American trypanosomiasis. Available treatment for American trypanosomiasis (p.827) is generally unsatisfactory, but benznidazole is of value especially in the acute phase. WHO[1] recommends that benznidazole should be given for 60 days but some in the USA[2] suggest courses of 30 to 90 days. Although treatment is usually confined to the acute phase of the disease, therapy during the early chronic phase was reported to be beneficial,[3] and long-term follow-up in patients who had received benznidazole has shown a reduction in cardiac complications and parasitaemia.[4]

1. WHO. Control of Chagas disease: second report of the WHO expert committee. *WHO Tech Rep Ser 905* 2002. Available at: http://libdoc.who.int/trs/WHO_TRS_905.pdf (accessed 17/07/08)
2. Abramowicz M, ed. *Drugs for parasitic infections*. 1st ed. New Rochelle NY: The Medical Letter, 2007.
3. de Andrade ALSS, *et al*. Randomised trial of efficacy of benznidazole in treatment of early Trypanosoma cruzi infection. *Lancet* 1996; **348:** 1407–13.
4. Viotti R, *et al*. Treatment of chronic Chagas' disease with benznidazole: clinical and serologic evolution of patients with long-term follow-up. *Am Heart J* 1994; **127:** 151–62.

Preparations

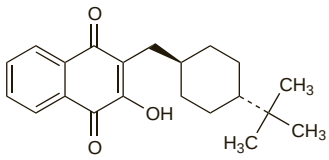
Proprietary Preparations (details are given in Part 3)
Arg.: Radanil; ***Braz.:*** Rochagan; ***Ecuad.:*** Ragonil.

Buparvaquone *(BAN, rINN)*

Buparvacuona; Buparvaquonum; BW-720C. *trans*-2-(4-*tert*-Butylcyclohexylmethyl)-3-hydroxy-1,4-naphthoquinone.

Бупарвахон

$C_{21}H_{26}O_3$ = 326.4.
CAS — 88426-33-9.
ATC Vet — QP51AX22.



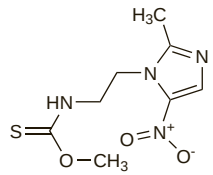
Profile
Buparvaquone is an antiprotozoal used in veterinary practice for the treatment of theileriosis in cattle.

Carnidazole *(BAN, USAN, pINN)*

Carnidazol; Carnidazolum; R-25831; R-28096 (carnidazole hydrochloride). *O*-Methyl [2-(2-methyl-5-nitroimidazol-1-yl)ethyl]-thiocarbamate.

Карнидазол

$C_8H_{12}N_4O_3S$ = 244.3.
CAS — 42116-76-7.
ATC Vet — QP51AA09.



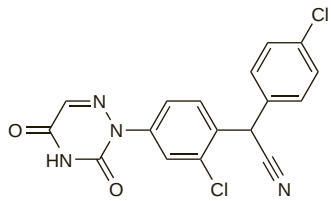
Profile
Carnidazole is a 5-nitroimidazole derivative similar to metronidazole. It is used in veterinary practice for the control of trichomoniasis in pigeons.

Clazuril *(BAN, USAN, rINN)*

Clazurilo; Clazurilum; Klatsuriili; Klazuril; R-62690. (±)-[2-Chloro-4-(4,5-dihydro-3,5-dioxo-*as*-triazin-2(3*H*)-yl)phenyl]-(*p*-chlorophenyl)acetonitrile.

Клазурил

$C_{17}H_{10}Cl_2N_4O_2$ = 373.2.
CAS — 101831-36-1.
ATC Vet — QP51AJ02.



Pharmacopoeias. In *Eur.* (see p.vii) for veterinary use only.
Ph. Eur. 6.2 (Clazuril for Veterinary Use; Clazuril BP(Vet) 2008). A white or light yellow powder. Practically insoluble in water; slightly soluble in alcohol and in dichloromethane; freely soluble in dimethylformamide. Protect from light.

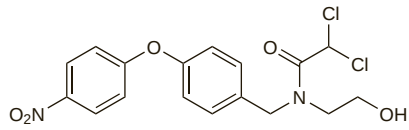
Profile
Clazuril is an antiprotozoal used in veterinary practice for the control of coccidiosis in pigeons.

