidrat; Piperazin hexahydrát; Piperazina hexahidrato; Piperazinas hidratas; Pipérazine, hydrate de; Piperazin-hidrát; Piperazinhydrat; Piperazini Hydras; Piperazinium Hexahydricum; Piperazinum hydricum; Piperazyna uwodniona. Piperazine hexahydrate.

Пиперазина Гидрат

$C_4H_{10}N_2,6H_2O$ = 194.2.

CAS — 142-63-2.

ATC — P02CB01.

Pharmacopoeias. In *Eur.* (see p.vii) and *Viet.*

Ph. Eur. 6.2 (Piperazine Hydrate). Colourless deliquescent crystals. M.p. about 43°. Freely soluble in water and in alcohol. A 5% solution in water has a pH of 10.5 to 12.0. Store in airtight containers. Protect from light.

Piperazine Phosphate

Piperazina, fosfato de; Piperazini Phosphas.

Пиперазина Фосфат

$C_4H_{10}N_2,H_3PO_4,H_2O$ = 202.1.

CAS — 14538-56-8 (anhydrous piperazine phosphate); 18534-18-4 (piperazine phosphate monohydrate).

ATC — P02CB01.

Pharmacopoeias. In *Br., Chin., Jpn,* and *Viet.*

BP 2008 (Piperazine Phosphate). A white odourless or almost odourless crystalline powder. Sparingly soluble in water; practically insoluble in alcohol. A 1% solution in water has a pH of 6.0 to 6.5.

Adverse Effects

Serious adverse effects are rare with piperazine and generally indicate overdosage or impaired excretion. Nausea, vomiting, diarrhoea, abdominal pain, headache, skin rashes, and urticaria occasionally occur. Severe neurotoxicity and EEG abnormalities have been reported with symptoms including somnolence, dizziness, nystagmus, muscular incoordination and weakness, ataxia, paraesthesia, myoclonic contractions, choreiform movements, tremor, convulsions, and loss of reflexes.

Transient visual disturbances such as blurred vision have occurred occasionally and there were reports of cataract formation after treatment with piperazine although they do not appear to have been substantiated.

Hypersensitivity reactions such as bronchospasm, Stevens-Johnson syndrome, and angioedema have occurred in some individuals.

◊ Piperazine has been taken off the market in some European countries because of general concern about its safety.[1] A study carried out in Sweden on 2 healthy subjects had indicated that mononitrosation of piperazine can occur in the stomach to produce the potential carcinogen *N*-mononitrosopiperazine; the more potent *N,N*-dinitrosopiperazine was not found.[2] However, the disease risk to man from such *N*-nitroso compounds has been questioned[3] and certainly reports of tumours associated with the use of piperazine have not been traced. Also, in the UK the CSM concluded that the incidence of serious adverse effects associated with piperazine was low and that, with appropriate pack warnings, piperazine products could remain as medicines available to the public through pharmacies.[1]

1. Anonymous. Data sheet changes for piperazine in pregnancy. *Pharm J* 1988; **240:** 367.
2. Bellander BTD, *et al.* Nitrosation of piperazine in the stomach. *Lancet* 1981; **ii:** 372.
3. Tannenbaum SR. N-nitroso compounds: a perspective on human exposure. *Lancet* 1983; **i:** 629–32.

Abuse. Derivatives of piperazine have been developed and abused as 'designer drugs'—see Benzylpiperazine (p.2152).

Effects on the blood. A 4-year-old African boy with G6PD deficiency developed haemolytic anaemia; no cause for the haemolysis was found except that 2 days previously he had taken *Pripsen* (piperazine and senna).[1] Severe thrombocytopenia with epistaxis and haemoptysis, which developed in a 61-year-old man after piperazine self-medication, was probably the result of sensitisation to piperazine 15 years earlier.[2]

1. Buchanan N, *et al.* G-6-PD deficiency and piperazine. *BMJ* 1971; **2:** 110.
2. Cork MJ, *et al.* Pruritus ani, piperazine, and thrombocytopenia. *BMJ* 1990; **301:** 1398.

Effects on the liver. A reaction resembling viral hepatitis occurred on 2 occasions in a 25-year-old woman after use of piperazine; it appeared to be a hypersensitivity reaction.[1]

1. Hamlyn AN, *et al.* Piperazine hepatitis. *Gastroenterology* 1976; **70:** 1144–7.

Hypersensitivity. A patient experienced a serum-sickness-like illness associated with piperazine,[1] which was followed by a delayed hypersensitivity vasculitis.

See also Effects on the Blood and Effects on the Liver, above.

1. Balzan M, Cacciottolo JM. Hypersensitivity vasculitis associated with piperazine therapy. *Br J Dermatol* 1994; **131:** 133–4.

Precautions

Piperazine is contra-indicated in patients with epilepsy or severe renal impairment and should be given with care to patients with neurological disturbances or mild to moderate renal impairment. It should also be avoided or given with extreme caution in patients with hepatic impairment.

Breast feeding. The UK licensed product information for *Pripsen* (piperazine and senna) states that piperazine is distributed into breast milk. Mothers should be advised to take a dose after breast feeding then not to breast feed for 8 hours during which period milk should be expressed and discarded at the regular feeding times.

