laemia. This may cause or exacerbate hypertension, heart failure, oedema, alkalosis, and muscle weakness and damage, and systemic carbenoxolone should therefore be used with caution, if at all, in patients with cardiovascular disease. If hypokalaemia is prolonged, renal impairment can occur. Care is needed in pre-existing hepatic or renal impairment. Regular monitoring of weight and blood pressure is advised; if hypokalaemia, oedema, or a significant rise in blood pressure occurs, carbenoxolone therapy should be stopped. Potassium depletion may be corrected with potassium supplements. Systemic use of carbenoxolone sodium is contra-indicated in patients with hypokalaemia, in pregnancy, in the elderly, and in children.

◊ Muscle weakness,[1-5] muscle necrosis,[4] myopathy,[1] hypertension,[2] headache,[2] cardiac failure,[2] mental confusion,[4] areflexia,[3] renal tubular dysfunction,[5] and acute tubular necrosis[4] have all been associated with carbenoxolone-induced hypokalaemia. Carbenoxolone-induced hypertension may have precipitated the onset of fatal polyarteritis in a patient predisposed to this condition.[6]

1. Fyfe T, *et al.* Myopathy and hypokalaemia in carbenoxolone therapy. *BMJ* 1969; **3:** 476.
2. Davies GJ, *et al.* Complications of carbenoxolone therapy. *BMJ* 1974; **3:** 400–2.
3. Royston A, Prout BJ. Carbenoxolone-induced hypokalaemia simulating Guillain-Barré syndrome. *BMJ* 1976; **2:** 150–1.
4. Descamps C, *et al.* Rhabdomyolysis and acute tubular necrosis associated with carbenoxolone and diuretic treatment. *BMJ* 1977; **1:** 272.
5. Dickinson RJ, Swaminathan R. Total body potassium depletion and renal tubular dysfunction following carbenoxolone therapy. *Postgrad Med J* 1978; **54:** 836–7.
6. Sloan J, Weaver JA. A case of polyarteritis developing after carbenoxolone therapy. *Ir Med J* 1968; **1:** 505–7.

Handling. Carbenoxolone sodium powder is irritant to nasal membranes.

Interactions
Because of the risk of toxicity, carbenoxolone should not be taken with digitalis glycosides unless serum-electrolyte concentrations are measured at weekly intervals and precautions are taken to avoid hypokalaemia.

Although amiloride or spironolactone relieve sodium and water retention, they antagonise the efficacy of systemic carbenoxolone and should not be used with it. The hypokalaemia associated with diuretics may be exacerbated by carbenoxolone.

Pharmacokinetics
Carbenoxolone sodium is absorbed from the gastrointestinal tract, mainly from the stomach. It is highly bound to plasma proteins. Carbenoxolone is chiefly excreted in the faeces via the bile. It appears to undergo enterohepatic circulation.

Uses and Administration
Carbenoxolone sodium is a synthetic derivative of glycyrrhizic acid (p.2316) that was formerly used as a mucosal protectant in peptic ulcer disease and has been given with antacids and alginic acid in gastro-oesophageal reflux disease.

Carbenoxolone sodium is one of many topical treatments for the symptomatic management of mouth ulceration (p.1700). It is usually used as a 2% gel; a 1% mouthwash has been used.

Mental function. High cortisol concentrations have been associated with poorer memory and neuronal loss in some patients. Carbenoxolone inhibits 11-β-hydroxysteroid dehydrogenase type 1, and thus may selectively lower intracellular cortisol. In a small crossover study in 10 healthy elderly men, carbenoxolone 100 mg three times daily by mouth for 4 weeks significantly improved verbal fluency compared with placebo, but did not influence visual or verbal memory, nonverbal reasoning, or processing speed. Twelve patients with stable type 2 diabetes were given carbenoxolone at the same dose for 6 weeks. Verbal memory was significantly improved compared with placebo, but verbal fluency and other scores were unaltered. All subjects were given amiloride 10 mg daily to prevent mineralocorticoid adverse effects (but see Interactions, above).[1]

1. Sandeep TC, *et al.* 11β-Hydroxysteroid dehydrogenase inhibition improves cognitive function in healthy elderly men and type 2 diabetics. *Proc Natl Acad Sci U S A* 2004; **101:** 6734–9.

