but antibacterial therapy is regarded as unnecessary in mild and self-limiting gastro-enteritis (see p.171).

Furazolidone is given orally in a dose of 100 mg four times daily; children and infants from 1 month of age may be given 1.25 mg/kg four times daily. It is usually given for 2 to 5 days, but may be given for up to 7 days in some patients, or for up to 10 days for giardiasis.

Peptic ulcer disease. Furazolidone is not one of the main antibacterials used in *Helicobacter pylori* eradication regimens for peptic ulceration (p.1702), but there are some studies suggesting its efficacy.[1-8]

1. Segura AM, *et al.* Furazolidone, amoxycillin, bismuth triple therapy for Helicobacter pylori infection. *Aliment Pharmacol Ther* 1997; **11:** 529–32.
2. Xiao S-D, *et al.* High cure rate of Helicobacter pylori infection using tripotassium dicitrato bismuthate, furazolidone and clarithromycin triple therapy for 1 week. *Aliment Pharmacol Ther* 1999; **13:** 311–15.
3. Liu W-Z, *et al.* Furazolidone-containing short-term triple therapies are effective in the treatment of Helicobacter pylori infection. *Aliment Pharmacol Ther* 1999; **13:** 317–22.
4. Dani R, *et al.* Omeprazole, clarithromycin and furazolidone for the eradication of Helicobacter pylori in patients with duodenal ulcer. *Aliment Pharmacol Ther* 1999; **13:** 1647–52.
5. Graham DY, *et al.* Furazolidone combination therapies for Helicobacter pylori infection in the United States. *Aliment Pharmacol Ther* 2000; **14:** 211–15.
6. Liu W-Z, *et al.* A new quadruple therapy for Helicobacter pylori using tripotassium dicitrato bismuthate, furazolidone, josamycin and famotidine. *Aliment Pharmacol Ther* 2000; **14:** 1519–22.
7. Fakheri H, *et al.* Clarithromycin vs furazolidone in quadruple therapy regimens for the treatment of Helicobacter pylori in a population with a high metronidazole resistance rate. *Aliment Pharmacol Ther* 2001; **15:** 411–16.
8. Lu H, *et al.* One-week regimens containing ranitidine bismuth citrate, furazolidone and either amoxicillin or tetracycline effectively eradicate Helicobacter pylori: a multicentre, randomized, double-blind study. *Aliment Pharmacol Ther* 2001; **15:** 1975–9.

Preparations

USP 31: Furazolidone Oral Suspension; Furazolidone Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Giardil; ***Braz.:*** Enterolidon†; Giarcid†; Giarlam†; Neo Furasil; ***Chile:*** Furoxona; ***Ger.:*** Nifuran†; ***India:*** Furoxone; ***Indon.:*** Neo Prodiar; ***Mex.:*** Furoxona; Fuxol; Kaodin; Rolidan†; Salmocide; ***Philipp.:*** Diafuran; Diapectolin; Furoxone; ***Thai.:*** Furasian; Furion; ***USA:*** Furoxone†; ***Venez.:*** Furoxil; Furoxona; Onetil†.

Multi-ingredient: ***Arg.:*** Endomicina†; ***Braz.:*** Atapec†; Colestase; Enterobion†; ***Chile:*** Furazolidona; ***Hong Kong:*** Enterocin Compound; ***Hung.:*** Noditran†; ***India:*** Aristogyl-F; Dysfur-M†; Emantid†; Flagyl-F†; Kaltin MF; Lomofen; Metrogyl-F†; ***Mex.:*** Caopecfar; Colfur; Contefur†; Coralzul; Dialgin; Dibapec Compuesto; Estibal; Exofur; Furoxona CP; Fuzotyl†; Kapecfuran; Neokap; Optazol; Reuginal; Solfurol; Threchop; Trilor†; Yodozona; ***Spain:*** Desinvag; ***Thai.:*** Coccila†; Di-Su-Frone†; Difuran; Disento; Disento PF; Furasian; Furopectin†; Med-Kafuzone†; Mediocin†; ***Venez.:*** Sendafur†.