Clefamide *(BAN, rINN)*

Chlorphenoxamide; Clefamida; Cléfamide; Clefamidum. 2,2-Dichloro-*N*-(2-hydroxyethyl)-*N*-[4-(4-nitrophenoxy)benzyl]-acetamide.

Клефамид

$C_{17}H_{16}Cl_2N_2O_5$ = 399.2.
CAS — 3576-64-5.
ATC — P01AC02.



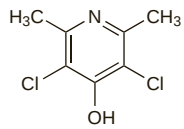
Profile
Clefamide is an antiprotozoal that has been used as a luminal amoebicide in the treatment of *Entamoeba histolytica* infections.

Clopidol *(BAN, USAN, rINN)*

Clopidolum; Clopindol; Meticlorpindol. 3,5-Dichloro-2,6-dimethylpyridin-4-ol.

Клопидол

$C_7H_7Cl_2NO$ = 192.0.
CAS — 2971-90-6.



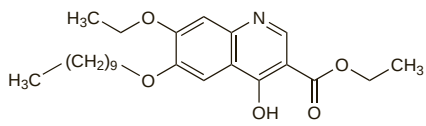
Profile
Clopidol is an antiprotozoal used in veterinary practice for the prevention of coccidiosis in poultry and rabbits either alone or with methyl benzoquate (p.837).

Decoquinate *(BAN, USAN, rINN)*

Décoquinate; Decoquinato; Decoquinatum; HC-1528; M&B-15497. Ethyl 6-decyloxy-7-ethoxy-4-hydroxyquinoline-3-carboxylate.

Декохинат

$C_{24}H_{35}NO_5$ = 417.5.
CAS — 18507-89-6.
ATC Vet — QP51AX14.



Pharmacopoeias. In *US* for veterinary use only. Also in *BP(Vet)*.
BP(Vet) 2008 (Decoquinate). A cream to buff-coloured, odourless or almost odourless, microcrystalline powder. Insoluble in water; practically insoluble in alcohol; very slightly soluble in chloroform and in ether.
USP 31 (Decoquinate). Store in airtight containers.

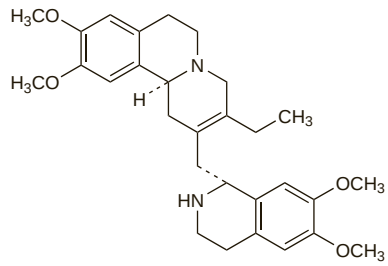
Profile
Decoquinate is an antiprotozoal used in veterinary practice for the control of coccidiosis in calves, sheep, and chickens. It is also used for toxoplasmosis in sheep.

Dehydroemetine Hydrochloride *(BANM, rINNM)*

BT-436; Déhydroémétine, Chlorhydrate de; 2,3-Dehydroemetine Hydrochloride; Dehydroemetini Hydrochloridum; DHE; Hidrocloruro de dehidroemetina; Ro-1-9334. 2,3-Didehydro-6′,7′,10,11-tetramethoxyemetan dihydrochloride; 3-Ethyl-1,6,7,11b-tetrahydro-9,10-dimethoxy-2-(1,2,3,4-tetrahydro-6,7-dimethoxy-1-isoquinolylmethyl)-4*H*-benzo[*a*]quinolizine dihydrochloride.

Дегидроэметина Гидрохлорид

$C_{29}H_{38}N_2O_4$,2HCl = 551.5.
CAS — 4914-30-1 (dehydroemetine); 2228-39-9 (dehydroemetine hydrochloride).



(dehydroemetine)

NOTE. The name DHE has been used to denote a preparation of dihydroergotamine mesilate.

Pharmacopoeias. In *Int.*

Profile
Dehydroemetine, a synthetic derivative of emetine (p.833), is a tissue amoebicide with similar actions and uses, although probably of a lower toxicity.

Dehydroemetine should be avoided in patients with cardiac, renal, or neuromuscular disease and patients should be monitored for cardiac toxicity during treatment.

When used in the treatment of amoebiasis (p.822), dehydroemetine hydrochloride is given by intramuscular injection in a dose of 1 mg/kg daily (maximum daily dose of 60 mg), generally for up to 4 to 6 days, but for no more than 5 days in children. A dose of 0.5 mg/kg has been suggested for elderly or severely ill patients. At least 6 weeks should elapse before treatment is repeated. Following treatment with dehydroemetine, all patients should receive a luminal amoebicide to eliminate organisms from the colon. Patients with hepatic amoebiasis may be given supplementary treatment with chloroquine.

