3. Matsumoto S. Cimetidine and survival with colorectal cancer. *Lancet* 1995; **346:** 115.
4. Langman MJS, *et al.* Prospective, double-blind, placebo-controlled randomized trial of cimetidine in gastric cancer. *Br J Cancer* 1999; **81:** 1356–62.
5. Primrose JN, *et al.* A prospective randomised controlled study of the use of ranitidine in patients with gastric cancer. *Gut* 1998; **42:** 17–19.

Mastocytosis. Cimetidine, alone or with an antihistamine (histamine H_1-antagonist), has been reported to relieve gastrointestinal symptoms,[1,2] pruritus, and urticaria[3,4] in patients with mastocytosis (p.1138).

1. Hirschowitz BI, Groarke JF. Effect of cimetidine on gastric hypersecretion and diarrhea in systemic mastocytosis. *Ann Intern Med* 1979; **90:** 769–71.
2. Linde R, *et al.* Combination H1 and H2 receptor antagonist therapy in mastocytosis. *Ann Intern Med* 1980; **92:** 716.
3. Simon RA. Treatment of systemic mastocytosis. *N Engl J Med* 1980; **302:** 231.
4. Frieri M, *et al.* Comparison of the therapeutic efficacy of cromolyn sodium with that of combined chlorpheniramine and cimetidine in systemic mastocytosis: results of a double-blind clinical trial. *Am J Med* 1985; **78:** 9–14.

Paracetamol toxicity. It has been suggested that cimetidine might be of use in the treatment of paracetamol poisoning (see p.108) because of its inhibition of the cytochrome P450 system. However, there appears to be no evidence to support the claims of benefit made in some anecdotal reports.[1]

1. Kaufenberg AJ, Shepherd MF. Role of cimetidine in the treatment of acetaminophen poisoning. *Am J Health-Syst Pharm* 1998; **55:** 1516–19.

Porphyria. There are reports[1-3] of patients with acute intermittent porphyria (p.1448) showing clinical and biochemical improvement during treatment with cimetidine. Cimetidine is, however, considered to be unsafe in patients with porphyria (see under Precautions, above).

1. Baccino E, *et al.* Cimetidine in the treatment of acute intermittent porphyria. *JAMA* 1989; **262:** 3000.
2. Horie Y, *et al.* Clinical usefulness of cimetidine treatment for acute relapse in intermittent porphyria. *Clin Chim Acta* 1995; **234:** 171–5.
3. Cherem JH, *et al.* Cimetidine and acute intermittent porphyria. *Ann Intern Med* 2005; **143:** 694–5.

Skin disorders. Cimetidine has been used alone[1-8] or with an antihistamine (H_1-antagonist)[5,8,9] in various skin disorders. H_2-antagonists such as cimetidine and ranitidine have produced improvement in certain types of *urticaria* (p.1584), especially those associated with cold or angioedema. Their routine use in urticaria is controversial, but in practice their addition to conventional treatment can be tried in resistant cases.[10-12] Little additional benefit has been found with combination therapy in dermographic urticaria.[13] Although they may act by antagonism of H_2-receptors on cutaneous blood vessels, other mechanisms of action may be involved.[8] Patients with *pruritus* (p.1582) of various causes may also respond to H_2-antagonists,[1,2,6,7,9] but studies in larger groups of patients have demonstrated no benefit.[3-5,14]