Pregnancy. It has been reported that piperazine is teratogenic in *rabbits* and that there have been isolated reports of fetal malformations after clinical use, though no causal relationship has been established. Two infants with malformations have been described briefly:[1] one had bilateral hare lip, cleft palate, and anophthalmia; the other had an abnormality of one foot. Both mothers had taken *Pripsen* (piperazine and senna). UK licensed product information for *Pripsen* advises against use in pregnancy, especially during the first trimester, unless immediate treatment with piperazine is essential.

1. Leach FN. Management of threadworm infestation during pregnancy. *Arch Dis Child* 1990; **65:** 399–400.

Interactions

The anthelmintic effects of piperazine and pyrantel may be antagonised when the two compounds are used together. The possibility that piperazine may enhance the adverse effects of phenothiazines such as chlorpromazine is discussed on p.975.

Pharmacokinetics

Piperazine is readily absorbed from the gastrointestinal tract and is excreted in the urine within 24 hours, partly as metabolites. The rate at which different individuals excrete piperazine has been reported to vary widely. It is distributed into breast milk.

Uses and Administration

Piperazine is an anthelmintic effective against the intestinal nematodes *Ascaris lumbricoides* (roundworm) and *Enterobius vermicularis* (pinworm, threadworm), although other anthelmintics are usually preferred (see the discussions on the treatment of ascariasis and enterobiasis on p.134 and p.136). In roundworms piperazine produces a neuromuscular block leading to a flaccid muscle paralysis in susceptible worms, which are then easily dislodged by the movement of the gut and expelled in the faeces.

Piperazine is usually given as the citrate or phosphate, but the adipate may also be used. The dosage of the salts of piperazine is usually expressed in terms of piperazine hydrate; 100 mg of piperazine hydrate is equivalent to about 44.4 mg of piperazine, 120 mg of piperazine adipate, 125 mg of piperazine citrate (110 mg of anhydrous piperazine citrate), and to 104 mg of piperazine phosphate.

For the treatment of ascariasis, a single dose, repeated once after 14 days, has been used. In adults and children over 12 years of age, a dose equivalent to 4.5 g of piperazine hydrate is given orally. Children aged 9 to 12 years may be given the equivalent of 3.75 g, those aged 6 to 8 years the equivalent of 3 g, those aged 4 to 5 years the equivalent of 2.25 g, and those aged 1 to 3 years the equivalent of 1.5 g. Children under 1 year should receive piperazine on medical advice only; a dose equivalent to 120 mg/kg has been suggested.

For enterobiasis, piperazine has been given for 7 days. A second course after a 7-day interval may be required. Adults and children over 12 years of age are given the equivalent of 2.25 g of the hydrate once daily, children aged 7 to 12 years the equivalent of 1.5 g daily, those aged 4 to 6 years the equivalent of 1.125 g daily, and those aged 1 to 3 years the equivalent of 750 mg daily. Children under 1 year should receive piperazine on medical advice only; a dose equivalent to 45 to 75 mg/kg has been suggested.

Piperazine is also used as a preparation with senna in a single dose of 4 g of the phosphate for adults and children over 6 years of age, repeated after 14 days for enterobiasis, or repeated monthly if necessary for up to 3 months to treat and prevent ascariasis.

Preparations

BP 2008: Piperazine Citrate Elixir; Piperazine Phosphate Tablets;
USP 31: Piperazine Citrate Syrup; Piperazine Citrate Tablets.

Proprietary Preparations (details are given in Part 3)
Braz.: Ascarinase†; Ortovermim†; Vermifran†; Vermilen†; ***Canad.:*** Entacyl†; ***Fr.:*** Vermifuge†; ***Indon.:*** Combicitrine; Piperacyl; Upixon; ***Ital.:*** Citropiperazina; ***Mex.:*** Desparasil†; Helmifar†; Lu-Peracina; Overpon; Piperawitt DS†; Piperazil; Pipergress; Pipermed†; Pirzinol; Verfid; Vermin; ***Port.:*** Lombrimade†; Pipermel; Pipertox; ***S.Afr.:*** Padax; Pipralen; Piprine; SB Tox Worm; ***Spain:*** Mimedran; Vermi; ***Thai.:*** Vermex; ***Turk.:*** Asepar; Askaripar; Helmicide; Helmipar; Oksiaskaril; Siropar; ***UK:*** Pripsen†; ***Venez.:*** Ciperina; Inquiper†; Jetsan†; Oxine†; Piperato; Piperazil; Piperdin; Piperzan; Verpirol.

Multi-ingredient: ***Braz.:*** Vermilen Composto†; ***India:*** Helmazan†; ***Irl.:*** Pripsen†; ***Port.:*** Biureol; ***UK:*** Pripsen.

Pomegranate Bark

Granado; Granati Cortex; Granatrinde; Granatum; Grenadier; Melograno; Pomegranate; Pomegranate Root Bark; Romeira.

Кора Гранатового Дерева

Profile

Pomegranate bark, the dried bark of the stem and root of *Punica granatum* (Punicaceae) containing about 0.4 to 0.9% of alkaloids,, has been used for the expulsion of tapeworms.

