

Cleboipride (BAN, USAN, rINN)

Cleboiprida; Cléboipride; Cleboipridum; LAS-9273. 4-Amino-N-(1-benzyl-4-piperidyl)-5-chloro-o-anisamide.

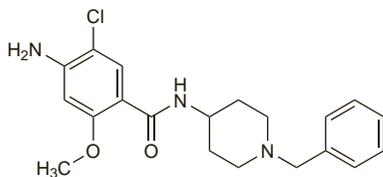
Клебоприда

$C_{20}H_{24}ClN_3O_2 = 373.9$.

CAS — 55905-53-8.

ATC — A03FA06.

ATC Vet — QA03FA06.

**Cleboipride Malate** (BANM, rINNMM)

Cléboipride, malate de; Cleboipridi malas; Cleboiprid malát; Cleboipridimalaatti; Kleboipridmalat; Kleboiprid-malát; Kleboipridomalatas; Malato de cleboiprida.

Клебоприда Малат

$C_{20}H_{24}ClN_3O_2 \cdot C_4H_6O_5 = 508.0$.

CAS — 57645-91-7.

ATC — A03FA06.

ATC Vet — QA03FA06.

Pharmacopoeias. In *Eur.* (see p.vii).

Ph. Eur. 6.2 (Cleboipride 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

Cleboipride 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. Cleboipride malate 679 micrograms is equivalent to about 500 micrograms of cleboipride.

Cleboipride malate is given in a usual oral dose equivalent to cleboipride 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 cleboipride malate orally in a dose equivalent to cleboipride 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.:** Motlex; **Port.:** Cleboflex; Clebutec; **Spain:** Clebonil.

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

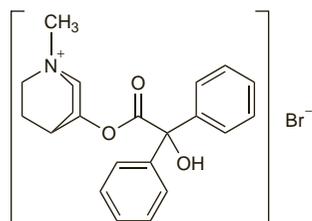
Clidinium Bromide (BAN, USAN, rINN)

Bromuro de clidinio; Clidini Bromidum; Clidinium, Bromure de; Klidiniumbromid; Klidiniumbromidi; Klidinyum Bromür; Ro-2-3773. 3-Benzilyloxy-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; Leroing; Libraxin; Lironex†; Sedogastrol†; Tensolv; **Fin.:** Librax; **Fr.:** Librax; **Gr.:** Distedon; Librax; **Hong Kong:** Bralix; Librax; Medocalum†; **India:** Equirax; Normaxin; Spasrax; **Indon.:** Braxidin; Clid; Klidibrax; Librax; Melidox; Renags; **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.

Colocyth

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

Colocyth 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.

Homeopathy. Colocyth has been used in homeopathic medicines under the following names: Colocynthis; Coloc.

Dantron (BAN, rINN)

Antrapuro; Chryszazin; Danthron; Dantrón; Dantrone; Dantroni; Dantronum; Dianthon; Dioxyanthracinonum. 1,8-Dihydroxyanthraquinone.

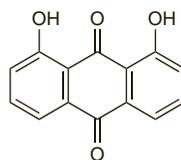
ДАНТРОН

$C_{14}H_8O_4 = 240.2$.

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-clin-

ical 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. Dantron 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 Pediatrics¹ 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.:** Fenogart; **Chile:** Modane; **Ir.:** Ailax; Codalax; Cotron; **Mex.:** Modaton; **NZ.:** Codalax†; Conthram†; **UK:** Ailax†; Capsu-
vac; Codalax; Danjax; Normax.

Dicycloverine Hydrochloride

(BANM, rINNM)

Cloridrato de Dicliverina; Dicliverin-hidroklorid; Dicliverino hidrokloridas; Dicyclomine Hydrochloride; Dicyclovérine, chlorhydrate de; Dicycloverini hydrochloridum; Dicycloverinhydrochlorid; Dicycloverinhydroklorid; Disykloverinhydroklorid; Hidrochloruro de dicliverina. 2-Diethylaminoethyl bicyclohexyl-1-carboxylate hydrochloride.

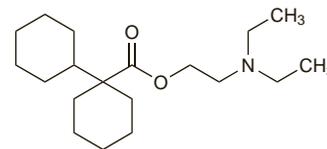
Дицикловерина Гидрохлорид

$C_{19}H_{35}NO_2 \cdot HCl = 345.9$.

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.