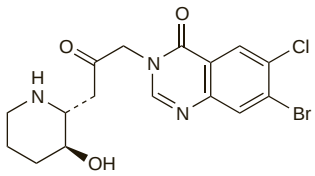
Halofuginone Hydrobromide *(BANM, USAN, rINNM)*

Halofuginone, Bromhydrate d'; Halofuginoni Hydrobromidum; Hidrobromuro de halofuginona; RU-19110. (±)-*trans*-7-Bromo-6-chloro-3-[3-(3-hydroxy-2-piperidyl)acetonyl]quinazolin-4(3*H*)-one hydrobromide.

Галофугинона Гидробромид

$C_{16}H_{17}BrClN_3O_3,HBr$ = 495.6.

CAS — 55837-20-2 (halofuginone); 64924-67-0 (halofuginone hydrobromide).



(halofuginone)

Profile
Halofuginone is an antiprotozoal used as the hydrobromide in veterinary practice for the prevention of coccidiosis in poultry and for the control of cryptosporidiosis in calves. It is also under investigation for use in neoplastic disease in humans and in the treatment of scleroderma (p.1817).

Imidocarb *(BAN, rINN)*

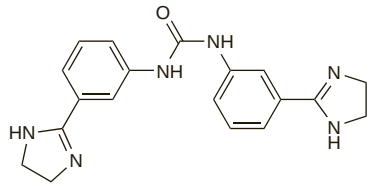
Imidocarbe; Imidocarbo; Imidocarbum. 1,3-Bis[3-(2-imidazolin-2-yl)phenyl]urea.

Имидокарб

$C_{19}H_{20}N_6O$ = 348.4.

CAS — 27885-92-3.

ATC Vet — QP51AE01.



Imidocarb Dipropionate *(BANM, rINNM)*

Dipropionato de imidocarbo; Imidocarbe, Dipropionate d'; Imidocarbi Dipropionas.

Имидокарба Дипропионат

$C_{19}H_{20}N_6O,2C_3H_6O_2$ = 496.6.

CAS — 55750-06-6.

Imidocarb Hydrochloride *(BANM, USAN, rINNM)*

4A65; Hidrocloruro de imidocarbo; Imidocarbe, Chlorhydrate d'; Imidocarbi Hydrochloridum. 3,3′-Di(2-imidazolin-2-yl)carbanilide dihydrochloride.

Имидокарба Гидрохлорид

$C_{19}H_{20}N_6O,2HCl$ = 421.3.

CAS — 5318-76-3.

Profile
Imidocarb has antiprotozoal and antibacterial activity and is used as the dipropionate in veterinary practice in the treatment of babesiosis and anaplasmosis in cattle. Imidocarb hydrochloride has also been used.

Isometamidium Chloride *(BAN, rINN)*

Cloruro de isometamidio; Isometamidii Chloridum; Isometamidium; Isométamidium, Chlorure d'. 8-[3-(*m*-Amidinophenyl)-2-triazeno]3-amino-5-ethyl-6-phenylphenanthridinium chloride.

Изометамидия Хлорид

$C_{28}H_{26}ClN_7$ = 496.0.

CAS — 34301-55-8.

Profile
Isometamidium is an antiprotozoal used as the chloride in veterinary practice for the control of trypanosomiasis.

Lasalocid *(BAN, USAN, rINN)*

Lasalocide; Lasalócido; Lasalocidum; Ro-02-2985. 6-[(3*R*,4*S*,5*S*,7*R*)-7-{(2*S*,3*S*,5*S*)-5-Ethyl-5-[(2*R*,5*R*,6*S*)-5-ethyltetrahydro-5-hydroxy-6-methyl-2*H*-pyran-2-yl]tetrahydro-3-methyl-2-furyl}4-hydroxy-3,5-dimethyl-6-oxononyl]-2-hydroxy-*m*-toluic acid.

Лазалоцид

$C_{34}H_{54}O_8$ = 590.8.

CAS — 11054-70-9; 25999-31-9.

ATC Vet — QP51AH02.

Lasalocid Sodium *(BANM, rINNM)*

Lasalocid sódico; Lasalocide Sodique; Lasalocidum Natricum.

Лазалоцид Натрий

$C_{34}H_{53}NaO_8$ = 612.8.

CAS — 25999-20-6.

