

Profile

Melarsomine is a trivalent arsenical derivative used in veterinary practice for the control of canine heartworm (dirofilariasis).

Metrifonate (BAN, rINN)

Bayer-L 1359; DETF; Metrifonaatti; Metrifonát; Metrifonat; Metrifonatas; Métrifonate; Metrifonato; Metrifonatum; Metrifonate; Trichlorfon (USAN); Trichlorphon. Dimethyl 2,2,2-trichloro-1-hydroxyethylphosphonate.

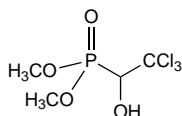
Метрифонат

$C_4H_8Cl_3O_4P = 257.4$.

CAS — 52-68-6.

ATC — P02BB01.

ATC Vet — QP52AB01; QP53AF02.



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

Ph. Eur. 6.2 (Metrifonate). A white or almost white, crystalline powder. M.p. is between 76° and 81°. Freely soluble in water, in alcohol, and in acetone; very soluble in dichloromethane. Protect from light.

USP 31 (Metrifonate). A white crystalline powder. M.p. about 78° with decomposition. Freely soluble in water, in alcohol, in acetone, in chloroform, in ether, and in benzene; very soluble in dichloromethane; very slightly soluble in hexane and in pentane. Decomposed by alkali. Store at a temperature not exceeding 25°.

Adverse Effects, Treatment, and Precautions

Metrifonate is generally well tolerated, but may cause nausea, vomiting, abdominal pain, diarrhoea, headache, dizziness, and weakness.

It is an organophosphorus compound and because of its anticholinesterase properties depresses plasma-cholinesterase concentrations. For a description of the toxic effects of organophosphorus compounds and the treatment of acute poisoning, see *Organophosphorus Insecticides*, p.2047. Atropine has been used to relieve cholinergic adverse effects without affecting metrifonate's activity against *Schistosoma haematobium*.

Anticholinesterase effects. Metrifonate depresses cholinesterase activity and there has been the occasional report of severe cholinergic adverse effects.¹ However, it does not usually give rise to troublesome effects at doses normally used, even though there may temporarily be almost complete inhibition of plasma cholinesterase and considerable inhibition of erythrocyte cholinesterase² (but see also under Alzheimer's Disease, below).

The environmental aspects of metrifonate usage have been considered by WHO.³

1. Jamnadas VP, Thomas JEP. Metrifonate and organophosphate poisoning. *Cent Afr J Med* 1979; **25**: 130.
2. Pleštin R, et al. Effect of metrifonate on blood cholinesterases in children during the treatment of schistosomiasis. *Bull WHO* 1972; **46**: 747–59.
3. WHO. Trichlorfon. *Environmental Health Criteria* 132. Geneva: WHO, 1992. Available at: <http://www.inchem.org/documents/ehc/ehc/ehc132.htm> (accessed 16/07/08)

Handling. Bulk metrifonate is very toxic when inhaled, swallowed, or spilled on the skin. It can be removed from the skin by washing with soap and water. Contaminated material should be immersed in a 2% aqueous solution of sodium hydroxide for several hours.

Pregnancy. WHO reported¹ that metrifonate had not shown embryotoxicity or teratogenicity, but did not recommend the use of metrifonate in pregnant patients unless immediate intervention was essential. There has been a report of an infant born with massive hydrocephalus and a large meningomyelocele whose mother had been treated twice with metrifonate during the second month of pregnancy.² A possible link between congenital abnormalities and the use of metrifonate to eradicate fish parasites has also been postulated.³

1. WHO. The control of schistosomiasis: second report of the WHO expert committee. *WHO Tech Rep Ser* 830 1993. Available at: http://libdoc.who.int/trs/WHO_TRS_830.pdf (accessed 16/07/08)
2. Monson MH, Alexander K. Metrifonate in pregnancy. *Trans R Soc Trop Med Hyg* 1984; **78**: 565.
3. Czeizel AE, et al. Environmental trichlorfon and cluster of congenital abnormalities. *Lancet* 1993; **341**: 539–42.

Interactions

Patients treated with metrifonate should not be given depolarising neuromuscular blockers such as suxamethonium for at least 48 hours. The use of metrifonate should be avoided in those recently exposed to insecticides or other agricultural chemicals with anticholinesterase activity.

Pharmacokinetics

Metrifonate is absorbed after oral doses and some is converted to dichlorvos which is considered to be the active moiety. Plasma concentrations of dichlorvos are about 1% of those of metrifonate with peak concentrations of both substances occurring within 2 hours. Excretion is via the kidney, mainly as glucuronides.

◇ References.

1. Nordgren I, et al. Plasma levels of metrifonate and dichlorvos during treatment of schistosomiasis with Bilarcil. *Am J Trop Med Hyg* 1980; **29**: 426–30.
2. Nordgren I, et al. Levels of metrifonate and dichlorvos in plasma and erythrocytes during treatment of schistosomiasis with Bilarcil. *Acta Pharmacol Toxicol (Copenh)* 1981; **49** (suppl V): 79–86.
3. Pettigrew LC, et al. Pharmacokinetics, pharmacodynamics, and safety of metrifonate in patients with Alzheimer's disease. *J Clin Pharmacol* 1998; **38**: 236–45.

Uses and Administration

Metrifonate is an organophosphorus compound and is converted in the body to the active metabolite dichlorvos (p.2040), an anticholinesterase.

Metrifonate has anthelmintic activity against *Schistosoma haematobium* and has been given orally as an alternative to praziquantel in the treatment of schistosomiasis due to *S. haematobium*. It has usually been given in three doses of 7.5 to 10 mg/kg at intervals of 2 weeks.

Metrifonate has also been used as an insecticide and as a parasiticide in fish and domestic animals.