Preparations

Proprietary Preparations (details are given in Part 3)
Fr.: Hexaporine.

Praziquantel *(BAN, USAN, rINN)*

EMBAY-8440; Pratsikvanteli; Prazicuantel; Prazikvantel; Prazikvantelis; Praziquantelum. 2-Cyclohexylcarbonyl-1,2,3,6,7,11b-hexahydropyrazino[2,1-*a*]isoquinolin-4-one.

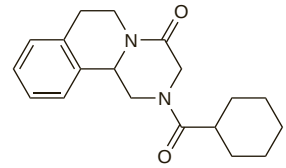
Празиквантел

$C_{19}H_{24}N_2O_2$ = 312.4.

CAS — 55268-74-1.

ATC — P02BA01.

ATC Vet — QP52AA01.



Pharmacopoeias. In *Chin., Eur.* (see p.vii), *Int.,* and *US.*

Ph. Eur. 6.2 (Praziquantel). White or almost white crystalline powder. It exhibits polymorphism. Very slightly soluble in water; freely soluble in alcohol and in dichloromethane. Protect from light.

USP 31 (Praziquantel). A white or practically white crystalline powder; odourless or with a faint characteristic odour. Very slightly soluble in water; freely soluble in alcohol and in chloroform. Protect from light.

Adverse Effects

Adverse effects with praziquantel may be common but are usually mild and transient. Headache, diarrhoea, dizziness, drowsiness, malaise, abdominal discomfort, nausea, and vomiting have been reported most frequently. Hypersensitivity reactions such as fever, urticaria, pruritic skin rashes, and eosinophilia can occur; they may be due to death of the infecting parasites. Raised liver enzyme values have been reported rarely.

Most patients with neurocysticercosis who are given praziquantel suffer CNS effects, including headache, hyperthermia, seizures, and intracranial hypertension, which are thought to result from an inflammatory re-

sponse to dead and dying parasites in the CNS. Use with corticosteroids is advised in such patients.

Effects on the gastrointestinal tract. Colicky abdominal pain and bloody diarrhoea occurred in a small community in Zaire shortly after treatment for *Schistosoma mansoni* infection with single oral doses of praziquantel 40 mg/kg.[1] A similar syndrome has been reported in some patients with *Schistosoma japonicum* infection given praziquantel.[2] The abdominal pain occurring in these patients was very different from the mild abdominal discomfort much more commonly reported with praziquantel therapy.

1. Polderman AM, *et al.* Side effects of praziquantel in the treatment of Schistosoma mansoni in Maniema, Zaire. *Trans R Soc Trop Med Hyg* 1984; **78:** 752–4.
2. Watt G, *et al.* Bloody diarrhoea after praziquantel therapy. *Trans R Soc Trop Med Hyg* 1986; **80:** 345–6.

Effects on the nervous system. Adverse nervous system effects are common in patients with neurocysticercosis given praziquantel. Neurological symptoms have also been reported[1] with the much lower doses of praziquantel used in the treatment of taeniasis in a patient with undiagnosed neurocysticercosis.

1. Flisser A, *et al.* Neurological symptoms in occult neurocysticercosis after single taenicidal dose of praziquantel. *Lancet* 1993; **342:** 748.

Precautions

Praziquantel should not be used in patients with ocular cysticercosis because of the risk of severe eye damage resulting from destruction of the parasite.

Patients should be warned that praziquantel may cause dizziness or drowsiness and if affected they should not drive or operate machinery during or for 24 hours after treatment.

Breast feeding. Praziquantel is distributed into breast milk and mothers should not breast feed during treatment or for 72 hours thereafter.

Pregnancy. In a review of 637 women given praziquantel in a mass distribution programme, 88 had had a single oral dose during pregnancy, including 37 in their first trimester. All pregnancies ended in full-term babies and there was no evidence of clinical abnormality. No difference was found in the rates of preterm delivery or abortion compared with a control group.[1]

1. Adam I,*et al.* Is praziquantel therapy safe during pregnancy? *Trans R Soc Trop Med Hyg* 2004; **98:** 540–3.

Interactions

Anthelmintics. For reference to plasma concentrations of the active metabolite of *albendazole* being increased by praziquantel, see p.139.

Antibacterials. A study[1] in healthy subjects found that oral *rifampicin* decreased plasma concentrations after single and multiple doses of oral praziquantel to subtherapeutic levels.

1. Ridtitid W, *et al.* Rifampin markedly decreases plasma concentrations of praziquantel in healthy volunteers. *Clin Pharmacol Ther* 2002; **72:** 505–13.

Antiepileptics. *Carbamazepine* and *phenytoin* have been reported to reduce the bioavailability of praziquantel.[1]

1. Quinn DI, Day RO. Drug interactions of clinical importance: an updated guide. *Drug Safety* 1995; **12:** 393–452.

Antimalarials. *Chloroquine* has been reported to reduce the bioavailability of praziquantel.[1]

1. Masimirembwa CM, *et al.* The effect of chloroquine on the pharmacokinetics and metabolism of praziquantel in rats and in humans. *Biopharm Drug Dispos* 1994; **15:** 33–43.

