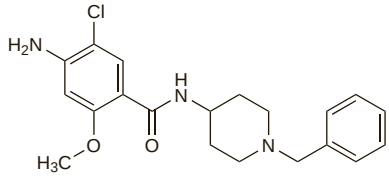
Clebopride *(BAN, USAN, rINN)*

Cleboprida; Clébopride; Clebopridum; LAS-9273. 4-Amino-*N*-(1-benzyl-4-piperidyl)-5-chloro-*o*-anisamide.

Клебоприд

$C_{20}H_{24}ClN_3O_2$ = 373.9.
CAS — 55905-53-8.
ATC — A03FA06.
ATC Vet — QA03FA06.



Clebopride Malate *(BANM, rINNM)*

Clébopride, malate de; Clebopridi malas; Kleboprid malát; Klebopridimalaatti; Klebopridmalat; Kleboprid-malát; Kleboprido malatas; Malato de clebopride.

Клебоприда Малат

$C_{20}H_{24}ClN_3O_2,C_4H_6O_5$ = 508.0.
CAS — 57645-91-7.
ATC — A03FA06.
ATC Vet — QA03FA06.

Pharmacopoeias. In *Eur.* (see p.vii)
Ph. Eur. 6.2 (Clebopride Malate). A white or almost white, crystalline powder. Sparingly soluble in water and in methyl alcohol; slightly soluble in dehydrated alcohol; practically insoluble in dichloromethane. The pH of a 1% solution in water is 3.8 to 4.2. Protect from light.

Profile
Clebopride is a substituted benzamide similar to metoclopramide (p.1747), that is used for its antiemetic and prokinetic actions in nausea and vomiting (p.1700) and various other gastrointestinal disorders. It is given as the malate but doses are expressed in terms of the base. Clebopride malate 679 micrograms is equivalent to about 500 micrograms of clebopride.

Clebopride malate is given in a usual oral dose equivalent to clebopride 0.5 mg three times daily before meals or 0.5 to 1 mg by intramuscular or intravenous injection for acute symptoms. For dosage in children see below.

Administration in children. Adolescents aged 12 to 20 years may be given clebopride malate orally in a dose equivalent to clebopride 250 micrograms three times daily. An oral dose of 15 to 20 micrograms/kg daily in 3 divided doses may be used for children under 12; the following doses have been recommended:

- 1 to 4 years: 50 micrograms 3 times daily
- 4 to 8 years: 100 micrograms 3 times daily
- 8 to 10 years: 150 micrograms 3 times daily
- 10 to 12 years: 200 micrograms 3 times daily

Preparations
Proprietary Preparations (details are given in Part 3)
Arg.: Gastridin; ***Indon.:*** Clast; ***Ital.:*** Motilex; ***Port.:*** Clebofex; Clebutec; ***Spain:*** Cleboril.

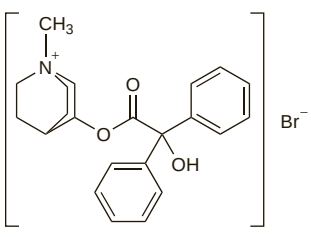
Multi-ingredient: *Arg.:* Eudon; Gastridin-E; Somasedan; ***Spain:*** Clanzoflat; Flatoril.

Clidinium Bromide *(BAN, USAN, rINN)*

Bromuro de clidinio; Clidinii Bromidum; Clidinium, Bromure de; Klidiniumbromid; Klidiniumbromidi; Klidinyum Bromür; Ro-2-3773. 3-Benziloyloxy-1-methylquinuclidinium bromide.

Клидиния Бромид

$C_{22}H_{26}BrNO_3$ = 432.4.
CAS — 7020-55-5 (clidinium); 3485-62-9 (clidinium bromide).



Pharmacopoeias. In *US.*
USP 31 (Clidinium Bromide). A white or nearly white, practically odourless, crystalline powder. Soluble in water and in alcohol; slightly soluble in ether and in benzene. Store in airtight containers. Protect from light.