Preparations
Proprietary Preparations (details are given in Part 3)

Austral.: Bioral; ***Austria:*** Rowadermat; ***Hong Kong:*** Herpesan; ***Hung.:*** Carbosan; ***Irl.:*** Carbosan; ***Malaysia:*** Herpesan; ***Philipp.:*** Rowagel; ***Singapore:*** Herpesan; ***Spain:*** Sanodin; ***UK:*** Bioplex†; Bioral†.

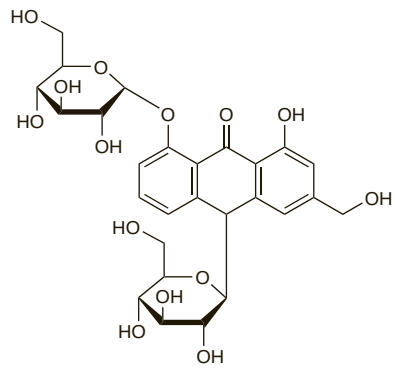
Multi-ingredient: ***Irl.:*** Pyrogastrone; ***UK:*** Pyrogastrone†.

Casanthranol *(USAN)*

Casantranol.

Казантранол

CAS — 8024-48-4.



(cascaroside A)

Pharmacopoeias. In *US*.

USP 31 (Casanthranol). It is obtained from cascara. It contains not less than 20% of total hydroxyanthracene derivatives calculated on the dried basis, of which not less than 80% consists of cascarosides, both calculated as cascaroside A ($C_{27}H_{32}O_{14}$ = 580.5).

It is a light tan to brown, amorphous, hygroscopic powder. Freely soluble in water with some residue; partially soluble in methyl alcohol and in hot isopropyl alcohol; practically insoluble in acetone. Store in airtight containers at a temperature not exceeding 30°. Protect from light.

Profile
Casanthranol is an anthraquinone stimulant laxative with general properties similar to those of senna (p.1769). It is given in usual oral doses of 30 to 60 mg daily with a faecal softener. In severe cases a dose of 90 mg daily, or 60 mg twice daily, may be given.

Preparations
Proprietary Preparations (details are given in Part 3)

Belg.: Cascalax†; ***Neth.:*** Cascalax.

Multi-ingredient: ***Arg.:*** Bil 13; En-Ga-Lax; ***Canad.:*** Peri-Colace†; ***Spain:*** Laxvital; ***USA:*** Black-Draught†; Docusoft Plus; Genasoft Plus Softgels†; Laxative & Stool Softener; Peri-Dos Softgels†; Silace-C†.

Cascara

Amerikinių šaltekšnių žievė; Cáscara sagrada; Cascararinde; Chittem Bark; Kaszkarabokor kéreg; Kůra řešetláku Purshova; Rhamni purshianae cortex; Rhamni Purshiani Cortex; Sacred Bark; Sagradabark; Sagradankuori.

Жостер Пурша; Крушина Пурша

CAS — 8047-27-6; 8015-89-2 (cascara sagrada extract).
ATC — A06AB07.
ATC Vet — QA06AB07.

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

Ph. Eur. 6.2 (Cascara). The dried, whole or fragmented bark of *Rhamnus purshianus* (=*Frangula purshiana*). It contains not less than 8.0% of hydroxyanthracene glycosides of which not less than 60% consists of cascarosides, both expressed as cascaroside A ($C_{27}H_{32}O_{14}$ = 580.5). and calculated with reference to the dried drug. Protect from light.

USP 31 (Cascara Sagrada). The dried bark of *Rhamnus purshianus* (Rhamnaceae). It contains not less than 7% of total hydroxyanthracene derivatives calculated on the dried basis, of which not less than 60% consists of cascarosides, both calculated as cascaroside A. It has a distinct odour.