Corticosteroids. Corticosteroids may be used to reduce the inflammatory reactions that often occur within 2 to 3 days of starting cysticidal therapy. However, use is complicated by the fact that dexamethasone roughly halves the plasma concentration of praziquantel. It has therefore been suggested that when praziquantel is given in the 2-week treatment regimen, corticosteroids should not be given prophylactically but only if an inflammatory reaction develops. Dexamethasone is then given daily for 2 or 3 days and most of the treatment period will be free of pharmacokinetic interaction. When the short course praziquantel regimen is used (3 doses given 2 hours apart), the corticosteroid may be given prophylactically. The first dose of dexamethasone is given 4 hours after the last dose of praziquantel (when the concentration of praziquantel is starting to decrease and the pharmacological action is assumed to have been accomplished) and then daily for 2 to 3 days. No pharmacokinetic interaction would be expected at this point.[1]

1. Sotelo J, Jung H. Pharmacokinetic optimisation of the treatment of neurocysticercosis. *Clin Pharmacokinet* 1998; **34:** 503–15.

Histamine H_2-antagonists. *Cimetidine* has been reported to increase praziquantel bioavailability.[1,2]

1. Metwally A, *et al.* Effect of cimetidine, bicarbonate and glucose on the bioavailability of different formulations of praziquantel. *Arzneimittelforschung* 1995; **45:** 516–18.
2. Jung H, *et al.* Pharmacokinetic study of praziquantel administered alone and in combination with cimetidine in a single-day therapeutic regimen. *Antimicrob Agents Chemother* 1997; **41:** 1256–9.

Pharmacokinetics

Praziquantel is rapidly absorbed after oral doses; more than 80% of a dose is reported to be absorbed. Peak plasma concentrations occur 1 to 3 hours after a dose, but there is a pronounced first-pass effect and praziquantel undergoes rapid and extensive metabolism in the liver, being hydroxylated to metabolites that are thought to be inactive. It is distributed into the CSF. The plasma elimination half-life of praziquantel is about 1 to 1.5 hours and that of the metabolites about 4 hours.

It is excreted in the urine, mainly as metabolites, about 80% of the dose being eliminated within 4 days and more than 90% of this in the first 24 hours.

Praziquantel is distributed into breast milk.

◊ References.

1. Leopold G, *et al.* Clinical pharmacology in normal volunteers of praziquantel, a new drug against schistosomes and cestodes: an example of a complex study covering both tolerance and pharmacokinetics. *Eur J Clin Pharmacol* 1978; **14:** 281–91.
2. Bühring KU, *et al.* Metabolism of praziquantel in man. *Eur J Drug Metab Pharmacokinet* 1978; **3:** 179–90.
3. Patzschke K, *et al.* Serum concentrations and renal excretion in humans after oral administration of praziquantel—results of three determination methods. *Eur J Drug Metab Pharmacokinet* 1979; **3:** 149–56.
4. Mandour M El M, *et al.* Pharmacokinetics of praziquantel in healthy volunteers and patients with schistosomiasis. *Trans R Soc Trop Med Hyg* 1990; **84:** 389–93.

Uses and Administration

Praziquantel is an anthelmintic with a broad spectrum of activity against trematodes (flukes) including all species of *Schistosoma* pathogenic to man, and against cestodes (tapeworms). It is used in the treatment of cysticercosis, diphyllobothriasis, hymenolepiasis, schistosomiasis, taeniasis, and intestinal, liver, and lung fluke infections. For discussions of these infections and their treatment, see under Choice of Anthelmintic, p.134, and under the individual headings below.

Praziquantel is given orally with food.

In the treatment of schistosomiasis in adults and children over 4 years it is given on one day as three doses of 20 mg/kg at intervals of 4 to 6 hours or it is given as a single dose of 40 to 60 mg/kg (but see below).

Doses in adults and children over 4 years in the liver fluke infections clonorchiasis and opisthorchiasis are 25 mg/kg three times daily for one or two days or a single dose of 40 mg/kg. Similar doses may be used in intestinal fluke and lung fluke infections (see below).

Single doses of 5 to 25 mg/kg are used in adults and children over 4 years in tapeworm infections.

Praziquantel is used in adults and children over 4 years in the treatment of neurocysticercosis in a dose of 50 mg/kg daily in 3 divided doses for 14 days. An alternative regimen of 3 doses of 25 mg/kg every 2 hours has been proposed.

◊ Reviews.

1. Pearson RD, Guerrant RL. Praziquantel: a major advance in anthelmintic therapy. *Ann Intern Med* 1983; **99:** 195–8. Correction. *ibid.*; 574.
2. King CH, Mahmoud AAF. Drugs five years later: praziquantel. *Ann Intern Med* 1989; **110:** 290–6.
3. Cioli D, Pica-Mattocia L. Praziquantel. *Parasitol Res* 2003; **90** (suppl 1): S3–S9.

Cysticercosis. Praziquantel is used in the treatment of neurocysticercosis (p.135) although albendazole is also considered to be the drug of choice.

References.