Profile
Clidinium bromide is a quaternary ammonium antimuscarinic with peripheral effects similar to those of atropine (p.1219). It has been used alone or more often with chlordiazepoxide in the symptomatic treatment of peptic ulcer disease and other gastrointestinal disorders.

Preparations
USP 31: Chlordiazepoxide Hydrochloride and Clidinium Bromide Capsules.

Proprietary Preparations (details are given in Part 3)
Multi-ingredient: *Arg.:* Libraxin; ***Canad.:*** Apo-Chlorax; Librax; ***Chile:*** Gastrolen; Lerogin; Libraxin; Lironex†; Sedogastrol†; Tensoliv; ***Fin.:*** Librax; ***Fr.:*** Librax; ***Gr.:*** Distedon; Librax; ***Hong Kong:*** Bralix; Librax; Medocalum†; ***India:*** Equirex; Normaxin; Spasrax; ***Indon.:*** Braxidin; Cliad; Klidibrax; Librax; Melidox; Renagas; ***Israel:*** Nirvaxal; ***Ital.:*** Librax; ***Malaysia:*** Apo-Chlorax†; Liblan; ***Port.:*** Librax; ***S.Afr.:*** Librax; ***Singapore:*** Apo-Chlorax; Chlobax; Librax; Medocalum; ***Switz.:*** Librax; Librocol; ***Thai.:*** Kenspa; Librax; Pobrax†; Tumax; Zepobrax†; ***Turk.:*** Klipaks; Librax; ***USA:*** Clindex; Librax; ***Venez.:*** Librax.

Colocynth

Bitter Apple; Bitter Cucumber; Colocinto; Colocynth Pulp; Colocynthis; Coloquinte; Coloquintidas; Koloquinthen.

Колоцинт

NOTE. The synonym Bitter Apple has also been applied to the fruits of *Solanum incanum*.

Profile
Colocynth is the dried pulp of the fruit of *Citrullus colocynthis* (Cucurbitaceae). It has a drastic purgative and irritant action and has been superseded by less toxic laxatives.

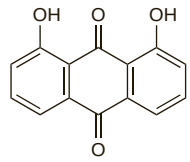
Homoeopathy. Colocynth has been used in homoeopathic medicines under the following names: Colocynthis; Coloc.

Dantron *(BAN, rINN)*

Antrapurol; Chrysazin; Danthron; Dantrón; Dantrone; Dantroni; Dantronum; Dianthon; Dioxyanthrachinonum. 1,8-Dihydroxyanthraquinone.

Дантрон

$C_{14}H_8O_4$ = 240.2.
CAS — 117-10-2.
ATC — A06AB03.
ATC Vet — QA06AB03.



NOTE. Compounded preparations of dantron may be represented by the following names:

- Co-danthramer *x*/*y* (*BAN*)—where *x* and *y* are the strengths in milligrams of dantron and poloxamer respectively
- Co-danthrusate (*BAN*)—dantron 5 parts and docusate sodium 6 parts (w/w).

Pharmacopoeias. In *Br.*
BP 2008 (Dantron). An orange, odourless or almost odourless, crystalline powder. Practically insoluble in water; very slightly soluble in alcohol; soluble in chloroform; slightly soluble in ether; dissolves in solutions of alkali hydroxides.

Adverse Effects and Precautions
As for Senna, p.1769. Dantron may colour the urine pink or red. Discoloration and superficial sloughing of perianal skin can occur after prolonged contact, therefore dantron should not be used in infants wearing nappies (diapers) and should be used with caution in incontinent patients. The mucosa of the large intestine may be discoloured with prolonged use or high dosage.

In *rodents*, dantron has been associated with the development of intestinal and liver tumours. Consequently, its use has been restricted, see Uses and Administration, below.