1. Easton P, Galbraith PR. Cimetidine treatment of pruritus in polycythemia vera. *N Engl J Med* 1978; **299:** 1134.
2. Hess CE. Cimetidine for the treatment of pruritus. *N Engl J Med* 1979; **300:** 370.
3. Harrison AR, *et al.* Pruritus, cimetidine and polycythemia. *N Engl J Med* 1979; **300:** 433–4.
4. Scott GL, Horton RJ. Pruritus, cimetidine and polycythemia. *N Engl J Med* 1979; **300:** 434. Correction. *ibid.*; 936.
5. Zappacosta AR, Hauss D. Cimetidine doesn't help pruritus of uremia. *N Engl J Med* 1979; **300:** 1280.
6. Schapira DV, Bennett JM. Cimetidine for pruritus. *Lancet* 1979; **i:** 726–7.
7. Aymard JP, *et al.* Cimetidine for pruritus in Hodgkin's disease. *BMJ* 1980; **280:** 151–2.
8. Theoharides TC. Histamine (H)-receptor antagonists in the treatment of urticaria. *Drugs* 1989; **37:** 345–55.
9. Deutsch PH. Dermatographism treated with hydroxyzine and cimetidine and ranitidine. *Ann Intern Med* 1984; **101:** 569.
10. Advenier C, Queille-Roussel C. Rational use of antihistamines in allergic dermatological conditions. *Drugs* 1989; **38:** 634–44.
11. Ormerod AD. Urticaria: recognition, causes, and treatment. *Drugs* 1994; **48:** 717–30.
12. Greaves MW. Chronic urticaria. *N Engl J Med* 1995; **332:** 1767–72.
13. Sharpe GR, Shuster S. In dermographic urticaria H receptor antagonists have a small but therapeutically irrelevant additional effect compared with H antagonists alone. *Br J Dermatol* 1993; **129:** 575–9.
14. Raisch DW, *et al.* Evaluation of a non-food and drug administration-approved use of cimetidine: treatment of pruritus resulting from epidural morphine analgesia. *DICP Ann Pharmacother* 1991; **25:** 716–8.

Preparations

BP 2008: Cimetidine Injection; Cimetidine Oral Solution; Cimetidine Oral Suspension; Cimetidine Tablets;
USP 31: Cimetidine in Sodium Chloride Injection; Cimetidine Injection; Cimetidine Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Tagamet†; Ulcerfen; ***Austral.:*** Cimehexal; Magicul; Sigmetadine†; Tagamet; ***Austria:*** Acidex; Cimetag; Neutromed; Neutronorm; Sodexx Cimetidine; Ulcometin; Ulcostad; ***Belg.:*** Doccimeti; Nuardin; Tagamet; ***Braz.:*** Cigamete; Cimetetax†; Cimetidan; Cimetil†; Cimetilab; Cimetin†; Cimetina†; Cimetinax; Cimetival; Cintidina; Cinton†; Climatidine†; Duomet†; Etidine; Gastidin†; Laveran†; Novacimet†; Pristonal; Prometidine; Stomakon†; Tagaliv; Tagamet; Tranimet†; Ulcedine; Ulcenon; Ulcerac; Ulceracid†; Ulcimet; Ulcinax; Ulcitag†; Ulcitrat; ***Canad.:*** Gaviscon Prevent†; Novo-Cimetine; Nu-Cimet; Tagamet†; ***Cz.:*** CimLich†; Lock-2†; Primamet; ***Denm.:*** Aciloc; Acinil; Cimecodan; Hocimin†; Novamet; ***Fr.:*** Stomedine; Tagamet; ***Ger.:*** Azucimet†; Cime; Cimebeta; Cimehexal; Cimet†; CimLich; duraH2†; Gastroprotect; H 2 Blocker; Sigacimet†; Tagamet; ***Gr.:*** Alkastom†; Besidin†; Cimeton†; Gastrolene†; Tagamet; Tamper; ***Hong Kong:*** Cementin; Cimedine; Cimeta; Cimulcer†; Citidine; Gastab; Gastidine; Maritidine; Simaglen; Syncomet; Tagadine†; Tagamet; Ulcomet; ***Hung.:*** Histodil; ***India:*** Cimet†; ***Indon.:*** Cimexol; Corsamet; Licomet; Nulcer; Sanmetidin; Tagamet; Ulcedine; Ulcumet; Ulcusan; Ulsikur; Xepamet; ***Irl.:*** Cedine; Cimagen; Cimeldine; Dyspamet; Galenamet; Geramet; Pinamet; Tagamet; ***Israel:*** Cemidin; Cimetag; Cimi†; Tagamet; ***Ital.:*** Biomag; Brumetidina; Dina†; Etideme; Notul†; Stomet; Tagamet; Temic; Ulcedin; Ulcodina†; Ulcomedina†; Ulis; ***Malaysia:*** Cimulcer; Shintamet; Tagamet; Ulcidine†; Xepamet†; ***Mex.:*** Alcatex†; Antil†; Cimebec; Cimedul; Cimeffer; Cimetase; Colimet; Columina†; Gastrodina; Metidisol†; Procimeti; Sercim; Sinegastrin; Tagamet; Ulcedine†; Ulmarin; Ulserral; ***Neth.:*** Tagamet; ***Norw.:*** Cimal; Tagamet; ***NZ:*** Cytine; ***Philipp.:*** Antag; Ciclem; Cimecid; Cimulcer; Duogastril; Montidin; Tagamet; Ulcenon; ***Pol.:*** Altramet; Cimegast; ***Port.:*** Cim; Evicer†; Tagamet; Ulceridine†; ***Rus.:*** Histodil (Гистодил); ***S.Afr.:*** Aci-Med; Cimlok; Cinadine; Cymi; Hexamet; Lenamet; Secadine; Tagamet; Ulcim; ***Singapore:*** Cementin; Cimulcer; Citidine; Erlmetin†; Gastromet†; Himetin; Shintamet; Tagamet; Xepamet; ***Spain:*** Ali Veg; Fremet; Mansal†; Tagamet; ***Swed.:*** Acinil; Tagamet; ***Switz.:*** Malimed†; Tagamet†; ***Thai.:*** Aidar†; Alserine†; Cencamet; Cidine; Cigamet; Cimet-P†; Cimetine; Cimidine†; Cimulcer†; Citidine; Clinimet; CMD†; Duotric; Gastrodin†; Iwamet; Manomet; Med-Gastramet†; Milamet; Peptica; Pondarmett; Promet; Rinadine; Sertidine; Siamidine; Simaglen; Simex; Tagamet†; Ulcedine; Ulcemet; Ulcimet; Umamett; ***UAE:*** Cimetag; ***UK:*** Acitak†; Dyspamet; Galenamet; Peptimax†; Tagamet; Ultec†; Zita; ***USA:*** Tagamet; ***Venez.:*** Cavimet†; Cimetix†; Gadol; Iscaten†; Mempotal†.