Liver fluke infections. Dehydroemetine has been given[1] in the treatment of the liver fluke infection fascioliasis (see p.137).

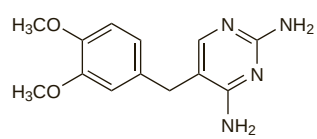
1. Farid Z, *et al*. Treatment of acute toxaemic fascioliasis. *Trans R Soc Trop Med Hyg* 1988; **82:** 299.

Diaveridine *(BAN, USAN, rINN)*

BW-49-210; Diaveridina; Diavéridine; Diaveridinum; NSC-408735. 5-Veratrylpyrimidine-2,4-diyldiamine.

Диаверидин

$C_{13}H_{16}N_4O_2$ = 260.3.
CAS — 5355-16-8.
ATC Vet — QP51AX18.



Pharmacopoeias. In *Fr.* for veterinary use.

Profile
Diaveridine is an antiprotozoal used in veterinary practice for the control of coccidiosis in poultry.

Diclazuril *(BAN, USAN, rINN)*

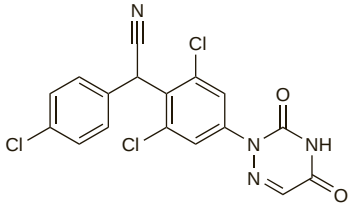
Diclazurilo; Diclazurilum; Diklatsuriili; Diklazuril; R-64433. (±)-4-Chlorophenyl[2,6-dichloro-4-(2,3,4,5-tetrahydro-3,5-dioxo-1,2,4-triazin-2-yl)phenyl]acetonitrile.

Диклазурил

$C_{17}H_9Cl_3N_4O_2$ = 407.6.

CAS — 101831-37-2.

ATC Vet — QP51AJ03.



Pharmacopoeias. In *Eur.* (see p.vii) for veterinary use only.
Ph. Eur. 6.2 (Diclazuril for Veterinary Use; Diclazuril BP(Vet) 2008). A white or light yellow powder. Practically insoluble in water, in alcohol, and in dichloromethane; sparingly soluble in dimethylformamide. Protect from light.

Profile

Diclazuril is an antiprotozoal that has been tried in AIDS patients for the management of diarrhoea associated with protozoal infection. It is used in veterinary practice for the control of coccidiosis in lambs and poultry.

◊ References.

1. Kayembe K, *et al.* Diclazuril for Isospora belli infections in AIDS. *Lancet* 1989; **i:** 1397.
2. Connolly GM, *et al.* Diclazuril in the treatment of severe cryptosporidial diarrhoea in AIDS patients. *AIDS* 1990; **4:** 700–701.
3. Menichetti F, *et al.* Diclazuril for cryptosporidiosis in AIDS. *Am J Med* 1991; **90:** 271–2.
4. Limson-Pobre RNR, *et al.* Use of diclazuril for the treatment of isospora in patients with AIDS. *Clin Infect Dis* 1995; **20:** 201–2.

Diiodohydroxyquinoline *(rINN)*

Diiodohidroxiquinoleína; Diiodohydroxyquin; Diiodohydroxyquinoléine; Di-iodohydroxyquinoline *(BAN)*; Diiodohydroxyquinolinum; Di-iodoxychinolinum; Diiodoxyquinoléine; Diiyodohidroksikinolin; Dijodhydroxikinolin; Dijodihydroksikinoliini; Iodoquinol *(USAN)*. 5,7-Di-iodoquinolin-8-ol.

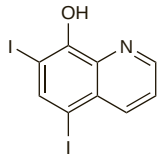
Дийодогидроксихинолин

$C_9H_5I_2NO$ = 397.0.

CAS — 83-73-8.

ATC — G01AC01.

ATC Vet — QG01AC01.



Pharmacopoeias. In *US.*
USP 31 (Iodoquinol). A light yellowish to tan, microcrystalline powder, not readily wetted in water, odourless or has a faint odour. Practically insoluble in water; sparingly soluble in alcohol and in ether.