◊ References to adverse effects occurring with dantron-containing laxatives include individual cases of leucopenia with liver damage,[1] greyish-blue skin discoloration,[2] and orange vaginal discharge.[3] There has also been a report of intestinal sarcoma in an 18-year-old girl with a history of prolonged use of a dantron-containing laxative.[4] In May 2000 the UK CSM restricted the use of dantron to terminally ill patients on the grounds that pre-clinical evidence had increased and dantron was now established as a potential human carcinogen.[5]

1. Tolman KG, *et al*. Possible hepatotoxicity of Doxidan. *Ann Intern Med* 1976; **84:** 290–2.
2. Darke CS, Cooper RG. Unusual case of skin discoloration. *BMJ* 1978; **1:** 1188–9.
3. Greer IA. Orange periods. *BMJ* 1984; **289:** 323.
4. Patel PM, *et al*. Anthraquinone laxatives and human cancer: an association in one case. *Postgrad Med J* 1989; **65:** 216–17.
5. Committee on Safety of Medicines/Medicine Control Agency. Danthron restricted to constipation in the terminally ill. *Current Problems* 2000; **26:** 4. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON007462&RevisionSelectionMethod=LatestReleased (accessed 08/11/06)

Breast feeding. The American Academy of Pediatrics[1] state that, although usually compatible with breast feeding, use of dantron by breast-feeding mothers has been reported to cause increased bowel activity in the infant.

1. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid.*; 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 08/11/06)

Pharmacokinetics
Dantron is metabolised by bacteria in the colon. Dantron or its metabolites are absorbed from the gastrointestinal tract, as indicated by discoloration of urine in some patients. Dantron or its metabolites are excreted in the faeces and the urine, and also in other secretions including breast milk.

Uses and Administration
Dantron is an anthraquinone stimulant laxative but, unlike senna (p.1769), it is not a glycoside. It is given orally to treat constipation (p.1693) and is effective within 6 to 12 hours. However, because of concern over *rodent* carcinogenicity it has been withdrawn in some countries, and its use restricted in others. In the UK, it may be used only in terminally ill patients.

Dantron is given in doses of 25 to 75 mg when given with poloxamer 188 (p.1918) as co-danthramer, and in doses of 50 to 150 mg when given with docusate sodium (p.1725) as co-danthrusate. Doses are usually given at bedtime. For doses in children, see below.

Administration in children. Children under 12 years have been given dantron 12.5 to 25 mg orally as co-danthramer or 50 mg as co-danthrusate. Doses are usually given at bedtime. Children aged 12 years and over may be treated with the adult dose (see Uses and Administration, above).

The *BNFC* recommends similar doses to these, but restricts the use of co-danthramer to children aged 2 years and over, and the use of co-danthrusate to those aged 6 years and over.

Dantron should not be used in infants wearing nappies (diapers) as it may cause discoloration and superficial sloughing of the skin.

Preparations
BP 2008: Co-danthrusate Capsules.

Proprietary Preparations (details are given in Part 3)
Multi-ingredient: *Braz.:* Fenogar†; ***Chile:*** Modane; ***Irl.:*** Ailax; Codalax; Cotron; ***Mex.:*** Modaton; ***NZ:*** Codalax†; Conthram†; ***UK:*** Ailax†; Capsuvac; Codalax; Danlax; Normax.

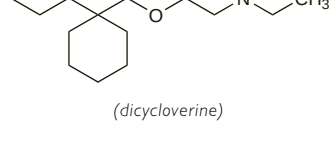
Dicycloverine Hydrochloride

(BANM, rINNM)

Cloridrato de Diciclоverina; Dicikloverin-hidroklorid; Dicikloverino hidrochloridas; Dicyclomine Hydrochloride; Dicyclovérine, chlorhydrate de; Dicycloverini hydrochloridum; Dicykloverin-hydrochlorid; Dicykloverinhydroklorid; Disykloveriinihydrokloridi; Hidrocloruro de diciclоverina. 2-Diethylaminoethyl bicyclohexyl-1-carboxylate hydrochloride.

Дицикловерина Гидрохлорид

$C_{19}H_{35}NO_2$,HCl = 345.9.
CAS — 77-19-0 (dicycloverine); 67-92-5 (dicycloverine hydrochloride).
ATC — A03AA07.
ATC Vet — QA03AA07.



(dicycloverine)

Pharmacopoeias. In *Eur.* (see p.vii) and *US.*
Ph. Eur. 6.2 (Dicycloverine Hydrochloride). A white or almost white, crystalline powder. It shows polymorphism. Soluble in water; freely soluble in alcohol and in dichloromethane. A 1% solution in water has a pH of 5.0 to 5.5.