ATC Vet — QP51AH02.

Profile
Lasalocid, an antibiotic produced by *Streptomyces lasaliensis*, is an antiprotozoal used as the sodium salt in veterinary practice for the prevention of coccidiosis in birds.

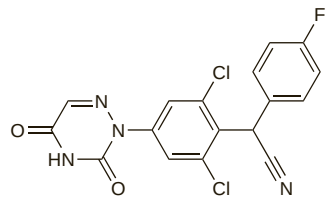
Letrazuril *(rINN)*

Létrazuril; Letrazurilo; Letrazurilum. (±)-[2,6-Dichloro-4-(4,5-dihydro-3,5-dioxo-*as*-triazin-2(3*H*)-yl)phenyl](*p*-fluorophenyl)acetonitrile.

Летразурил

$C_{17}H_9Cl_2FN_4O_2$ = 391.2.

CAS — 103337-74-2.



Profile
Letrazuril is an antiprotozoal that has been investigated in the treatment of cryptosporidiosis (p.823) in patients with AIDS.

Maduramicin *(BAN, USAN, rINN)*

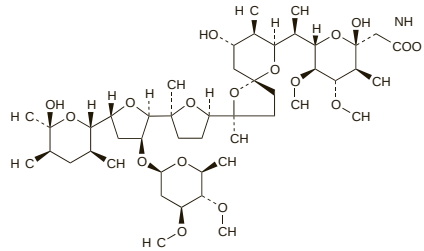
CL-273703; Maduramicin Ammonium; Maduramicina; Maduramicine; Maduramicinum. Ammonium (2*R*,3*S*,4*S*,5*R*,6*S*)-tetrahydro-2-hydroxy-6-{(*R*)-1-[(2*S*,5*R*,7*S*,8*R*,9*S*)-9-hydroxy-2,8-dimethyl-2-{(2*S*,2′*R*,3′*S*,5*R*,5′*R*)-octahydro-2-methyl-3′-[(2*R*,4*S*,5*S*,6*S*)-tetrahydro-4,5-dimethoxy-6-methyl-2*H*-pyran-2-yl]oxy}-5′-[(2*S*,3*S*,5*R*,6*S*)-tetrahydro-6-hydroxy-3,5,6-trimethyl-2*H*-pyran-2-yl](2,2′-bifuran-5-yl)-1,6-dioxaspiro[4.5]dec-7-yl]ethyl}-4,5-dimethoxy-3-methyl-2*H*-pyran-2-acetate.

Мадурамицин

$C_{47}H_{80}O_{17},NH_3$ = 934.2.

CAS — 84878-61-5.

ATC Vet — QP51AX10.



NOTE. The name maduramicin has also been used to denote the acid.

Profile
Maduramicin is an antiprotozoal used in veterinary practice for the prevention of coccidiosis in poultry.

Melarsoprol *(BAN, rINN)*

Mel B; Melarsen Oxide-BAL; Mélarsoprol; Melarsoprolum; RP-3854. 2-[4-(4,6-Diamino-1,3,5-triazin-2-ylamino)phenyl]-1,3,2-dithiarsolan-4-ylmethanol.

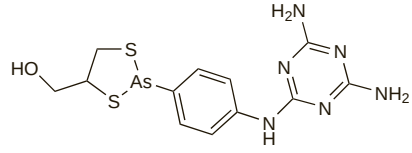
Меларсопрол

$C_{12}H_{15}AsN_6OS_2$ = 398.3.

CAS — 494-79-1.

ATC — P01CD01.

ATC Vet — QP51AD04.



Adverse Effects and Treatment
Adverse effects are common and may be severe during the treatment of African trypanosomiasis with melarsoprol. It may be difficult to distinguish between effects of the disease, Jarisch-Herxheimer reactions resulting from the release of antigens from trypanosomes killed by melarsoprol, and adverse effects due to the drug's arsenic content or to hypersensitivity. For the adverse effects of arsenic and their treatment, see Arsenic Trioxide, p.2260.

A severe febrile reaction may occur after the first injection of melarsoprol, especially in patients with large numbers of trypanosomes in their blood. It is therefore

common practice to give 2 or 3 injections of suramin or pentamidine before starting melarsoprol therapy.