Alzheimer's disease. Metrifonate, like a number of other cholinesterase inhibitors, has been tried in the treatment of Alzheimer's disease (see Dementia, p.362). Clinical studies^{1,2} produced modest benefits but research was stopped after reports of muscle weakness, sometimes requiring respiratory support.

1. Becker RE, et al. Effects of metrifonate on cognitive decline in Alzheimer disease: a double-blind, placebo-controlled, 6-month study. *Alzheimer Dis Assoc Disord* 1998; **12**: 54–7.
2. Morris JC, et al. Metrifonate benefits cognitive, behavioral, and global function in patients with Alzheimer's disease. *Neurology* 1998; **50**: 1222–30.

Schistosomiasis. While praziquantel is now the main treatment for schistosomiasis (p.138), metrifonate is an alternative for infection due to *Schistosoma haematobium*. Cure rates with standard doses in schistosomiasis control programmes range from 40 to more than 80%, with a reduction of more than 80% in egg counts among those not cured, but a comparison with praziquantel has shown praziquantel to be the more effective drug.¹ In addition, metrifonate's dosage schedule of 3 doses at intervals of 2 weeks has caused problems of patient compliance;² giving 5 mg/kg three times in one day has produced similar results to a standard dosage schedule.³

1. Squires N. Interventions for treating schistosomiasis haematobium. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 1997 (accessed 16/05/05).
2. Aden Abdi Y, Gustafsson LL. Poor patient compliance reduces the efficacy of metrifonate treatment of *Schistosoma haematobium* in Somalia. *Eur J Clin Pharmacol* 1989; **36**: 161–4.
3. Aden Abdi Y, Gustafsson LL. Field trial of the efficacy of a simplified and standard metrifonate treatments of *Schistosoma haematobium*. *Eur J Clin Pharmacol* 1989; **37**: 371–4.

Milbemycin Oxime

CGA-179246; Milbemicina oxima. A mixture of milbemycin A₄ 5-oxime and milbemycin A₃ 5-oxime.

Мильбемицин Оксим

CAS — 129496-10-2.

ATC Vet — QP54AB01.

Profile

Milbemycin oxime is an anthelmintic used in veterinary medicine.

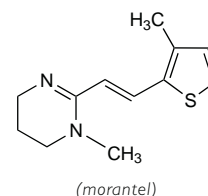
Morantel Citrate (BANM, pINNMM)

Citrato de morantel; Morantel, Citrate de; Moranteli Citras. (E)-1,4,5,6-Tetrahydro-1-methyl-2-[2-(3-methyl-2-thienyl)vinyl]pyrimidine citrate monohydrate.

Морантела Цитрат

$C_{12}H_{16}N_2S_2C_6H_8O_7 \cdot H_2O = 430.5$.

CAS — 20574-50-9 (morantel); 69525-81-1 (morantel citrate).



(morantel)

Morantel Tartrate (BANM, USAN, pINNMM)

CP-12009-18; Moranteelivetytartraatti; Morantel, hidrogénotartrate de; Morantel, Tartrate de; Morantel-hidrogén-tartarát; Morantel-hydrogen-tartarát; Moranteli hydrogenotartras; Moranteli Tartras; Morantelvetetartrat; Tartrato de morantel; UK-2964-18.

Морантела Тартрат

$C_{12}H_{16}N_2S_2C_6H_8O_6 = 370.4$.

CAS — 20574-50-9 (morantel); 26155-31-7 (morantel tartrate).

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

Ph. Eur. 6.2 (Morantel Hydrogen Tartrate for Veterinary Use; Morantel Tartrate BP(Vet) 2008). A white or pale yellow, crystalline powder. Very soluble in water and in alcohol; practically insoluble in ethyl acetate. A 1% solution in water has a pH of 3.3 to 3.9. Protect from light.

USP 31 (Morantel Tartrate). A white or pale yellow, crystalline powder. Very soluble in water and in alcohol; practically insoluble in ethyl acetate. pH of a 1% solution in water is between 2.8 and 3.9. Store at a temperature of 25°, excursions permitted between 15° and 30°. Protect from light.

Profile

Morantel is an analogue of pyrantel. The citrate and the tartrate are used as anthelmintics in veterinary medicine for the treatment of gastrointestinal roundworms.

Moxidectin (BAN, USAN, rINN)

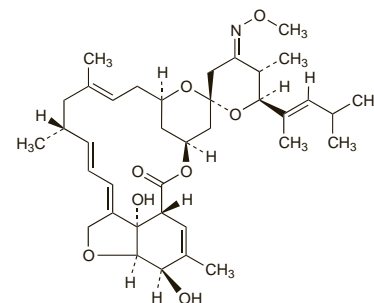
CL-301423; Moksidektiini; Moxidectina; Moxidectine; Moxidectinum; Moxidektin. (6R,15S)-5-O-Demethyl-28-deoxy-25-[(E)-1,3-dimethylbut-1-enyl]-6,28-epoxy-23-oxomilbemycin B (E)-23-O-methylxime.

МОКСИДЕКТИН

$C_{37}H_{53}NO_8 = 639.8$.

CAS — 113507-06-5.

ATC Vet — QP54AB02.



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

Ph. Eur. 6.2 (Moxidectin for Veterinary Use). A white or pale yellow, amorphous powder. Practically insoluble in water; very soluble in alcohol; slightly soluble in hexane.

Profile

Moxidectin is an anthelmintic used in veterinary medicine. It is also used as a systemic veterinary ectoparasiticide and is under investigation for the treatment of human onchocerciasis.

◇ References.

1. Cotreau MM, et al. The antiparasitic moxidectin: safety, tolerability, and pharmacokinetics in humans. *J Clin Pharmacol* 2003; **43**: 1108–15.