1. Sotelo J, Jung H. Pharmacokinetic optimisation of the treatment of neurocysticercosis. *Clin Pharmacokinet* 1998; **34:** 503–15.
2. Del Brutto OH, *et al.* Single-day praziquantel versus 1-week albendazole for neurocysticercosis. *Neurology* 1999; **52:** 1079–81.
3. OH Del Brutto, *et al.* Meta-analysis: cysticidal drugs for neurocysticercosis: albendazole and praziquantel. *Ann Intern Med* 2006; **145:** 43–51.

Echinococcosis. Praziquantel may be used as an adjunct to surgery in echinococcosis (p.136). Praziquantel has been reported to possess a scolicidal effect *in vitro* against *Echinococcus granulosus*[1] and there has been a report of the successful treatment of disseminated peritoneal hydatid disease with praziquantel and surgery.[2] In this case praziquantel was effective against the small cysts; 2 large cysts were removed surgically, one before praziquantel was started. However, activity in 9 other patients given praziquantel was disappointing.[3] A combination of praziquantel with albendazole may be effective.[4]

1. Morris DL, *et al.* Protoscolicidal effect of praziquantel— in vitro and electron microscopical studies on Echinococcus granulosus. *J Antimicrob Chemother* 1986; **18:** 687–91.
2. Henriksen T-H, *et al.* Treatment of disseminated peritoneal hydatid disease with praziquantel. *Lancet* 1989; **i:** 272.
3. Piens MA, *et al.* Praziquantel dans l'hydatidose humaine: évaluation par traitement médical pré-opératoire. *Bull Soc Pathol Exot Filiales* 1989; **82:** 503–12.
4. Ayles HM, *et al.* A combined medical and surgical approach to hydatid disease: 12 years' experience at the Hospital for Tropical Diseases, London. *Ann R Coll Surg Engl* 2002; **84:** 100–105.

Intestinal fluke infections. Praziquantel is used in the treatment of intestinal fluke infections (p.136). In the treatment of fasciolopsiasis, heterophyiasis, and metagonimiasis, the usual recommended dose is 25 mg/kg three times daily for one day.[1] However, a single dose of 25 mg/kg has also been recommended.[2] Single doses of 15 mg/kg, 25 mg/kg, or 40 mg/kg all yielded a cure rate of 100% in a study in 72 primary-school children in Thailand who were harbouring *Fasciolopsis buski*, suggesting that a single dose of 15 mg/kg at bedtime might be tried.[3] In another study, 9 patients infected with the trematode *Nanophyetus salmincola* were treated with praziquantel 20 mg/kg three times daily for one day and were negative for eggs in their stools 2 to 12 weeks later,[4] and this has become the usual recommended dose.[1]

1. Abramowicz M, ed. *Drugs for parasitic infections*. 1st ed. New Rochelle NY: The Medical Letter, 2007.
2. WHO. *WHO model formulary*. Geneva: WHO, 2004.
3. Harinasuta T, *et al.* Efficacy of praziquantel on fasciolopsiasis. *Arzneimittelforschung* 1984; **34:** 1214–15.
4. Fritsche TR, *et al.* Praziquantel for treatment of human Nanophyetus salmincola (Troglotrema salmincola) infection. *J Infect Dis* 1989; **160:** 896–9.

Liver fluke infections. Praziquantel is used in the treatment of clonorchiasis and opisthorchiasis, and has also been used in the treatment of fascioliasis (p.137) although in this latter infection bithionol or triclabendazole are preferred.

Various studies have shown praziquantel to be effective in clonorchiasis[1-4] and opisthorchiasis,[5,6] although one study in opisthorchiasis[7] showed that re-infection was common despite praziquantel therapy, particularly in those with heavy initial infection. A study in Thailand[8] confirmed that mass treatment for opisthorchiasis with a single dose of praziquantel was beneficial, although it was suggested that ideally treatment should be given twice a year.

While praziquantel is not the drug of choice for fascioliasis, there has been a report[9] of successful treatment of a patient with severe infection. Subsequent studies[10-12] have, however, shown praziquantel to be of little benefit.

1. Soh C-J. Clonorchis sinensis: experimental and clinical studies with praziquantel in Korea. *Arzneimittelforschung* 1984; **34:** 1156–9.
2. Chen C-Y, Hsieh W-C. Clonorchis sinensis: epidemiology in Taiwan and clinical experience with praziquantel. *Arzneimittelforschung* 1984; **34:** 1160–2.
3. Kuang Q-H, *et al.* Clonorchiasis: treatment with praziquantel in 50 cases. *Arzneimittelforschung* 1984; **34:** 1162–3.
4. Lee S-H. Large scale treatment of clonorchis sinensis infections with praziquantel under field conditions. *Arzneimittelforschung* 1984; **34:** 1227–8.
5. Bunnag D, *et al.* Opisthorchis viverrini: clinical experience with praziquantel in hospital for tropical diseases. *Arzneimittelforschung* 1984; **34:** 1173–4.
6. Ambroise-Thomas P, *et al.* Therapeutic results in opisthorchiasis with praziquantel in a reinfection-free environment in France. *Arzneimittelforschung* 1984; **34:** 1177–9.
7. Upatham ES, *et al.* Rate of re-infection by Opisthorchis viverrini in an endemic northeast Thai community after chemotherapy. *Int J Parasitol* 1988; **18:** 643–9.
8. Pungpak S, *et al.* Opisthorchis viverrini infection in Thailand: studies on the morbidity of the infection and resolution following praziquantel treatment. *Am J Trop Med Hyg* 1997; **56:** 311–14.
9. Schiappacasse RH, *et al.* Successful treatment of severe infection with Fasciola hepatica with praziquantel. *J Infect Dis* 1985; **152:** 1339–40.
10. Farag HF, *et al.* A short note on praziquantel in human fascioliasis. *J Trop Med Hyg* 1986; **89:** 79–80.
11. Farid Z, *et al.* Unsuccessful use of praziquantel to treat acute fascioliasis in children. *J Infect Dis* 1986; **154:** 920–1.
12. Farid Z, *et al.* Treatment of acute toxaemic fascioliasis. *Trans R Soc Trop Med Hyg* 1988; **82:** 299.