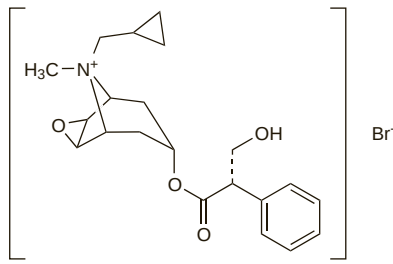
Multi-ingredient: ***Neth.:*** Aciflux.

Cimetropium Bromide *(rINN)*

Bromuro de cimetropio; Cimetropii Bromidum; Cimétropium, Bromure de; DA-3177; Hyoscine-*N*-(cyclopropylmethyl) Bromide. 8-(Cyclopropylmethyl)-6β,7β-epoxy-3α-hydroxy-1αH,5αH-tropanium bromide, (–)-(*S*)-tropate.

Циметропия Бромид

$C_{21}H_{28}BrNO_4$ = 438.4.
CAS — 51598-60-8.
ATC — A03BB05.
ATC Vet — QA03BB05.



Profile

Cimetropium bromide is a quaternary ammonium antimuscarinic with peripheral effects similar to those of atropine (p.1219). It has been used as an antispasmodic in the treatment of gastrointestinal disorders, in usual doses of 50 mg two or three times daily orally or by rectal suppository. It has also been given intramuscularly or intravenously in usual doses of 5 mg.

◊ References.

1. Dobrilla G, *et al.* Longterm treatment of irritable bowel syndrome with cimetropium bromide: a double blind placebo controlled clinical trial. *Gut* 1990; **31:** 355–8.
2. Marzio L, *et al.* Effect of cimetropium bromide on esophageal motility and transit in patients affected by primary achalasia. *Dig Dis Sci* 1994; **39:** 1389–94.
3. Savino F, *et al.* Cimetropium bromide in the treatment of crisis in infantile colic. *J Pediatr Gastroenterol Nutr* 2002; **34:** 417–9.

Preparations

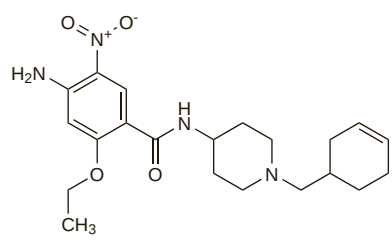
Proprietary Preparations (details are given in Part 3)
Ital.: Alginor.

Cinitapride *(rINN)*

Cinitaprida; Cinitapridum. 4-Amino-*N*-[1-(3-cyclohexen-1-ylmethyl)-4-piperidyl]-2-ethoxy-5-nitrobenzamide.

Цинитаприд

$C_{21}H_{30}N_4O_4$ = 402.5.
CAS — 66564-14-5.



