ca. Diethylcarbamazine is also used in the treatment of toxocariasis (visceral larva migrans). For discussions of these infections and their treatment, see under Choice of Anthelmintic, p.134, and under the individual headings below.

Diethylcarbamazine is usually given orally as the citrate.

In the treatment of **lymphatic filariasis** the recommended dose of diethylcarbamazine citrate is 6 mg/kg daily in 3 divided doses for 3 weeks, given in an initial dosage of 1 mg/kg daily and then gradually increased to 6 mg/kg daily over 3 days to reduce the incidence and severity of hypersensitivity reactions due to the destruction of microfilariae. However, adverse effects of diethylcarbamazine may be reduced, without loss of efficacy, by giving a single dose of 6 mg/kg at weekly or monthly intervals. In areas where lymphatic filariasis is endemic, mass treatment campaigns can reduce the intensity of transmission and incidence of disease. Diethylcarbamazine may also be used in the form of medicated salt to control lymphatic filariasis. For further details, see below.

In the treatment of **loiasis** diethylcarbamazine citrate 6 mg/kg daily in 3 divided doses for 2 to 4 weeks has been given. In heavy infections rapid killing of microfilariae can cause severe adverse effects including encephalitis and treatment should start with very small doses, increasing gradually over 4 days. A corticosteroid has been given concurrently. In the prophylaxis of loiasis, a dose of 300 mg weekly is recommended by WHO.

In the treatment of **toxocariasis** diethylcarbamazine citrate 9 mg/kg daily in 3 divided doses for 21 days has been given. Diethylcarbamazine is considered by some to be the treatment of choice while others do not recommend its use due to higher rates of severe adverse effects.

Administration. Diethylcarbamazine was first used as the chloride, but was subsequently produced as the dihydrogen citrate which contains only half its weight as base. In reporting doses it was therefore important to indicate whether they referred to a specific salt or to the base; unless otherwise stated, it could generally be assumed that the dose referred to the citrate.[1]

1. WHO. Lymphatic filariasis: fourth report of the WHO expert committee on filariasis. *WHO Tech Rep Ser 702* 1984. Available at: http://libdoc.who.int/trs/WHO_TRS_702.pdf (accessed 16/07/08)

Loiasis. Diethylcarbamazine is the main drug used in the management of loiasis (p.137).

References.

1. Nutman TB, *et al.* Loa loa infection in temporary residents of endemic regions: recognition of a hyperresponsive syndrome with characteristic clinical manifestations. *J Infect Dis* 1986; **154:** 10–18.
2. Nutman TB, *et al.* Diethylcarbamazine prophylaxis for human loiasis: results of a double-blind study. *N Engl J Med* 1988; **319:** 752–6.
3. Nutman TB, Ottesen EA. Diethylcarbamazine and human loiasis. *N Engl J Med* 1989; **320:** 320.
4. Klion AD, *et al.* Effectiveness of diethylcarbamazine in treating loiasis acquired by expatriate visitors to endemic regions: long-term follow-up. *J Infect Dis* 1994; **169:** 604–10.

Lymphatic filariasis. Diethylcarbamazine is used in the management of lymphatic filariasis (p.137). In endemic areas mass treatment of the entire population (excluding neonates, pregnant women, and debilitated individuals) can reduce the intensity of transmission and the incidence of disease. In countries where there is no co-endemic loiasis or onchocerciasis, the Global Programme to Eliminate Lymphatic Filariasis launched by WHO together with other international agencies, advocates a single dose of diethylcarbamazine citrate 6 mg/kg with a single dose of albendazole 400 mg, given once each year for at least 5 years. If diethylcarbamazine-medicated salt is to be employed then intake of salt needs to be on a daily basis for 6 to 12 months.

Preparations

BP 2008: Diethylcarbamazine Tablets;
USP 31: Diethylcarbamazine Citrate Tablets.

Proprietary Preparations (details are given in Part 3)

Fr.: Notezine; ***Gr.:*** Hetrazan†; Notezine; ***India:*** Banocide; Hetrazan; ***Thai.:*** Diethizine.