USP 31 (Dicyclomine Hydrochloride). A fine white, practically odourless, crystalline powder. Soluble 1 in 13 of water, 1 in 5 of alcohol, 1 in 2 of chloroform and of glacial acetic acid, and 1 in 770 of ether. pH of a 1% solution in water is between 5.0 and 5.5.

Adverse Effects, Treatment, and Precautions

As for Atropine Sulfate, p.1219. Dicycloverine hydrochloride should not be given to infants younger than 6 months of age.

Apnoea. Reports[1-3] of severe apnoea in infants aged 5 to 10 weeks associated with the use of dicycloverine.

1. Williams J, Watkin-Jones R. Dicyclomine: worrying symptoms associated with its use in some small babies. *BMJ* 1984; **288:** 901.
2. Edwards PDL. Dicyclomine in babies. *BMJ* 1984; **288:** 1230.
3. Spoudeas H, Shribman S. Dicyclomine in babies. *BMJ* 1984; **288:** 1230.

Pregnancy. For a review of the risks to the fetus of antiemetic therapy during pregnancy, with particular reference to *Debendox* (*Bendectin*: dicycloverine with doxylamine and pyridoxine), see under Antihistamines on p.563.

Interactions

As for antimuscarinics in general (see Atropine Sulfate, p.1220).

Uses and Administration

Dicycloverine hydrochloride is a tertiary amine antimuscarinic with effects similar to but weaker than those of atropine (p.1219); it also has a direct antispasmodic action.

Dicycloverine is used in gastrointestinal spasm, particularly that associated with the irritable bowel syndrome. For adults, 10 to 20 mg of dicycloverine hydrochloride is given orally 3 times daily; in the USA, up to 40 mg four times daily has been recommended where adverse effects permit. Children aged 6 months to 2 years may be given 5 to 10 mg up to 3 or 4 times daily; doses are usually given 15 minutes before meals. Children aged 2 to 12 years may be given 10 mg three times daily.

Dicycloverine hydrochloride may be given intramuscularly in doses of 20 mg given 4 times daily to patients in whom oral therapy is temporarily impractical, but should not be used for longer than 1 to 2 days.

Preparations

BP 2008: Dicycloverine Oral Solution; Dicycloverine Tablets;
USP 31: Dicyclomine Hydrochloride Capsules; Dicyclomine Hydrochloride Injection; Dicyclomine Hydrochloride Syrup; Dicyclomine Hydrochloride Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Babypasmil; ***Austral.:*** Merbentyl†; ***Braz.:*** Bentyl; ***Canad.:*** Bentylol; Formulex†; Lomine; ***Hong Kong:*** Dicymine; ***India:*** Cyclominol; Cyclopam; Dysmen; Spasmo-Proxyvon; Spasmonil; ***Irl.:*** Merbentyl†; ***Israel:*** Notensyl; ***Mex.:*** Bentyl; Clominal; Dicigon; Diclomin; Sediclon; ***NZ:*** Merbentyl†; ***Philipp.:*** Bentyl; Dilomin; Relestal; Spasdon; ***Port.:*** Optimal†; ***Rus.:*** Trigan (Триган); ***S.Afr.:*** Clomin†; Medicyclomine†; Merbentyl; ***Thai.:*** Dicomin; Dicymine; ***UK:*** Merbentyl; ***USA:*** Antispas; Bentyl; Byclomine; Dibent; Or-Tyl; ***Venez.:*** Ciclan†; Diciclor†; Mabex.

