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)*

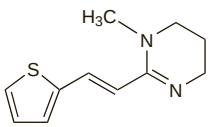
CP-10423-16; Embonato de pirantel; Pirantel Pamoat; Pirantel Pamoate; Pirantelio embonatas; Pyranteeliembonaatti; Pyrantel, embonate de; Pyrantel Pamoate *(USAN)*; Pyrantelembonat; Pyrantel-embonát; Pyranteli embonas; Pyrantelu embonian. 1,4,5,6-Tetrahydro-1-methyl-2-[(*E*)-2-(2-thienyl)vinyl]pyrimidine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

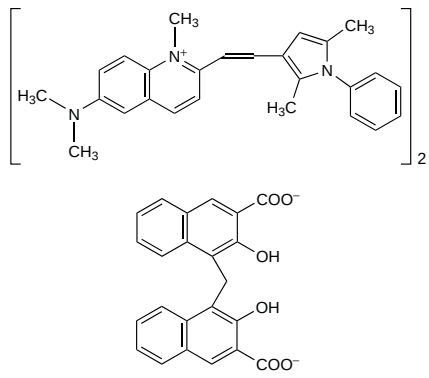
Embonato de pirvinio; Pirvinyum Pamoat; Pyrvinii Embonas; Pyrvinium, Embonate de; Pyrvinium Pamoate *(BAN)*; Viprynium Embonate; Viprynium Pamoate. Bis{6-dimethylamino-2-[2-(2,5-dimethyl-1-phenylpyrrol-3-yl)vinyl]-1-methylquinolinium} 4,4′-methylenebis(3-hydroxy-2-naphthoate).

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)*

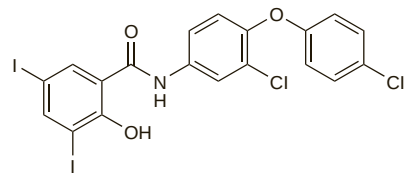
MK-990; Rafoxanida; Rafoxanidum. 3′-Chloro-4′-(4-chlorophenoxy)-3,5-di-iodosalicylanilide.

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.

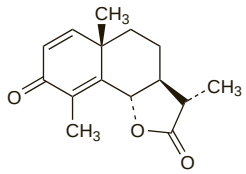
### Santonin

Santoniini; Santonina; Santoninum. (3*S*,3a*S*,5a*S*,9b*S*)-3a,5,5a,9b-Tetrahydro-3,5a,9-trimethylnaphtho[1,2-*b*]furan-2,8(3*H*,4*H*)-dione.

Сантонин

$C_{15}H_{18}O_3$ = 246.3.

*CAS — 481-06-1.*



**Pharmacopoeias.** In *Jpn*.

#### Profile

Santonin is a crystalline lactone obtained from the dried unexpanded flowerheads of *Artemisia cina* (santonica, wormwood) and other species of *Artemisia* (Compositae). It was formerly used as an anthelmintic in the treatment of roundworm (*Ascaris*) infection, but has been superseded by other less toxic anthelmintics.

It is used as a flavour in food.

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### Selamectin *(USAN, rINN)*

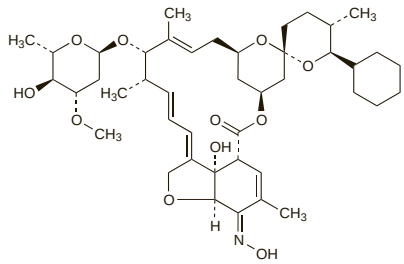
Selamectina; Sélamectine; Selamectinum; Selamektiini; Selamektin; UK-124114. (2a*E*,4*E*,5′*S*,6*S*,6′*S*,7*S*,8*E*,11*R*,13*R*,15*S*,17a*R*,20a*R*,20b*S*)-6′-Cyclohexyl-7-[(2,6-dideoxy-3-*O*-methyl-α-L-*arabino*-hexopyranosyl)oxy]-3′,4′,5′,6,6′,7,10,11,14,15,20a,20b-dodecahydro-20b-hydroxy-5′,6,8,19-tetramethylspiro(11,15-methano-2*H*,13*H*,17*H*-furo[4,3,2-*p*,*q*][2,6]benzodioxacyclooctadecin-13,2′-[2*H*]pyran)-17,20(17a*H*)-dione 20-oxime.