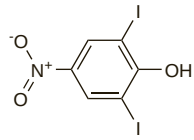
Multi-ingredient: ***India:*** Helmazan†; Unicarbazan.

Disophenol

Disofenol. 2,6-Diiodo-4-nitrophenol.

$C_6H_3I_2NO_3$ = 390.9.

CAS — 305-85-1.



Profile

Disophenol is an anthelmintic used in veterinary medicine.

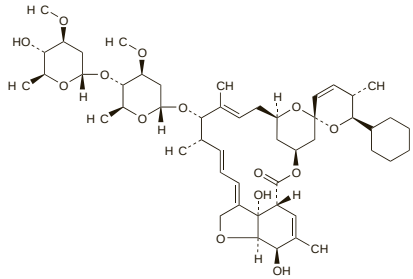
Doramectin *(BAN, USAN, rINN)*

Doramectina; Doramectine; Doramectinum; Doramektiini; Doramektin; UK-67994.

Дорамектин

CAS — 117704-25-3.

ATC Vet — QP54AA03.



Profile

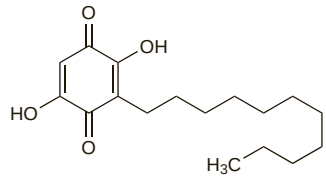
Doramectin is an avermectin anthelmintic used in veterinary medicine for nematode infections. It is also used as a systemic veterinary ectoparasiticide.

Embelia

Vidang.

Виданга

CAS — 550-24-3 (embelic acid).



(embelic acid)

Profile

Embelia consists of the dried fruits of *Embelia ribes* and *E. robusta* (= *E. tsjeriamcottam*) (Myrsinaceae), containing about 2.5% of embelic acid (embelin). It has been used in India and other Asian countries for the expulsion of tapeworms.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***India:*** Happy'tizer.

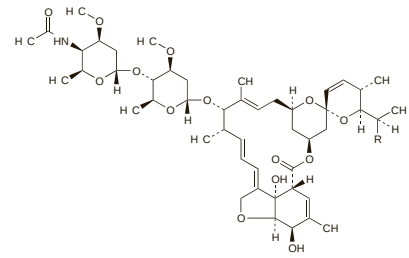
Eprinomectin *(USAN, rINN)*

Eprinomectina; Éprinomectine; Eprinomectinum; Eprinomektiini; Eprinomektin; MK-397. A mixture of eprinomectin component B_{1a} and eprinomectin component B_{1b}.

Эприномектин

CAS — 159628-36-1 (eprinomectin); 123997-26-2 (eprinomectin); 133305-88-1 (component B_{1a}); 133305-89-2 (component B_{1b}).

ATC Vet — QP54AA04.



Pharmacopoeias. In *US.*

USP 31 (Eprinomectin). Eprinomectin is a mixture of component B_{1a} ($C_{50}H_{75}NO_{14}$ = 914.1) and component B_{1b} ($C_{49}H_{73}NO_{14}$ = 900.1). It contains not less than 90% of component B_{1a} and not less than 95% of components B_{1a} and B_{1b}, calculated on the anhydrous, solvent-free, and antoxidant-free basis. Antoxidants may be added. A white to off-white powder. Insoluble in cold water. Store in airtight containers at 2° to 8°.

Profile

Eprinomectin is an avermectin anthelmintic used in veterinary medicine for nematode infections. It is also used as a systemic veterinary ectoparasiticide.

Epsiprantel *(BAN, rINN)*

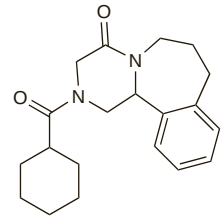
BRL-38705; Epsipranteeli; Epsiprantelum. 2-Cyclohexylcarbonyl-1,2,3,4,6,7,8,12b-octahydropyrazino[2,1-*a*][2]benzazepin-4-one.

Эпсипрантел

$C_{20}H_{26}N_2O_2$ = 326.4.

CAS — 98123-83-2.