Multi-ingredient: ***Arg.:*** Dafne; ***Chile:*** Profisin; ***Hong Kong:*** Colimix; Dicymine Co; Epilon; Veragel; ***India:*** Colimex; Colirid; Cyclo-Meff; Cyclopam; Diclospa; Dysmen; Nicispas; Normaxin; Parvon-Spas; Spasmo-Proxyvon; Spasmo-Proxyvon Forte; Spasmocip Plus; Spasmoflexon†; Spasmonil; Spasmonil Plus; Trigan-D; Ze-Spas; ***Ital.:*** Merankol Pastiglie; ***Malaysia:*** Colimix; Uphaco†; ***Mex.:*** Alphalox-D; Exhidrol; Farcolan; ***Port.:*** Nausefe; ***Rus.:*** Trigan-D (Триган-Д); ***S.Afr.:*** Acugel; Alkalite D; Alumag D; Alumite D; Asic; Betaclomin; Co-Gel; Gelumen; Kolantyl; Medigel; Microgel; Neutragel-D; pH 550†; Propan Gel-S; Remotrox; Spasmogel; ***Singapore:*** Colimix; Meclosil; Veragel DMS; ***Spain:*** Colchimax; Neocolan; ***Thai.:*** Berclomine; Biodan†; Cymine; Difemic; Kremil-S; Mainnox; Med-Anspasmic†; Spasticone; Veragel; ***UK:*** Kolanticon; ***Venez.:*** Clopina†; Dicigel.

Difemerine Hydrochloride *(rINNM)*

Difémérine, Chlorhydrate de; Difemerini Hydrochloridum; Hidrocloruro de difemerina; UP-57. 2-Dimethylamino-1,1-dimethylethyl benzilate hydrochloride.

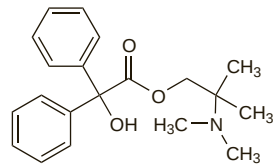
Дифемерина Гидрохлорид

$C_{20}H_{25}NO_3$,HCl = 363.9.

CAS — 80387-96-8 (difemerine); 70280-88-5 (difemerine hydrochloride).

ATC — A03AA09.

ATC Vet — QA03AA09.



(difemerine)

Profile

Difemerine hydrochloride is an antimuscarinic with effects similar to those of atropine (p.1219) and was used in the symptomatic treatment of visceral spasms.

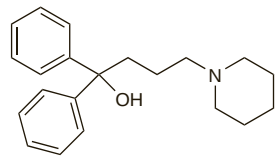
Difenidol Hydrochloride *(BANM, rINNM)*

Difénidol, Chlorhydrate de; Difenidoli Hydrochloridum; Diphenidol Hydrochloride *(USAN)*; Hidrocloruro de difenidol; SKF-478 (difenidol); SKF-478-A; SKF-478-J (difenidol embonate). 1,1-Diphenyl-4-piperidinobutan-1-ol hydrochloride.

Дифенидола Гидрохлорид

$C_{21}H_{27}NO$,HCl = 345.9.

CAS — 972-02-1 (difenidol); 3254-89-5 (difenidol hydrochloride); 26363-46-2 (difenidol embonate).



(difenidol)

Pharmacopoeias. In *Chin.* and *Jpn.*

Profile

Difenidol hydrochloride is an antiemetic that probably acts through the chemoreceptor trigger zone. It is claimed to control vertigo by means of a specific effect on the vestibular apparatus. Difenidol also has a weak peripheral antimuscarinic action.

It has been used in the treatment of some forms of nausea and vomiting (p.1700) such as those associated with surgery, radiotherapy, and cancer chemotherapy. It has also been used for the symptomatic treatment of vertigo (p.565), nausea and vomiting due to Ménière's disease (p.564), and other labyrinthine disturbances.

It has been given in oral doses equivalent to 25 to 50 mg of difenidol every 4 hours as required. Difenidol hydrochloride has also been given parenterally.

Preparations

Proprietary Preparations (details are given in Part 3)

Braz.: Vontrol†; ***Chile:*** Vontrol; ***Hong Kong:*** Cephadol; ***Jpn:*** Cephadol; ***Malaysia:*** Cephadol; ***Mex.:*** Biomitin; Diphafen; Hemetiken; Lansenol; Nautrol; Normavom; Serratol; Sons; Vontrol; Voxamine; ***Philipp.:*** Cephadol; ***Singapore:*** Cephadol†; ***Thai.:*** Cephadol.

Difenoxin *(BAN, USAN, rINN)*

Difenoxilic Acid; Difenoxina; Difénoxine; Difenoxinum; Diphenoxylic Acid; McN-JR-15403-11. 1-(3-Cyano-3,3-diphenylpropyl)-4-phenylpiperidine-4-carboxylic acid.

