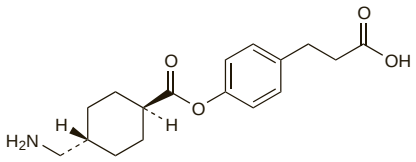
Cetraxate Hydrochloride *(USAN, rINNM)*

Cétraxate, Chlorhydrate de; Cetraxati Hydrochloridum; DV-1006; Hidrocloruro de cetraxato. 4-(2-Carboxyethyl)phenyl tranexamate hydrochloride; 4-(2-Carboxyethyl)phenyl *trans*-4-aminomethylcyclohexanecarboxylate hydrochloride.

Цетраксата Гидрохлорид

$C_{17}H_{23}NO_4$,HCl = 341.8.

CAS — 34675-84-8 (cetraxate); 27724-96-5 (cetraxate hydrochloride).



(cetraxate)

Pharmacopoeias. In *Jpn*.

Profile

Cetraxate hydrochloride is stated to be a mucosal protectant with actions on gastric microcirculation as well as prostaglandin synthesis and kallikrein. It is used in the treatment of gastritis and peptic ulcer disease (p.1702) in oral doses of 600 to 800 mg daily in divided doses.

Preparations

Proprietary Preparations (details are given in Part 3)
Jpn: Neuer.

Chalk

Creta; Prepared Chalk.

Мел

$CaCO_3$ = 100.1.

CAS — 13397-25-6.

Pharmacopoeias. In *Br.*

BP 2008 (Chalk). A native form of calcium carbonate freed from most of its impurities by elutriation and dried. It consists of the calcareous shells and detritus of various foraminifera and contains not less than 97.0% and not more than 100.5% of $CaCO_3$, calculated with reference to the dried substance.

White or greyish-white, odourless or almost odourless, amorphous, earthy, small friable masses, usually conical in form, or in powder. Practically insoluble in water; slightly soluble in water containing carbon dioxide; it absorbs water readily.

Profile

Chalk has been used as an adsorbent antidiarrhoeal. Calcium carbonate (precipitated chalk) is used as an antacid, calcium supplement, and phosphate binder, see p.1714.

Calabash chalk, also known as Calabar stone, la craie or argile, nzu, mabele, ebumba, or ulo, is ingested by some pregnant women to alleviate morning sickness. It is traditionally used by Nigerian or West African women in the form of blocks, pellets, or powders. Calabash chalk either occurs naturally or is produced from clay and mud which may be mixed with other ingredients including sand, wood ash, and sometimes, salt. However, it contains high levels of lead, as well as arsenic (see Contamination, below).

Contamination. Concern with regard to the safety of calabash chalk has arisen, particularly with regard to its lead and arsenic content.[1-3] Analysis of calabash chalk samples available in the UK found that the major component of calabash chalk was an aluminium silicate hydroxide from the kaolin clay group. Lead concentrations in the samples were found to be about 40 mg/kg, almost 40 times the EU recommended guidelines. Potentially toxic chromium concentrations (dependent on the oxidation state) were also found. Arsenic, cadmium, and mercury were not detectable in any of the analysed samples. Persistent organic pollutants were also identified in one sample.[1] Calabash chalk is traditionally used by pregnant women, often those from Nigerian and West African communities, as a remedy for morning sickness. Health authorities in various countries have issued warnings, and advised people, especially pregnant and breast-feeding women, not to consume calabash chalk.[2,3]

1. Dean JR, *et al.* Characterisation and analysis of persistent organic pollutants and major, minor and trace elements in calabash chalk. *Chemosphere* 2004; **57:** 21–5.
2. Health Canada. Calabash chalk may pose health risk for pregnant and breastfeeding women (issued 2nd October 2007). Available at: http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2007/2007_136_e.html (accessed 03/10/07)
3. Food Standards Agency. Lead contamination of calabash chalk (issued 15th October 2002). Available at: http://www.food.gov.uk/enforcement/alerts/2002/oct/94151 (accessed 03/10/07)

Preparations

BP 2008: Compound Magnesium Trisilicate Oral Powder.
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***S.Afr.:*** Behoedmiddel vir Kinders.