Селамектин

$C_{43}H_{63}NO_{11}$ = 770.0.

*CAS — 165108-07-6.*

*ATC Vet — QP54AA05.*



**Pharmacopoeias.** In *Eur.* (see p.vii) for veterinary use only.

**Ph. Eur. 6.2** (Selamectin for Veterinary Use). A semi-synthetic product derived from a fermentation product. A white or almost white, hygroscopic powder. Practically insoluble in water; soluble in acetone and in dichloromethane; freely soluble in isopropyl alcohol; sparingly soluble in methyl alcohol. Store in airtight containers.

#### Profile

Selamectin is an avermectin anthelmintic and ectoparasiticide used in veterinary medicine.

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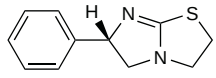
### Tetramisole Hydrochloride *(BANM, USAN, rINNM)*

Hidrocloruro de tetramisol; ICI-50627; McN-JR-8299-11; R-8299; Tétramisole, Chlorhydrate de; Tetramisoli Hydrochloridum. (±)-2,3,5,6-Tetrahydro-6-phenylimidazo[2,1-*b*]thiazole hydrochloride.

Тетрамизола Гидрохлорид

$C_{11}H_{12}N_2S,HCl$ = 240.8.

*CAS — 5036-02-2 (tetramisole); 5086-74-8 (tetramisole hydrochloride).*



*(tetramisole)*

**Pharmacopoeias.** In *Fr.* for veterinary use only.

#### Profile

Tetramisole hydrochloride is an anthelmintic used in veterinary medicine for the control of nematode infections. It is a racemic mixture and the laevo-isomer, levamisole hydrochloride (p.147), accounts for most of its activity.

#### Preparations

**Proprietary Preparations** (details are given in Part 3)
***Braz.:*** Ascarizole†; Tetramizotil†.

**Multi-ingredient:** ***India:*** Jetomisol-P.

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### Thiacetarsamide *(rINNM)*

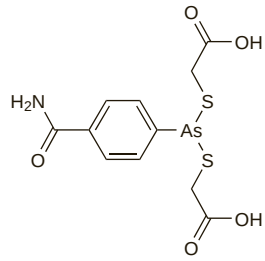
Thiacétarsamide; Thiacetarsamidum; Tiacetarsamida. *p*-[Bis(carboxymethylmercapto)arsino]benzamide; 4-Carbamylphenyl bis[carboxymethylthio]arsenite.

Тиацетарсамид

$C_{11}H_{12}AsNO_5S_2$ = 377.3.

*CAS — 531-72-6.*

*ATC Vet — QP52AX08.*



#### Profile

Thiacetarsamide is an anthelmintic used in veterinary medicine.

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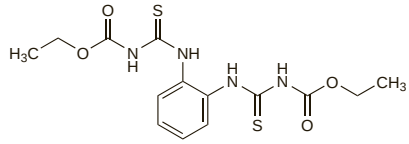
### Thiophanate *(BAN)*

Tiofanato. 4,4′-*o*-Phenylenebis(ethyl 3-thioallophanate).

$C_{14}H_{18}N_4O_4S_2$ = 370.4.

*CAS — 23564-06-9.*

*ATC Vet — QP52AC04.*



#### Profile

Thiophanate is an anthelmintic used in veterinary medicine for the control of nematode infections.

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## Tiabendazole *(BAN, rINN)*

E233; MK-360; Thiabendazole *(USAN)*; Tiabendatsoli; Tiabendazol; Tiabendazolas; Tiabendazolum. 2-(Thiazol-4-yl)-1*H*-benzimidazole.

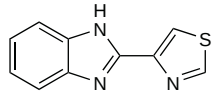
Тиабендазол

$C_{10}H_7N_3S$ = 201.2.

*CAS — 148-79-8.*

*ATC — D01AC06; P02CA02.*

*ATC Vet — QD01AC06; QP52AC10.*



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

**Ph. Eur. 6.2** (Tiabendazole). A white or almost white crystalline powder. Practically insoluble in water; slightly soluble in alcohol and in dichloromethane; it dissolves in dilute mineral acids. Protect from light.