ATC Vet — QP52AA04.



Profile

Epsiprantel is an anthelmintic closely related to praziquantel. It is used in veterinary medicine.

Febantel *(BAN, USAN, rINN)*

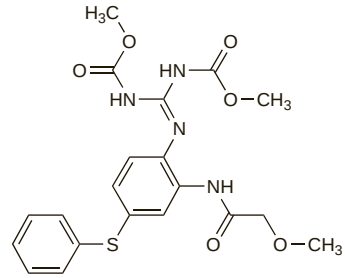
Bay-h-5757; Bay-Vh-5757; Febanteeli; Fébantel; Febantelum. 2′-[2,3-Bis(methoxycarbonyl)guanidino]-5′-phenylthio-2-methoxyacetanilide; Dimethyl {2-[2-(2-methoxyacetamido)-4-(phenylthio)phenyl]imidocarbonyl}dicarbamate.

Фебантел

$C_{20}H_{22}N_4O_6S$ = 446.5.

CAS — 58306-30-2.

ATC Vet — QP52AC05.



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

Ph. Eur. 6.2 (Febantel for Veterinary Use; Febantel BP(Vet) 2008). A white or almost white, crystalline powder. It exhibits polymorphism. Practically insoluble in water; slightly soluble in dehydrated alcohol; soluble in acetone.

Profile

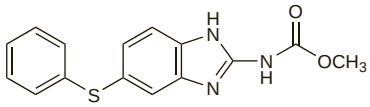
Febantel is an anthelmintic used in veterinary medicine for the treatment of nematode infections of the gastrointestinal tract and lungs and in tapeworm infections.

Fenbendazole *(BAN, USAN, rINN)*

Fenbendatsoli; Fenbendazol; Fenbendazolum; Hoe-881V. Methyl 5-phenylthio-1*H*-benzimidazol-2-ylcarbamate.

Фенбендазол

$C_{15}H_{13}N_3O_2S$ = 299.3.
CAS — 43210-67-9.
ATC — P02CA06.
ATC Vet — QP52AC13.



Pharmacopoeias. In *Eur.* (see p.vii) and *US* for veterinary use only.
Ph. Eur. 6.2 (Fenbendazole for Veterinary Use; Fenbendazole BP(Vet) 2008). A white or almost white powder. Practically insoluble in water; sparingly soluble in dimethylformamide; very slightly soluble in methyl alcohol. Protect from light.
USP 31 (Fenbendazole). A white to off-white powder. Practically insoluble in water; sparingly soluble in dimethylformamide; very slightly soluble in methyl alcohol. Store at a temperature of 25°, excursions permitted between 15° and 30°. Protect from light.

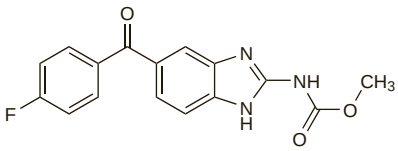
Profile
Fenbendazole is a benzimidazole carbamate anthelmintic structurally related to mebendazole (p.148). It is used in veterinary medicine.

Flubendazole *(BAN, USAN, rINN)*

Flubendatsoli; Flubendazol; Flubendazolas; Flubendazolum; Fluoromebendazole; R-17889. Methyl 5-(4-fluorobenzoyl)-1*H*-benzimidazol-2-ylcarbamate.

Флубендазол

$C_{16}H_{12}FN_3O_3$ = 313.3.
CAS — 31430-15-6.
ATC — P02CA05.
ATC Vet — QP52AC12.



Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Flubendazole). A white or almost white powder. It exhibits polymorphism. Practically insoluble in water, in alcohol, and in dichloromethane. Protect from light.

Profile
Flubendazole, a benzimidazole carbamate anthelmintic, is an analogue of mebendazole (p.148) and has similar actions and uses.

For the treatment of enterobiasis in adults and children, flubendazole 100 mg is given as a single oral dose, repeated after 2 to 3 weeks. For ascariasis, hookworm infections, and trichuriasis 100 mg is given twice daily for 3 days. For discussions of these infections and their treatment, see under Choice of Anthelmintic, p.134.