The greatest risk is from reactive encephalopathy which occurs in about 10% of patients treated with melarsoprol and is usually seen between the end of the first 3- or 4-day course of injections and the start of the second course. Encephalopathy may be sudden in onset or develop slowly. Symptoms include fever, headache, tremor, slurring of speech, convulsions, and coma; death has occurred in up to 5% of patients treated with melarsoprol. Less commonly, haemorrhagic encephalopathy may occur. The prophylactic use of corticosteroids has been suggested during treatment courses of melarsoprol (see African Trypanosomiasis, below). Treatment of reactive encephalopathy has included the use of corticosteroids, hypertonic solutions to combat cerebral oedema, anticonvulsants such as diazepam, and subcutaneous adrenaline; dimercaprol has been given on the assumption that encephalopathy resulted from arsenic poisoning, but has not generally been of benefit.

Hypersensitivity reactions to melarsoprol may occur during the second and subsequent courses of treatment. Desensitisation with gradually increasing doses of melarsoprol has been attempted; corticosteroids may help to control symptoms during this procedure. Some authorities consider that the use of small doses of melarsoprol may increase the risk of resistance.

Melarsoprol injection is very irritant and extravasation during intravenous use should be avoided. Vomiting and abdominal colic may occur if it is injected too rapidly. Other adverse effects reported include agranulocytosis, hypertension, peripheral neuropathy, proteinuria, severe diarrhoea, myocardial damage, exfoliative dermatitis, and hepatic disturbances.

◊ References.

1. Pepin J, *et al.* Trial of prednisolone for prevention of melarsoprol-induced encephalopathy in gambiense sleeping sickness. *Lancet* 1989; **i:** 1246–50.
2. Pepin J, Milord F. African trypanosomiasis and drug-induced encephalopathy: risk factors and pathogenesis. *Trans R Soc Trop Med Hyg* 1991; **85:** 222–4.
3. Pepin J, *et al.* Risk factors for encephalopathy and mortality during melarsoprol treatment of Trypanosoma brucei gambiense sleeping sickness. *Trans R Soc Trop Med Hyg* 1995; **89:** 92–7.

Precautions

Use of melarsoprol in febrile patients has been associated with an increased incidence of reactive encephalopathy, and therefore it should not be given during epidemics of influenza. Intercurrent infections such as malaria and pneumonia should be treated before melarsoprol is used. Severe haemolytic reactions have been reported in patients with G6PD deficiency. It may precipitate erythema nodosum when given to patients with leprosy.

Patients should be in hospital when they are treated with melarsoprol and dosage decided after taking into account their general condition.

Treatment of pregnant women with trypanosomiasis should be deferred until after delivery. Pregnant women with meningoencephalitis may be treated with pentamidine (*Trypanosoma brucei gambiense*) or suramin (*T. b. rhodesiense*).

Pharmacokinetics

Melarsoprol is reported to be unreliably absorbed if given orally and is usually given by intravenous injection. A small amount penetrates into the CSF where it has a local trypanocidal action. It is rapidly metabolised and excreted in the faeces and urine so any prophylactic effect is short-lived.

Uses and Administration

Melarsoprol, a trivalent arsenical derivative, is a trypanocide which appears to act by inhibiting trypanosomal pyruvate kinase. It is effective in the treatment of all stages of African trypanosomiasis due to *Trypanosoma brucei gambiense* or *T. brucei rhodesiense*, but because of its toxicity its use is usually reserved for stages of the disease involving the CNS. Resistance has been reported to develop.

Patients undergoing therapy with melarsoprol should be treated in hospital. Melarsoprol is given by intravenous injection as a 3.6% solution in propylene glycol. The injection should be given slowly, care being taken to prevent leakage into the surrounding tissues, and the patient should remain supine and fasting for several hours after the injection.

Treatment protocols vary, but in general melarsoprol is given in low doses initially, especially in children and debilitated patients, increased gradually to the maximum daily dose of 3.6 mg/kg. Doses are given daily for 3 or 4 days and the course repeated 2 or 3 times with an interval of 7 to 10 days between courses. Since massive destruction of parasites resulting in a Jarisch-Herxheimer reaction is particularly dangerous during treatment with melarsoprol, several doses of suramin or pentamidine may be given to induce the reaction before melarsoprol is started.