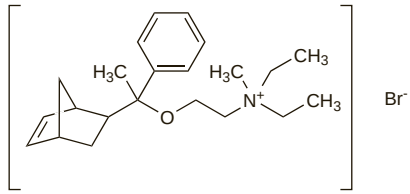
Ciclonium Bromide *(rINN)*

Asta-3746; Bromuro de ciclonio; Ciclonii Bromidum; Ciclonium, Bromure de. Diethylmethyl{2-[(α-methyl-α-5-norbornen-2-ylbenzyl)oxy]ethyl}ammonium bromide.

Циклония Бромид

$C_{22}H_{34}BrNO$ = 408.4.

CAS — 29546-59-6.



NOTE. The name cyclonium or ciclonium iodide has been used to describe an unrelated antispasmodic, oxapium iodide (p.1759).

Profile

Ciclonium bromide is an antimuscarinic that has been used in the treatment of gastrointestinal and urinary-tract disorders associated with smooth muscle spasm.

Preparations

Proprietary Preparations (details are given in Part 3)
Thai.: Adamon†.
Multi-ingredient: ***Arg.:*** Espasmo Motrax†; ***Turk.:*** Doladamon-P.

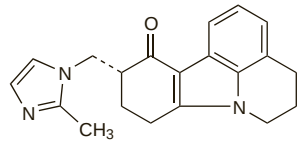
Cilansetron *(USAN, rINN)*

Cilansétron; Cilansetrón; Cilansetronum; KC-9946. (–)-(*R*)-5,6,9,10-Tetrahydro-10-[(2-methylimidazol-1-yl)methyl]-4*H*-pyrido[3,2,1-*jk*]carbazol-11(8*H*)-one.

Цилансетрон

$C_{20}H_{21}N_3O$ = 319.4.

CAS — 120635-74-7.
ATC — A03AE03.
ATC Vet — QA03AE03.



Profile

Cilansetron is a 5-HT_3 antagonist under investigation for the treatment of diarrhoea-predominant irritable bowel syndrome.

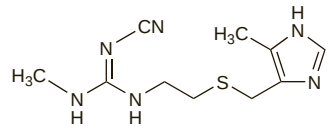
Cimetidine *(BAN, USAN, rINN)*

Cimetidin; Cimetidina; Cimetidinas; Cimétidine; Cimetidinum; Cymetydyna; Simetidiini; Simetidin; SKF-92334. 2-Cyano-1-methyl-3-[2-(5-methylimidazol-4-ylmethylthio)ethyl]guanidine.

Циметидин

$C_{10}H_{16}N_6S$ = 252.3.

CAS — 51481-61-9.
ATC — A02BA01.
ATC Vet — QA02BA01.



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

Ph. Eur. 6.2 (Cimetidine). A white or almost white, polymorphic powder. Slightly soluble in water; soluble in alcohol; practically insoluble in dichloromethane. It dissolves in dilute mineral acids. Store in airtight containers. Protect from light.

USP 31 (Cimetidine). A white to off-white crystalline powder, odourless or with a slight mercaptan odour. Slightly soluble in water and in chloroform; soluble in alcohol and in macrogol 400; practically insoluble in ether; sparingly soluble in isopropyl alcohol; freely soluble in methyl alcohol. Store in airtight containers. Protect from light.

Cimetidine Hydrochloride *(BANM, USAN, rINNM)*

Cimétidine, chlorhydrate de; Cimetidin-hidroklorid; Cimetidinhydroklorid; Cimetidini hydrochloridum; Cimetidino hidrochloridas; Hidrocloruro de cimetidina; Simetidiinihydrokloridi.