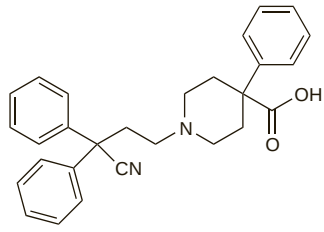
Дифеноксин

$C_{28}H_{28}N_2O_2$ = 424.5.

CAS — 28782-42-5.

ATC — A07DA04.

ATC Vet — QA07DA04.



Difenoxin Hydrochloride *(BANM, rINNM)*

Difénoxine, Chlorhydrate de; Difenoxini Hydrochloridum; Difenoxylic Acid Hydrochloride; Diphenoxylic Acid Hydrochloride; Hidrocloruro de difenoxina; R-15403.

Дифеноксина Гидрохлорид

$C_{28}H_{28}N_2O_2$,HCl = 461.0.

CAS — 35607-36-4.

ATC — A07DA04.

ATC Vet — QA07DA04.

Profile

Difenoxin is the principal active metabolite of diphenoxylate (p.1724) and has similar actions and uses. It is given orally as the hydrochloride, but doses are in terms of the base; difenoxin hydrochloride 1.1 mg is equivalent to about 1 mg of difenoxin.

In the treatment of diarrhoea (p.1694), the usual dose in adults is the equivalent of difenoxin 2 mg initially, followed by 1 mg after each loose stool or every 3 to 4 hours as required, up to a maximum of 8 mg daily.

Preparations of difenoxin usually contain subclinical amounts of atropine sulfate in an attempt to discourage abuse.

Preparations

Proprietary Preparations (details are given in Part 3)

USA: Motofen.

Dihexyverine Hydrochloride *(USAN, rINNM)*

Dihexiverine Hydrochloride; Dihexyvérine, Chlorhydrate de; Dihexyverini Hydrochloridum; Hidrocloruro de dihexiverina; JL-1078. 2-Piperidinoethyl bicyclohexyl-1-carboxylate hydrochloride.

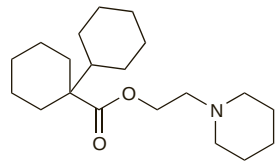
Дигексиверина Гидрохлорид

$C_{20}H_{35}NO_2$,HCl = 358.0.

CAS — 561-77-3 (dihexyverine); 5588-25-0 (dihexyverine hydrochloride).

ATC — A03AA08.

ATC Vet — QA03AA08.



(dihexyverine)

Profile

Dihexyverine hydrochloride is an antimuscarinic with effects similar to those of atropine (p.1219). It has been given in the symptomatic treatment of gastrointestinal spasm.

Preparations

Proprietary Preparations (details are given in Part 3)

Fr.: Spasmodex†.

Dihydroxyaluminum Sodium Carbonate

Aluminium Sodium Carbonate Hydroxide; Carbonato sódico de dihidroxialuminio; Dihidroksialüminyum Sodyum Karbonat; Dihydroksialuminiumnatriumkarbonaatti; Dihydroxialuminiinatrii Carbonas; Dihydroxialuminiumnatriumkarbonat; Dihydroxyaluminium Sodium Carbonate. Sodium (carbonato)dihydroxyaluminate(1-).

Дигидрооксиалюминия Натрия Карбонат

CH_2AlNaO_5 = 144.0.

CAS — 41342-54-5 (carbaldrate); 12011-77-7 (dihydroxyaluminium sodium carbonate); 16482-55-6 (dihydroxyaluminium sodium carbonate).

ATC — A02AB04.

ATC Vet — QA02AB04.

NOTE. The name Carbaldrate (*rINN*) has been applied to (CH_2AlNaO_5,*n*H_2O), a form of sodium (carbonato)dihydroxyaluminate(1-) hydrate.

Pharmacopoeias. In *US*.

USP 31 (Dihydroxyaluminum Sodium Carbonate). A fine white odourless powder. It loses not more than 14.5% of its weight on drying. Practically insoluble in water and in organic solvents;