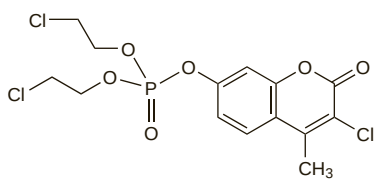
Preparations
Proprietary Preparations (details are given in Part 3)
Arg.: Flumoxal; ***Fr.:*** Fluvermal; ***Port.:*** Fluvermal; Teniverme; ***Spain:*** Flicum; ***Venez.:*** Fluvermox.

Haloxon *(BAN, rINN)*

Haloxón; Haloxone; Haloxonum. Bis(2-chloroethyl) 3-chloro-4-methylcoumarin-7-yl phosphate.

Галоксон

$C_{14}H_{14}Cl_3O_6P$ = 415.6.
CAS — 321-55-1.
ATC Vet — QP52AB04.



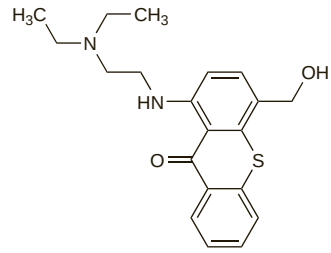
Profile
Haloxon is an organophosphorus compound (see Organophosphorus Insecticides, p.2047) used as an anthelmintic in veterinary medicine.

Hycanthone *(USAN, rINN)*

Hicantona; Hycanthonum; NSC-134434; Win-24933. 1-(2-Diethylaminoethylamino)-4-hydroxymethylthioxanthen-9-one.

Гикантон

$C_{20}H_{24}N_2O_2S$ = 356.5.
CAS — 3105-97-3.



Hycanthone Mesilate *(rINNM)*

Hycanthone, Mésilate d'; Hycanthone Mesylate; Hycanthoni Mesilas; Hydroxylucanthone Methanesulphonate; Mesilato de hicantona.

Гикантона Мезилат

$C_{20}H_{24}N_2O_2S,CH_3SO_3H$ = 452.6.
CAS — 23255-93-8.

Profile
Hycanthone has been used as a schistosomicide in the individual or mass treatment of infection with *Schistosoma haematobium* and *S. mansoni*.

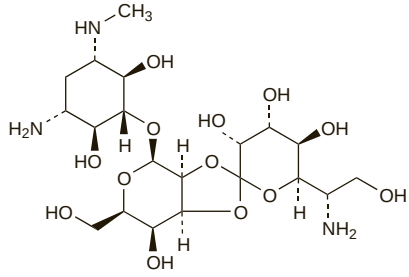
Owing to its toxicity and concern about possible carcinogenicity, mutagenicity, and teratogenicity, hycanthone has been replaced by other drugs such as praziquantel.

Hygromycin B

Higromicina B. *O*-6-Amino-6-deoxy-L-glycero-D-galacto-heptopyranosylidene-(1→2-3)-*O*-β-D-talopyranosyl-(1→5)-2-deoxy-*N*^{3}-methyl-D-streptamine.

Гигромицин Б

$C_{20}H_{37}N_3O_{13}$ = 527.5.



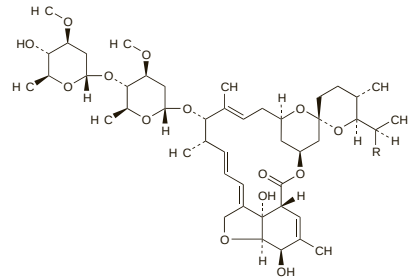
Profile
Hygromycin B is an anthelmintic used in veterinary medicine for nematode infections.

Ivermectin *(BAN, USAN, rINN)*

Ivermectina; Ivermectine; Ivermectinum; Ivermektiini; Ivermektin; Ivermektinas.

Ивермектин

CAS — 70288-86-7 (ivermectin); 70161-11-4 (component B_{1a}); 70209-81-3 (component B_{1b}).
ATC — P02CF01.
ATC Vet — QP54AA01; QS02QA03.