Циметидина Гидрохлорид

$C_{10}H_{16}N_6S$,HCl = 288.8.

CAS — 70059-30-2.
ATC — A02BA01.
ATC Vet — QA02BA01.

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

Ph. Eur. 6.2 (Cimetidine Hydrochloride). A white or almost white, crystalline powder. Freely soluble in water; sparingly soluble in dehydrated alcohol. A 1% solution in water has a pH of 4.0 to 5.0. Store in airtight containers. Protect from light.

USP 31 (Cimetidine Hydrochloride). Store in airtight containers. Protect from light.

Adverse Effects

Adverse reactions to cimetidine and other histamine H_2-antagonists are generally infrequent. The commonest adverse effects reported have been diarrhoea and other gastrointestinal disturbances, dizziness, tiredness, headache, and rashes.

Altered liver function tests have occurred and there have been rare reports of hepatotoxicity. Reversible confusional states, especially in the elderly or in seriously ill patients such as those with renal failure, have occasionally occurred. Other adverse effects that have been reported rarely are hypersensitivity reactions and fever, arthralgia and myalgia, blood disorders including agranulocytosis, leucopenia, and thrombocytopenia, acute pancreatitis, interstitial nephritis, hallucinations and depression, and cardiovascular disorders including bradycardia, tachycardia, and heart block. Rapid intravenous injection should be avoided as there have been rare associations with cardiac arrest and arrhythmias; transient hypotension has also been seen.

In patients such as the elderly, those with chronic lung disease, diabetes mellitus, or the immunocompromised, treatment with H_2-antagonists may be associated with an increased risk of developing community-acquired pneumonia.

Cimetidine has a weak anti-androgenic effect and gynaecomastia and impotence have also occasionally occurred in men; these are usually reversible.

Incidence of adverse effects. In a meta-analysis of 24 double-blind placebo-controlled studies,[1] the incidence of adverse effects with cimetidine was not significantly different from placebo. The most common adverse effects reported by patients taking cimetidine who were followed up for at least one year[2,3] were diarrhoea, headache, fatigue, skin rash or pruritus, and gynaecomastia. The incidence of adverse effects was dose-related and decreased with length of treatment.[3] No fatal adverse effect of cimetidine could be found in a mortality survey involving 9928 patients taking cimetidine and 9351 controls;[4] although the mortality rate was higher in the cimetidine patients, this was explained by the presence of underlying disease (known or unknown) before starting cimetidine treatment and the use of cimetidine to counter adverse gastric effects of other drugs. Follow-up of 9377 of these cimetidine-treated patients for a further 3 years[5] still revealed no fatal disorder attributable to cimetidine treatment and a steady fall in the excess death rate in cimetidine users was seen with increasing length of follow-up; by the fourth year there was little difference between the observed and expected death rate. Cimetidine still appeared to be safe after 10 years of follow-up.[6]

1. Richter JM, *et al.* Cimetidine and adverse reactions: a meta-analysis of randomized clinical trials of short-term therapy. *Am J Med* 1989; **87:** 278–84.
2. Colin Jones DG, *et al.* Post-marketing surveillance of the safety of cimetidine: twelve-month morbidity report. *Q J Med* 1985; **54:** 253–68.
3. Bardhan KD, *et al.* Safety of longterm cimetidine (CIM) treatment: the view from one centre. *Gut* 1990; **31:** A599.
4. Colin-Jones DG, *et al.* Postmarketing surveillance of the safety of cimetidine: 12 month mortality report. *BMJ* 1983; **286:** 1713–16.
5. Colin-Jones DG, *et al.* Postmarketing surveillance of the safety of cimetidine: mortality during second, third, and fourth years of follow up. *BMJ* 1985; **291:** 1084–8.
6. Colin-Jones DG, *et al.* Postmarketing surveillance of the safety of cimetidine: 10 year mortality report. *Gut* 1992; **33:** 1280–4.