Profile

Cinitapride is a substituted benzamide used for its prokinetic properties. It is given as the acid tartrate in oral doses of 1 mg three times daily before meals in the management of gastroparesis and gastro-oesophageal reflux disease (p.1696).

Preparations

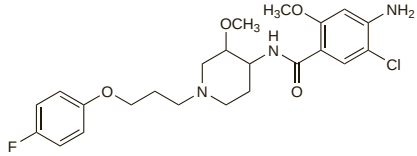
Proprietary Preparations (details are given in Part 3)
Arg.: Cinigest; Paxapride; Rogastril; ***Mex.:*** Pemix; ***Spain:*** Blaston; Cidine.

Cisapride *(BAN, USAN, rINN)*

Cisaprid; Cisaprida; Cisapridas; Cisapride monohydraté; Cisapridum; Cisapridum monohydricum; Ciszaprid; Cyzapryd jednowodny; R-51619; Sisapridi. *cis*-4-Amino-5-chloro-*N*-{1-[3-(4-fluorophenoxy)propyl]-3-methoxy-4-piperidyl}-2-methoxybenzamide monohydrate.

Цизаприд

$C_{23}H_{29}ClFN_3O_4.H_2O$ = 484.0.
CAS — 81098-60-4 (anhydrous cisapride).
ATC — A03FA02.
ATC Vet — QA03FA02.



Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Cisapride Monohydrate; Cisapride BP 2008). A white or almost white powder; it exhibits polymorphism. Practically insoluble in water; soluble in dichloromethane; freely soluble in dimethylformamide; sparingly soluble in methyl alcohol. Protect from light.

Cisapride Tartrate *(BANM, rINNM)*

Cisapride, tartrate de; Cisapridi tartras; Cisapridо tartratas; Cisaprid-tartarát; Cisapridtartrat; Ciszaprid-tartarát; Sisapridi-tartraatti; Tartrato de cisaprida.

Цизаприда Тартрат

$C_{27}H_{35}ClFN_3O_{10}$ = 616.0.

Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Cisapride Tartrate). A white or almost white powder. It exhibits polymorphism. Slightly soluble in water and in methyl alcohol; very slightly soluble in alcohol; freely soluble in dimethylformamide. Protect from light.

Adverse Effects

The most commonly reported adverse effects with cisapride are gastrointestinal disturbances including abdominal cramps, borborygmi, and diarrhoea. Headache and lightheadedness may also occur. Hypersensitivity (including rash, pruritus, and bronchospasm), convulsions, extrapyramidal effects, and increased urinary frequency, have occasionally been reported. Cases of arrhythmia, including ventricular tachycardia, ventricular fibrillation, torsade de pointes, and QT interval prolongation have occurred rarely; fatalities have resulted, and have led to severe restrictions on its use (see Effects on the Heart, below). There have been a few cases of disturbances in liver function among patients receiving cisapride.

Incidence of adverse effects. A comparison of data from prescription-event monitoring in over 13 000 recipients of cisapride and from a further 9726 recipients involved in a controlled study showed that diarrhoea, in about 2 to 4% of patients, was the commonest adverse effect reported.[1] Other relatively common adverse effects were headache, abdominal pain, nausea and vomiting, and constipation, all in around 1 to 1.5% of patients. There were 46 reports in the prescription-event monitoring data of increased urinary frequency (plus a further 20 among the controlled study patients), and 5 reports of arrhythmias.

1. Wager E, *et al.* A comparison of two cohort studies evaluating the safety of cisapride: prescription-event monitoring and a large phase IV study. *Eur J Clin Pharmacol* 1997; **52:** 87–94.

Effects on the heart. Seven reports[1] of cardiac effects associated with cisapride were submitted to the WHO Programme for International Drug Monitoring between 1989 and 1991. They included palpitations in 4, tachycardia and hypertension in 1, and extrasystole in 2. Subsequent reports implicated cisapride in the development of prolonged QT interval and torsade de pointes or ventricular fibrillation or both.[2,3] By December 1999 the FDA had received 341 reports of heart rhythm abnormalities associated with cisapride use, including 80 reports of deaths. Most patients were either receiving other drugs known to impair cisapride metabolism (see Interactions, below) or had other factors predisposing to arrhythmias. In the light of earlier reports of cardiac effects and of evidence for a direct effect of cisapride on the heart at therapeutic concentrations, in 1998 the UK CSM **contra-indicated**[2] the use of cisapride in patients receiving drugs that could inhibit cisapride metabolism or that prolong the QT