Lung fluke infections. Praziquantel is used in the treatment of the lung fluke infection paragonimiasis (p.137).

References.

1. Vanijanonta S, *et al.* Paragonimus heterotremus and other Paragonimus spp. in Thailand: pathogenesis clinic and treatment. *Arzneimittelforschung* 1984; **34:** 1186–8.
2. Pachucki CT, *et al.* American paragonimiasis treated with praziquantel. *N Engl J Med* 1984; **311:** 582–3.
3. De NV, *et al.* Epidemiology, symptoms and treatment of paragonimiasis in Sin Ho district, Lai Chau province, Vietnam. *Southeast Asian J Trop Med Public Health* 2000; **31** (suppl 1): 26–30.

Schistosomiasis. Praziquantel is the main drug[1,2] used in the treatment of schistosomiasis (p.138). It is effective against all species of schistosomes.[1] Doses are either 20 mg/kg given three times in one day or a single dose of 40 mg/kg. WHO considers[1] that in the field such a single-dose treatment will produce a cure rate of 60 to 90% with a reduction in egg count in those not cured

of 90 to 95%. Good as such results are, a single dose or one day's sole treatment should not be considered to be all that is required to achieve a permanent cure or prevent re-infection, and any treatment plan should be reassessed after 6 or 12 months.[3,4] Such an approach with annual screening and targeted chemotherapy can provide, at least in some endemic areas, successful protection for children against intense infection and consequent hepatic disease.[4]

Several studies indicate that doses lower than those recommended above might be effective and in some control programmes 20 mg/kg might be enough for *S. haematobium*[5-7] or 30 mg/kg for *S. mansoni*.[5] The extent to which low doses contribute to resistance, as has been suggested with oxamniquine,[8] is unclear, but refractory infections have been reported. A 4-day treatment course was needed to produce a complete cure in a patient who relapsed twice following standard one-day treatment regimens.[9] Hepatic impairment, specifically hepatic fibrosis, is a feature of some schistosomal infections and patients with such liver involvement have benefited from treatment with praziquantel.[4,10]

1. WHO. The control of schistosomiasis: second report of the WHO expert committee. *WHO Tech Rep Ser 830* 1993.
2. Doenhoff MJ, Pica-Mattocia L. Praziquantel for the treatment of schistosomiasis: its use for control in areas with endemic disease and prospects for drug resistance. *Expert Rev Anti Infect Ther* 2006; **4:** 199–210.
3. Anonymous. The chemotherapy of schistosomiasis control. *Bull WHO* 1986; **64:** 23–5.
4. Anonymous. Mass treatment of schistosomiasis with praziquantel. *WHO Drug Inf* 1988; **2:** 184–5.
5. Taylor P, *et al.* Efficacy of low doses of praziquantel for Schistosoma mansoni and S. haematobium. *J Trop Med Hyg* 1988; **91:** 13–17.
6. King CH, *et al.* Dose-finding study for praziquantel therapy of Schistosoma haematobium in Coast Province, Kenya. *Am J Trop Med Hyg* 1989; **40:** 507–13.
7. Hatz C, *et al.* Ultrasound scanning for detecting morbidity due to Schistosoma haematobium and its resolution following treatment with different doses of praziquantel. *Trans R Soc Trop Med Hyg* 1990; **84:** 84–8.
8. Coles GC, *et al.* Tolerance of Kenyan Schistosoma mansoni to oxamniquine. *Trans R Soc Trop Med Hyg* 1987; **81:** 782–5.
9. Murray-Smith SQ, *et al.* A case of refractory schistosomiasis. *Med J Aust* 1996; **165:** 458.
10. Zwingenberger K, *et al.* Praziquantel in the treatment of hepatosplenic schistosomiasis: biochemical disease markers indicate deceleration of fibrogenesis and diminution of portal flow obstruction. *Trans R Soc Trop Med Hyg* 1990; **84:** 252–6.

Taeniasis. Praziquantel is used in the treatment of taeniasis (p.139). It has been studied in the mass control of taeniasis when a single dose of 5 mg/kg was used.[1]

Praziquantel is also effective against the larval form of *Taenia solium* and is used to treat neurocysticercosis (see above).