Profile
Cascara is an anthraquinone stimulant laxative with general properties similar to those of senna (p.1769). It has been used in the treatment of constipation in oral doses equivalent to about 20 mg of total hydroxyanthracene derivatives daily.

Breast feeding. No adverse effects have been seen in breast-fed infants whose mothers were receiving cascara, and the American Academy of Pediatrics considers[1] that it is therefore usually compatible with breast feeding.

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)

Preparations
BP 2008: Cascara Dry Extract; Cascara Tablets;
USP 31: Aromatic Cascara Fluidextract; Cascara Sagrada Extract; Cascara Sagrada Fluidextract; Cascara Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Natulax; ***Braz.:*** Laxsotrin; ***Fr.:*** Peristaltine; ***Ger.:*** Legapas; ***Port.:*** Laxolen†.

Multi-ingredient: ***Arg.:*** Bilidren; Calculina†; Cascara Sagrada Bouzen†; Cascara Sagrada Oligoplex; Cascara Sagrada Puler†; Veracolate; Yuyo; ***Austral.:*** Colax; Peritone; ***Austria:*** Cascara-Salax; Dragees Neunzehn†; Silberne; ***Belg.:*** Grains de Vals; Vethoine; ***Braz.:*** Bilifel†; Boldopeptan†; Chofranina; Composto Emagrecedor†; Emagrevit†; Eparema; Jurubileno†; Pílulas De Witt's†; Prisoventnl†; Solvobil; Ventre Livre†; ***Canad.:*** Bicholate; Cholasyn II; Cholasyn†; Control; Doulax; Extra Strong Formula 12†; Herbal Laxative; Herbal Laxative plus Yogurt; Herbal Laxative†; Herbalax†; Herbolax; Herborex; Laxaco; Laxative†; Mucinum†; Thunas Laxative†; ***Chile:*** Bulgarolax; ***Fr.:*** Dragees Fuca; Dragees Vegetales Rex; Grains de Vals; Imegul†; Mucinum a l'Extrait de Cascara; ***Hong Kong:*** Mucinum Cascara†; ***Ital.:*** Amaro Medicinale; Coladren; Combilax; Confetti Lassativi CM; Critichol; Digelax†; Dis-Cinil Complex; Draverex; Eparema; Eparema-Levul; Eupatol; Fave di Fuca; Grani di Vals; Hepatos; Hepatos B12; Lassatina†; Magisbile†; Mepalax; Schias-Amaro Medicinale†; Solvobil; Stimolfit; Vadolax†; ***Norw.:*** Cosylan; ***Port.:*** Caroid†; Mucinum; ***S.Afr.:*** Moultons Herbal Extract; Veracolate†; ***Spain:*** Crislaxo; Lipograsil; Menabil Complex†; Nico Hepatocyn; Píldoras Zeninas; ***Swed.:*** Emulax; ***Switz.:*** Padma-Lax; Padmed Laxan; ***Thai.:*** Flatulence; Hemolax; Veracolate; ***UK:*** Dual-Lax Extra Strong; Dual-Lax Normal Strength; Jacksons Herbal Laxative; Laxative Tablets; Modern Herbals Laxative; Modern Herbals Pile; Natural Herb Tablets; Out-of-Sorts; Pileabs; Piletabs; Rhuaka; Senokot Dual Relief; Skin Eruptions Mixture; ***USA:*** Concentrated Milk of Magnesia-Cascara; ***Venez.:*** Gameral.

Cassia Pulp

Fístula, pulpa de caña.

Мякоть Амалтас

Profile
Cassia pulp is the evaporated aqueous extract of crushed ripe cassia fruits (cassia pods), *Cassia fistula* (Leguminosae). It is a mild anthraquinone stimulant laxative with general properties similar to those of senna (p.1769).