Melarsonyl potassium is a water-soluble derivative of melarsoprol which was formerly used as an alternative to melarsoprol but was probably more toxic and less effective.

African trypanosomiasis. Melarsoprol, which is effective against both *Trypanosoma brucei gambiense* and *T. b. rhodesiense*, is usually only given to treat the meningoencephalitic stage of African trypanosomiasis (p.827) because it may produce potentially fatal encephalopathy. However, protection against this toxicity may be provided by prophylaxis with prednisolone.[1,2] Therapy with melarsoprol and eflornithine was reported to be effective in a patient who had not responded to either drug alone.[3] A comparative study[4] in 500 patients with second-stage infection with *T. b. gambiense* found that a more concise dosage regimen of melarsoprol 2.2 mg/kg daily, as a single course over 10 days, was similar in efficacy to standard regimens of 1.2 to 3.6 mg/kg daily for 3 or 4 days repeated twice over a 26-day period with 7-day intervals between series, although there was no difference between the regimens in the incidence of associated encephalopathy.

1. Pepin J, *et al.* Trial of prednisolone for prevention of melarsoprol-induced encephalopathy in gambiense sleeping sickness. *Lancet* 1989; **i:** 1246–50.
2. Pepin J, *et al.* Risk factors for encephalopathy and mortality during melarsoprol treatment of Trypanosoma brucei gambiense sleeping sickness. *Trans R Soc Trop Med Hyg* 1995; **89:** 92–7.
3. Simarro PP, Asumu PN. Gambian trypanosomiasis and synergism between melarsoprol and eflornithine: first case report. *Trans R Soc Trop Med Hyg* 1996; **90:** 315.
4. Burri C, *et al.* Efficacy of new, concise schedule for melarsoprol in treatment of sleeping sickness caused by Trypanosoma brucei gambiense: a randomised trial. *Lancet* 2000; **355:** 1419–25.

Mepacrine Hydrochloride *(BANM, rINNM)*

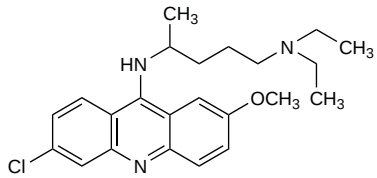
Acrichinum; Acrinamine; Antimalarinae Chlorhydras; Chinacrina; Hidrocloruro de mepacrina; Mépacrine, Chlorhydrate de; Mepacrini Hydrochloridum; Mepakrin Hidroklorür; Quinacrine Hydrochloride. 6-Chloro-9-(4-diethylamino-1-methylbutylamino)-2-methoxyacridine dihydrochloride dihydrate.

Мепакрина Гидрохлорид

$C_{23}H_{30}ClN_3O,2HCl,2H_2O$ = 508.9.

CAS — 83-89-6 (mepacrine); 69-05-6 (anhydrous mepacrine dihydrochloride); 6151-30-0 (mepacrine dihydrochloride dihydrate).

ATC — P01AX05.



(mepacrine)

Adverse Effects

The most common adverse effects associated with mepacrine are dizziness, headache, and gastrointestinal disturbances such as nausea and vomiting. Reversible yellow discoloration of the skin, conjunctiva, and urine may occur during long-term use or after large doses; blue/black discoloration of the palate and discoloration of the nails have also been reported. Doses such as those used in the treatment of giardiasis may occasionally cause transient acute toxic psychosis and CNS stimulation. Convulsions have been reported at high doses. Ocular toxicity similar to that seen with chloroquine (p.600) and chronic dermatoses, including severe exfoliative dermatitis and lichenoid eruptions, have also occurred after prolonged use of mepacrine. Hepatotoxicity and aplastic anaemia occur rarely.

Effects on the nervous system. Two patients had convulsions a few hours after mepacrine hydrochloride 400 mg was given intrapleurally for malignant effusions. One developed status epilepticus and died and the other was successfully treated with anticonvulsants.[1]

1. Borda I, Krant M. Convulsions following intrapleural administration of quinacrine hydrochloride. *JAMA* 1967; **201:** 1049–50.