1. Cruz M, *et al.* Operational studies on the control of Taenia solium taeniasis/cysticercosis in Ecuador. *Bull WHO* 1989; **67:** 401–7.

Preparations

USP 31: Praziquantel Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Prazitral; ***Austral.:*** Biltricide; ***Braz.:*** Cestox; Cisticid; ***Canad.:*** Biltricide; ***Chile:*** Cesol; Cisticid; ***Fr.:*** Biltricide; ***Ger.:*** Biltricide; Cesol; Cysticide; ***Gr.:*** Biltricide; ***Hong Kong:*** Biltricide; ***Israel:*** Biltricide; ***Mex.:*** Bio-Cest†; Cesol; Cisticid; Extiser-Q†; Prozitel†; Tecprazin; Teniken; Zifartel; ***Neth.:*** Biltricide; ***Rus.:*** Biltricid (Бильтрицид); ***S.Afr.:*** Biltricide; Cysticide; ***Thai.:*** Mycotricide; Opticide; Praquantel; Prasikon; Prazite; Wormicide; ***USA:*** Biltricide; ***Venez.:*** Cestox; Cisticid†.

Pyrantel Embonate *(BANM, rINNM)*

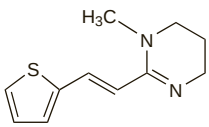
CP-10423-16; Embonato de pirantel; Pirantel Pamoat; Pirantel Pamoate; Pirantelio embonatas; Pyranteeliembonaatti; Pyrantel, embonate de; Pyrantel Pamoate *(USAN)*; Pyrantelembonat; Pyrantel-embonát; Pyranteli embonas; Pyrantelu embonian. 1,4,5,6-Tetrahydro-1-methyl-2-[(*E*)-2-(2-thienyl)vinyl]pyrimidine 4,4′-methylenebis(3-hydroxy-2-naphthoate).

Пирантела Эмбонат

$C_{11}H_{14}N_2S$,$C_{23}H_{16}O_6$ = 594.7.

CAS — 15686-83-6 (pyrantel); 22204-24-6 (pyrantel embonate); 33401-94-4 (pyrantel tartrate).

ATC — P02CC01.



(pyrantel)

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, and *US.*

Ph. Eur. 6.2 (Pyrantel Embonate). A pale yellow or yellow powder. Practically insoluble in water and in methyl alcohol; soluble in dimethyl sulfoxide. Protect from light.

USP 31 (Pyrantel Pamoate). A yellow to tan solid. Practically insoluble in water and in methyl alcohol; soluble in dimethyl sulfoxide; slightly soluble in dimethylformamide. Protect from light.

Adverse Effects and Precautions

The adverse effects of pyrantel embonate are generally mild and transient. The most frequent are gastrointestinal effects such as nausea and vomiting, anorexia, abdominal pain, and diarrhoea. Other adverse effects reported include headache, dizziness, drowsiness, insomnia, skin rashes, and raised liver enzyme values.

Pyrantel embonate should be used with caution in patients with hepatic impairment.

Interactions

The anthelmintic effects of both pyrantel and piperazine may be antagonised when the two drugs are used together.

Pharmacokinetics

Only a small proportion of a dose of pyrantel embonate is absorbed from the gastrointestinal tract. Up to about 7% is excreted as unchanged drug and metabolites in the urine but over half of the dose is excreted unchanged in the faeces.

Uses and Administration

Pyrantel embonate is an anthelmintic effective against intestinal nematodes including roundworms (*Ascaris lumbricoides*), threadworms (*Enterobius vermicularis*), and *Trichostrongylus* spp., the tissue nematode *Trichinella spiralis*, and hookworms, although it is possibly less effective against *Necator americanus* hookworms than against *Ancylostoma duodenale*. Pyrantel embonate is one of the anthelmintics that may be used in the treatment of infections with these worms, as discussed under Choice of Anthelmintic, p.134. It appears to act by paralysing susceptible worms which are then dislodged by peristaltic activity.

Pyrantel is given orally as the embonate, but doses are described in terms of the base. Pyrantel embonate 2.9 g is equivalent to about 1 g of pyrantel.

Single or mixed infections due to susceptible worms in adults and children may be treated with the equivalent of pyrantel 10 mg/kg as a single oral dose. Ascariasis occurring alone may only require 5 mg/kg; a single dose of 2.5 mg/kg given three or four times a year has been used in mass treatment programmes. In necatoriasis, 10 mg/kg daily for 3 or 4 days or 20 mg/kg daily for 2 days may be necessary. The response in enterobiasis may be improved by repeating the 10 mg/kg dose after 2 to 4 weeks. In trichinosis, a dose of 10 mg/kg daily for 5 days has been used.

Pyrantel tartrate has been used as a veterinary anthelmintic.

Preparations

USP 31: Pyrantel Pamoate Oral Suspension.