**USP 31** (Thiabendazole ). A white to practically white, odourless or practically odourless, powder. Practically insoluble in water; slightly soluble in alcohol and in acetone; very slightly soluble in chloroform and in ether.

### Adverse Effects

Dizziness and gastrointestinal disturbances, especially anorexia, nausea and vomiting, diarrhoea, and abdominal pain are common during treatment with tiabendazole. Other adverse effects occurring occasionally include pruritus, skin rashes, headache, fatigue, drowsiness, drying of mucous membranes, hyperglycaemia, disturbance of vision including colour vision, leucopenia, tinnitus, effects on the liver including cholestasis and parenchymal damage (in some cases severe and irreversible), enuresis, crystalluria, and bradycardia and hypotension. There have also been reports of erythema multiforme, fatal Stevens-Johnson syndrome, toxic epidermal necrolysis, convulsions, and effects on mental state.

Fever, chills, angioedema, and lymphadenopathy have been reported, but may represent allergic response to dead parasites rather than to tiabendazole.

The urine of some patients taking tiabendazole may have a characteristic odour similar to that after eating asparagus; it is attributed to the presence of a tiabendazole metabolite.

**Effects on the salivary glands.** Dry mouth with swollen parotid and salivary glands suggestive of the sicca complex preceded the development of cholestatic jaundice in a 17-year-old boy given tiabendazole.[1]

1. Davidson RN, *et al.* Intrahepatic cholestasis after thiabendazole. *Trans R Soc Trop Med Hyg* 1988; **82:** 620.

**Hypersensitivity.** Severe erythema multiforme developed in a patient 16 days after a course of tiabendazole.[1] Many of the lesions encircled pre-existing melanocytic naevi.

1. Humphreys F, Cox NH. Thiabendazole-induced erythema multiforme with lesions around melanocytic naevi. *Br J Dermatol* 1988; **118:** 855–6.

### Precautions

Tiabendazole should be used with caution in patients with hepatic or renal impairment. Tiabendazole causes drowsiness in some patients and those affected should not drive or operate machinery.

Tiabendazole should not be used in mixed worm infections involving *Ascaris lumbricoides* as it can cause these roundworms to migrate; live roundworms have emerged through the mouth or nose.

**Pregnancy.** Tiabendazole is teratogenic in *mice* although there are no adequate and well controlled studies in human pregnancy.

**Renal impairment.** Tiabendazole and its 5-hydroxy metabolite did not accumulate in an anephric patient on haemodialysis and haemoperfusion who was treated for severe strongyloidiasis.[1] However, the potentially toxic conjugated glucuronide and sulfate metabolites did accumulate. The clearance of all 3 metabolites was poor by haemodialysis; haemoperfusion was much more efficient, although for rapid removal the haemoperfusion columns should be changed every hour.

1. Bauer L, *et al.* The pharmacokinetics of thiabendazole and its metabolites in an anephric patient undergoing hemodialysis and hemoperfusion. *J Clin Pharmacol* 1982; **22:** 276–80.

### Interactions

**Xanthines.** For the effect of tiabendazole on serum concentrations of *theophylline*, see p.1145.

### Pharmacokinetics

Tiabendazole is readily absorbed from the gastrointestinal tract and reaches peak concentrations in the plasma after 1 to 2 hours. It is metabolised to 5-hydroxythiabendazole and excreted principally in the urine as glucuronide or sulfate conjugates; about 90% is recovered in the urine within 48 hours of ingestion, but only 5% in the faeces. Absorption may occur from preparations applied to the skin or eyes.

◊ References.

1. Tocco DJ, *et al.* Absorption, metabolism, and excretion of thiabendazole in man and laboratory animals. *Toxicol Appl Pharmacol* 1966; **9:** 31–9.

### Uses and Administration

Tiabendazole, a benzimidazole derivative, is an anthelmintic with activity against most nematode worms; activity against some larval stages and ova has also been demonstrated. The mode of action is not certain, but tiabendazole may inhibit the fumarate-reductase system of worms thereby interfering with their source of energy.

Tiabendazole is used in the treatment of cutaneous larva migrans, dracunculiasis (guinea worm infection),