Preparations
Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Braz.:*** Fitolax; Florlax; Fontolax; Forlax; Frutalax†; Laxarine†; Laxtam; Naturetti; Sene Composta†; Tamaril; Tamarine; Tamarix†; ***Fr.:*** Benetransit; ***Ital.:*** Miracolon; Tamarine; ***Mex.:*** Naturetti†; ***S.Afr.:*** Entressdruppels HM; ***Spain:*** Pruina.

Cerium Oxalate

Cerii Oxalas; Cerio, oxalato de; Ceriumoksalaatti; Ceriumoxalat.

Церия Оксалат

CAS — 139-42-4 (anhydrous cerous oxalate); 15053-73-3 (cerous oxalate decahydrate).
ATC — A04AD02.
ATC Vet — QA04AD02.

NOTE. Cerium oxalate has been defined as consisting of about 50% of cerous oxalate ($(C_2O_4)_3Ce_2,10H_2O$) with the oxalates of numerous other rare earths, especially lanthanum, praseodymium, and neodymium. Oxalates of the form $(C_2O_4)_3Ce_2,xH_2O$ are also referred to as cerium or cerous oxalate.

Profile
Cerium oxalate has been used as an antiemetic.

Preparations
Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Spain:*** Novonausin†.

Certolizumab Pegol *(BAN, USAN, rINN)*

CDP-870; Certolizumab Pégol; Certolizumabum Pegolum; PHA-738144.

Цертолизумаб Пегол

CAS — 428863-50-7.
ATC — L04AB05.
ATC Vet — QL04AB05.

Adverse Effects and Precautions
As for Infliximab, p.69.

Interactions
As for Infliximab, p.71

Uses and Administration
Certolizumab pegol is a pegylated tumour necrosis factor antibody fragment. It is used in the treatment of patients with moderate to severe, active Crohn's disease (p.1697) who have had an inadequate response to conventional treatment. The initial dose is 400 mg given as two subcutaneous injections of 200 mg, repeated after 2 and 4 weeks. Patients who have a clinical response may then receive a maintenance dose of 400 mg every 4 weeks. Certolizumab pegol is also under investigation in the treatment of rheumatoid arthritis and psoriasis.

◊ References.

1. Schreiber S, *et al.* A randomized, placebo-controlled trial of certolizumab pegol (CDP870) for treatment of Crohn's disease. *Gastroenterology* 2005; **129:** 807–18. Correction. *ibid.*; 1808. [dose]
2. Sandborn WJ, *et al.* PRECISE 1 Study Investigators. Certolizumab pegol for the treatment of Crohn's disease. *N Engl J Med* 2007; **357:** 228–38.
3. Schreiber S, *et al.* PRECISE 2 Study Investigators. Maintenance therapy with certolizumab pegol for Crohn's disease. *N Engl J Med* 2007; **357:** 239–50. Correction. *ibid.*: 1357.

Preparations
Proprietary Preparations (details are given in Part 3)

Switz.: Cimzia; ***USA:*** Cimzia.

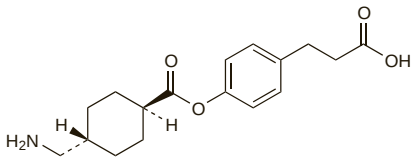
Cetraxate Hydrochloride *(USAN, rINNM)*

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.

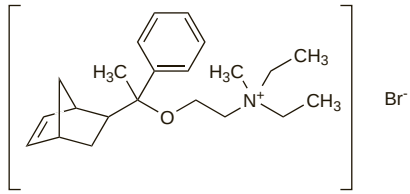
Ciclonium Bromide *(rINN)*

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.

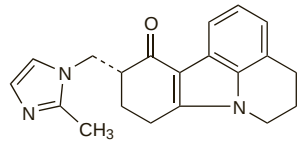
Cilansetron *(USAN, rINN)*

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.

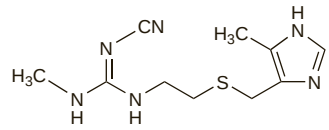
Cimetidine *(BAN, USAN, rINN)*

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.