Pharmacopoeias. In *Eur.* (see p.vii) and *US*.
Ph. Eur. 6.2 (Ivermectin). A mixture of ivermectin component H_2B_{1a} (5-*O*-demethyl-22,23-dihydroavermectin A_{1a}; $C_{48}H_{74}O_{14}$ = 875.1) and ivermectin component H_2B_{1b} (5-*O*-demethyl-25-de(1-methylpropyl)-25-(1-methylethyl)-22,23-dihydroavermectin A_{1a}; $C_{47}H_{72}O_{14}$ = 861.1).
A white or yellowish-white, slightly hygroscopic, crystalline powder. Practically insoluble in water; soluble in alcohol; freely soluble in dichloromethane. Store in airtight containers.
USP 31 (Ivermectin). A mixture of component H_2B_{1a} (5-*O*-demethyl-22,23-dihydro-avermectin A_{1a}; $C_{48}H_{74}O_{14}$ = 875.1) and component H_2B_{1b} (5-*O*-demethyl-25-de(1-methylpropyl)-22,23-dihydro-25-(1-methylethyl)-avermectin A_{1a}; $C_{47}H_{72}O_{14}$ = 861.1). It may contain small amounts of suitable antoxidant and chelating agents.
A white to yellowish-white, slightly hygroscopic, crystalline powder. Practically insoluble in water and in petroleum spirit; soluble in acetone and in acetonitrile; freely soluble in dichloromethane and in methyl alcohol. Store in airtight containers at a temperature of 2° to 8°. Where the use of an antoxidant is allowed, store at 25°, excursions permitted between 15° and 30°.

Adverse Effects and Precautions
The adverse effects reported with ivermectin in patients with filariasis are generally consistent with a mild Mazzotti reaction arising from its effect on microfilariae. They include fever, pruritus, skin rashes, arthralgia, myalgia, asthenia, orthostatic hypotension, tachycardia, oedema, lymphadenopathy, gastrointestinal symptoms, sore throat, cough, and headache. The effects tend to be transient and if treatment is required they respond to analgesics and antihistamines.

Ivermectin may cause mild ocular irritation. Somnolence, transient eosinophilia, and raised liver enzyme values have also been reported.

Ivermectin is not recommended during pregnancy. Mass treatment is generally withheld from pregnant women (see Pregnancy, below), children under 15 kg, and the seriously ill.

Incidence of adverse effects. Some studies have shown quite a high incidence of adverse effects with ivermectin and have associated the effects with the severity of infection.[1-3] However, in none of these studies were the reactions considered to be life-threatening and only symptomatic treatment was required. The severity, incidence, and duration of adverse reactions was reported to be reduced after repeated annual administration.[4] When larger groups of patients were considered in the Onchocerciasis Control Programme (OCP) in West Africa, a much lower incidence of adverse reactions was seen in patients given ivermectin for the first time[5] and when treatment was repeated a year later that incidence was reduced even further. The results from several studies in this programme[6] showed 93 severe reactions in 50 929 patients (1.83%), most of the reactions being orthostatic hypotension or dizziness (53). In a 3-year randomised, double-blind, controlled study of ivermectin for onchocerciasis control in 572 patients,[7] 3-monthly treatment with the standard dose of 150 micrograms/kg was associated with a reduced risk of adverse reactions, especially oedema, pruritus, and back pain, when compared with the same dose given annually. Higher doses of 400 then 800 micrograms/kg, given either 3-monthly or annually, were associated with subjective ocular problems. Another study[8] found 22 severe reactions in 17 877 patients treated for onchocerciasis in an area also endemic for *Loa loa* infection, and demonstrated a relationship to heavy *L. loa* microfilaraemia. The Mectizan® Expert Committee and the Technical Consultative Committee have reported the incidence of encephalopathy after ivermectin treatment of onchocerciasis in *Loa loa* endemic areas to be less than 1 case in 10 000 treatments[9] and have implemented recommendations for ivermectin mass treatment programmes