Precautions

Mepacrine should be used with caution in elderly patients or patients with a history of psychosis, or in the presence of hepatic disease. Mepacrine can cause exacerbation of psoriasis and should be avoided in psoriatic patients.

Porphyria. Mepacrine should be used with caution in patients with porphyria.

Interactions

Mepacrine has been reported to produce a mild disulfiram-like reaction (see p.2296) when taken with alcohol.

Theoretically, mepacrine may increase the plasma concentrations of primaquine resulting in a higher risk of toxicity, and it has been recommended that these drugs should not be used together.

Pharmacokinetics

Mepacrine is readily absorbed from the gastrointestinal tract and widely distributed throughout the body. It accumulates in body tissues, particularly the liver, and is liberated slowly. It is excreted slowly mainly in the urine, and is still detectable in the urine after 2 months. Mepacrine crosses the placenta.

Intrapleural administration. Peak plasma concentrations of mepacrine far above those associated with CNS effects were rapidly attained in 3 of 4 patients after intrapleural instillation of a solution of mepacrine hydrochloride and remained at these levels for several hours.[1]

1. Björkman S, *et al.* Pharmacokinetics of quinacrine after intrapleural instillation in rabbits and man. *J Pharm Pharmacol* 1989; **41:** 160–73.

Uses and Administration

Mepacrine is a 9-aminoacridine antiprotozoal used as the hydrochloride mainly as an alternative to the nitroimidazoles in the treatment of giardiasis (p.824).

In giardiasis, mepacrine hydrochloride is given orally in doses of 100 mg three times daily after food for 5 to 7 days. A dose for children is 2 mg/kg given three times daily (maximum 300 mg daily).

Mepacrine hydrochloride may also be used, alone or with hydroxychloroquine, for the treatment of discoid and subcutaneous lupus erythematosus. It has also been used locally in the treatment of some forms of cutaneous leishmaniasis, as a sterilisation technique for contraception, and in the management of malignant effusions. It was formerly used to treat malaria.

The mesilate was also formerly used.

Mepacrine is under investigation for the treatment of variant Creutzfeldt-Jakob Disease.

Contraception. Sterilisation with intra-uterine mepacrine has been attempted as an irreversible method of contraception (p.2070). It produces occlusion of the fallopian tube and has been reported to be an effective nonsurgical means of female sterilisation,[1] although it may be less effective than other methods.[2] There has been speculation about the risk of cancer from this technique but there appeared to be no evidence to confirm such a risk.[3-5] However, the method remains controversial and a full evaluation of its safety and efficacy has been recommended.[6] The Indian government has banned the use of mepacrine for sterilisation.

1. Hieu DT, *et al.* 31 781 Cases of non-surgical female sterilisation with quinacrine pellets in Vietnam. *Lancet* 1993; **342:** 213–17.
2. Sokal DC, *et al.* Contraceptive effectiveness of two insertions of quinacrine: results from 10-year follow-up in Vietnam. *Contraception* 2008; **78:** 61–5.
3. Anonymous. Death of a study: WHO, what, and why. *Lancet* 1994; **343:** 987–8.
4. Hieu DT. Quinacrine method of family planning. *Lancet* 1994; **343:** 1040.
5. Sokal DC, *et al.* Safety of quinacrine contraceptive pellets: results from 10-year follow-up in Vietnam. *Contraception* 2008; **78:** 66–72.
6. Benagiano G. Sterilisation by quinacrine. *Lancet* 1994; **344:** 689.

Leishmaniasis. Mepacrine has been suggested for intralesional injection in the treatment of early noninflamed nodular lesions of cutaneous leishmaniasis (p.824) due to *Leishmania tropica, L. major, L. mexicana, L. panamensis*, or *L. peruviana*.[1] The suggested course of treatment was 3 intralesional injections of a 5% solution of mepacrine given at intervals of 3 to 5 days. However, local infiltration of drugs can be difficult and painful.

1. WHO. Control of the leishmaniases. *WHO Tech Rep Ser 793* 1990.

Sclerotherapy. Intrapleural instillations of mepacrine hydrochloride or mesilate have been used as sclerosants in the management of malignant pleural effusions (p.659) and recurrent pneu-