Adverse Effects

Major concerns have been expressed about the safety of the halogenated hydroxyquinolines since the recognition of severe neurotoxicity with clioquinol (p.254). In Japan, the epidemic development of subacute myelo-opticoneuropathy (SMON) in the 1960s was associated with the ingestion of normal or high doses of clioquinol for prolonged periods and the sale of clioquinol and related hydroxyquinolines was subsequently banned there. Symptoms of SMON are principally those of peripheral neuropathy, including optic atrophy, and myelopathy. Abdominal pain and diarrhoea often precede neurological symptoms such as paraesthesias in the legs, progressing to paraplegia in some patients, and loss of visual acuity sometimes leading to blindness. Cerebral disturbances, including confusion and retrograde amnesia, have also been reported. Although many patients improved when clioquinol was withdrawn, others had residual disability.

It was suggested that the Japanese epidemic might have been due to genetic susceptibility, but a few cases of SMON associated with clioquinol or related hydroxyquinoline derivatives, including broxyquinoline and diiodohydroxyquinoline, have been reported elsewhere.

Diiodohydroxyquinoline has also been associated with gastrointestinal effects such as abdominal cramps, nausea, and diarrhoea. Adverse effects which may be attributable to the iodine content of diiodohydroxyquinoline include pruritus ani, skin eruptions, and enlargement of the thyroid gland. Fever, chills, headache, and vertigo have also occurred.

Precautions

Diiodohydroxyquinoline is contra-indicated in patients known to be hypersensitive to iodine or halogenated hydroxyquinolines and in those with hepatic or renal impairment. It should be used with caution in thyroid disease and may interfere with determinations of protein-bound iodine in tests for thyroid function for up to 6 months after therapy. Its use is best avoided in patients with neurological disorders. Long-term use should be avoided.

Children. The Committee on Drugs of the American Academy of Pediatrics[1] considered that there was a potential risk of toxicity to infants and children from clioquinol and diiodohydroxyquinoline applied topically. Since alternative effective preparations are available for dermatitis, the Committee recommended that products containing either of these compounds should not be used.

WHO considers that the use of halogenated hydroxyquinolines for the treatment of acute diarrhoea or amoebiasis in children cannot be justified.[2] There is no evidence of their efficacy in acute diarrhoea and they have been associated with severe neurological effects. On the rare occasions when a luminal amoebicide is required, other less toxic and more effective agents are available.

1. Kauffman RE, *et al.* American Academy of Pediatrics Committee on Drugs. Clioquinol (iodochlorhydroxyquin, Vioform) and iodoquinol (diiodohydroxyquin): blindness and neuropathy. *Pediatrics* 1990; **86:** 797–8.
2. WHO. The rational use of drugs in the management of acute diarrhoea in children. Geneva: WHO, 1990.

Pharmacokinetics

Diiodohydroxyquinoline is poorly absorbed from the gastrointestinal tract. Concern has been expressed about possible absorption after application to the skin (see Children, under Precautions, above).

Uses and Administration

Diiodohydroxyquinoline, a halogenated hydroxyquinoline, is a luminal amoebicide acting principally in the bowel lumen and is used in the treatment of intestinal amoebiasis, although a less toxic amoebicide such as diloxanide furoate is usually preferred; children should not be treated with diiodohydroxyquinoline (see Precautions, above). It is given alone in the treatment of asymptomatic cyst passers and with an amoebicide that acts in the tissues, such as metronidazole, in patients with invasive amoebiasis (p.822). The usual oral dosage in the treatment of amoebiasis is 630 or 650 mg three times daily for 20 days.

Diiodohydroxyquinoline has also been given in the treatment of *Dientamoeba fragilis* infections, in balantidiasis (p.823) as an alternative to tetracycline, and in *Blastocystis hominis* infections (p.823).

Diiodohydroxyquinoline was formerly used in the treatment of acrodermatitis enteropathica; it is reported to act by enhancing zinc absorption and has now been superseded by oral zinc therapy.

Diiodohydroxyquinoline is claimed to have some antibacterial and antifungal activity and has been used topically (but see Children, under Precautions, above).

Preparations

USP 31: Iodoquinol Tablets.

Proprietary Preparations (details are given in Part 3)

Canad.: Diodoquin; ***Mex.:*** Ameban; Antidifar; Carsuquin; Diameb; Diodoquin; Diyosul; Drioquilen†; Entero-Diyod; Entodiba; Exoquin; Flanoquin†; Quinosul; Versamiv; ***Turk.:*** Floraquin; ***USA:*** Sebaquin; Yodoxin; ***Venez.:*** Diodoquin.