Proprietary Preparations (details are given in Part 3)

Arg.: Aut†; ***Austral.:*** Anthel; Combantrin; Early Bird; ***Austria:*** Combantrin; ***Braz.:*** Ascarical; ***Canad.:*** Combantrin; Jaa Pyral; ***Chile:*** Combantrin; ***Fr.:*** Combantrin; Helmintox; ***Ger.:*** Helmex; ***Gr.:*** Combantrin†; ***Hong Kong:*** Combantrin; Pyrantin; Pyrantrin†; ***India:*** Nemocid; ***Indon.:*** Combantrin; Konvermex; Medicomtrin; Piraska; Proworm; ***Israel:*** Combantrin†; ***Ital.:*** Combantrin; ***Mex.:*** Combantrin; Pirantrim; ***NZ:*** Combantrin; ***Philipp.:*** Combantrin; Gelminthic; ***Port.:*** Combantrin; Vertel†; ***Rus.:*** Helmintox (Гельминтокс); Nemocid (Немоцид); ***S.Afr.:*** Combantrin; ***Singapore:*** Bearantel; ***Spain:*** Lombriareu; Trilombrin; ***Switz.:*** Cobantril; ***Thai.:*** Bantel†; Pyrapam; ***Turk.:*** Kontil; ***USA:*** Antiminth†; Pin-Rid; Pin-X; Reese's Pinworm; ***Venez.:*** Combantrin; Etimex†; Pamoval†; Pleosan†; Tamoa; Tenecha†.

Multi-ingredient: ***India:*** Mebex Plus; ***Indon.:*** Quantrel; ***Philipp.:*** Quantrel; ***Venez.:*** Dualid; Quantrel.

Pyrvinium Embonate *(rINNM)*

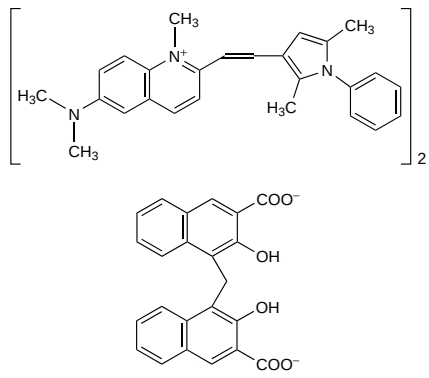
Embonato de pirvinio; Pirvinyum Pamoat; Pyrvinii Embonas; Pyrvinium, Embonate de; Pyrvinium Pamoate *(BAN)*; Viprynium Embonate; Viprynium Pamoate. Bis{6-dimethylamino-2-[2-(2,5-dimethyl-1-phenylpyrrol-3-yl)vinyl]-1-methylquinolinium} 4,4′-methylenebis(3-hydroxy-2-naphthoate).

Пирвиния Эмбонат

$C_{52}H_{56}N_6$,$C_{23}H_{14}O_6$ = 1151.4.

CAS — 3546-41-6.

ATC — P02CX01.



Pharmacopoeias. In *US.*

USP 31 (Pyrvinium Pamoate). A bright orange or orange-red to practically black crystalline powder. Practically insoluble in water and in ether; slightly soluble in chloroform and in methoxyethanol; freely soluble in glacial acetic acid; very slightly soluble in methyl alcohol. Store in airtight containers. Protect from light.

Adverse Effects

Pyrvinium occasionally causes nausea, vomiting, abdominal pain, and diarrhoea. Hypersensitivity reactions and photosensitivity have been reported. Headache may occur.

Pyrvinium stains the stools bright red and may stain clothing if vomiting occurs.

Pharmacokinetics

Pyrvinium embonate is not significantly absorbed from the gastrointestinal tract.

Uses and Administration

Pyrvinium embonate is an effective anthelmintic in the treatment of enterobiasis (p.136), but has generally been superseded by other drugs.

Pyrvinium is given as the embonate but doses are described in terms of the base. Pyrvinium embonate 7.5 mg is equivalent to about 5 mg of pyrvinium.

It has been given orally in a single dose equivalent to pyrvinium 5 mg/kg, repeated after 2 to 3 weeks.

Preparations

USP 31: Pyrvinium Pamoate Oral Suspension; Pyrvinium Pamoate Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Tru; ***Austria:*** Molevac; ***Braz.:*** Enterocid†; Pyr-Pam†; Pyverm; ***Canad.:*** Vanquin†; ***Denm.:*** Vanquin; ***Fin.:*** Pyrvin; ***Fr.:*** Povanyl; ***Ger.:*** Molevac; Pyrcon; ***Norw.:*** Vanquin; ***Spain:*** Pamoxan; ***Swed.:*** Vanquin; ***Turk.:*** Pirok.

Rafoxanide *(BAN, USAN, rINN)*

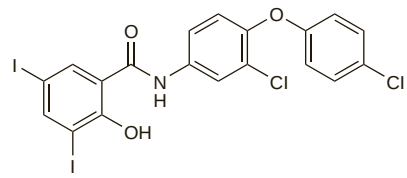
MK-990; Rafoxanida; Rafoxanidum. 3′-Chloro-4′-(4-chlorophenoxy)-3,5-di-iodosalicylanilide.

Рафоксанид

$C_{19}H_{11}Cl_2I_2NO_3$ = 626.0.

CAS — 22662-39-1.

ATC Vet — QP52AG05.



Profile

Rafoxanide is an anthelmintic used in veterinary medicine for the treatment of fascioliasis in cattle and sheep.