Multi-ingredient: ***Arg.:*** Hipoglos Cicatrizante; Plusderm†; ***Chile:*** Dexagin; Kordinol Compuesto†; ***Mex.:*** Ameban; Amebyl; Bontal; Coralzul; Depofin; Dialgin; Diodolina; Dipecfur; Facetin-D; Farmeban; Flagenase 400; Flagocil; Lambliquin; Metodine; Metrodiyod; Metroviform†; Norecil; Novageon; Stomffler Plus; Threchop; ***S.Afr.:*** Vagarsol; Viocort; Viodor; ***Thai.:*** Coccila†; Disento; Gynecon; Gynecon-T; Gynoco; Gynova; Gyracon; Medicocin†; Nystin; Quinradon-N; Vagicin; ***USA:*** Alcortin; Vytone; ***Venez.:*** Diodonato†.

Diloxanide Furoate *(BANM, rINNM)*

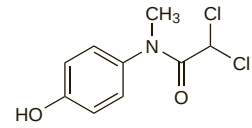
Diloksanid Furoat; Diloxanide, Furoate de; Diloxanidi Furoas; Furoato de diloxanida. 4-(*N*-Methyl-2,2-dichloroacetamido)-phenyl 2-furoate.

Дилоксанида Фуроат

$C_{14}H_{11}Cl_2NO_4$ = 328.1.

CAS — 579-38-4 (diloxanide); 3736-81-0 (diloxanide furoate).

ATC — P01AC01.



(diloxanide)

Pharmacopoeias. In *Br.*, *Int.*, and *US.*
BP 2008 (Diloxanide Furoate). A white or almost white, odourless or almost odourless, crystalline powder. Very slightly soluble in water; slightly soluble in alcohol and in ether; freely soluble in chloroform. Protect from light.
USP 31 (Diloxanide Furoate). A white or almost white, crystalline powder. Very slightly soluble in water; slightly soluble in alcohol and in ether; freely soluble in chloroform. Store in airtight containers. Protect from light.

Adverse Effects

Flatulence is the most common adverse effect during treatment with diloxanide furoate. Vomiting, pruritus, and urticaria may occasionally occur.

Pharmacokinetics

Diloxanide furoate is hydrolysed before absorption from the gastrointestinal tract. The resulting diloxanide is readily absorbed and excreted mainly in the urine as the glucuronide; less than 10% of a dose appears in the faeces.

Uses and Administration

Diloxanide furoate, a dichloroacetamide derivative, is a luminal amoebicide acting principally in the bowel lumen and is used in the treatment of intestinal amoebiasis (p.822). It is given alone in the treatment of asymptomatic cyst passers and with an amoebicide that acts in the tissues, such as metronidazole, in patients with invasive amoebiasis.

Diloxanide furoate is given orally in a dosage of 500 mg three times daily for 10 days; children weighing more than 25 kg may be given 20 mg/kg daily, in 3 divided doses, for 10 days. The course of treatment may be repeated if necessary.

Preparations

BP 2008: Diloxanide Tablets.

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***India:*** Aristogyl Plus; Dyrade-M; Entamizole; Entrolate†; Qugyl; Tinidafyl Plus; Wotinex.

Dimetridazole *(BAN, pINN)*

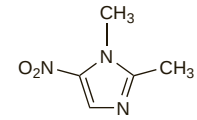
Dimetridatsoli; Dimetridazol; Dimétridazole; Dimetridazolum. 1,2-Dimethyl-5-nitroimidazole.

Диметридазол

$C_5H_7N_3O_2$ = 141.1.

CAS — 551-92-8.

ATC Vet — QP51AA07.



Pharmacopoeias. In *Fr.* for veterinary use. Also in *BP(Vet).*
BP(Vet) 2008 (Dimetridazole). An almost white to brownish-yellow, odourless or almost odourless powder which darkens on exposure to light. Slightly soluble in water; sparingly soluble in alcohol; freely soluble in chloroform; slightly soluble in ether. Protect from light.

Profile

Dimetridazole is a 5-nitroimidazole derivative similar to metronidazole. It is used in veterinary practice for the control of various protozoal infections in birds, fish, and reptiles. It is also used for swine dysentery.