patients with spinal cord injuries,[1] and it is sometimes used in palliative care to control night sweats. The *BNF* notes that propantheline may be used for gustatory sweating in patients with diabetic neuropathy.

1. Canaday BR, Stanford RH. Propantheline bromide in the management of hyperhidrosis associated with spinal cord injury. *Ann Pharmacother* 1995; **29:** 489–92.

Urinary incontinence. In the UK, guidelines issued by NICE suggest that propantheline should not be recommended for the treatment of urinary incontinence (p.2180) or overactive bladder in women; other antimuscarinics are preferred.[1]

1. National Institute for Health and Clinical Excellence. Urinary incontinence: the management of urinary incontinence in women (issued October 2006). Available at: http://www.nice.org.uk/nicemedia/pdf/CG40fullguideline.pdf (accessed 03/07/08)

Preparations

BP 2008: Propantheline Tablets;
USP 31: Propantheline Bromide Tablets.

Proprietary Preparations (details are given in Part 3)
Austral.: Pro-Banthine; ***Canad.:*** Propanthel†; ***Denm.:*** Erconil; ***India:*** Pro-Banthine; ***Indon.:*** Pro-Banthine; ***Mex.:*** Propantel†; ***NZ:*** Pro-Banthine; ***S.Afr.:*** Pro-Banthine; ***UK:*** Pro-Banthine; ***USA:*** Pro-Banthine.

Multi-ingredient: ***Indon.:*** Methaphyllin; ***Ital.:*** Lexil.

Prune

Ameixa; Ciruela; Prunus.

Слива Домашняя (*Prunus domestica*)

Profile

Prune is the dried ripe fruits of the plum *Prunus domestica* and some other species of *Prunus* (Rosaceae). It has laxative and demulcent properties.

◊ References.

1. Stacewicz-Sapuntzakis M, *et al.* Chemical composition and potential health effects of prunes: a functional food? *Crit Rev Food Sci Nutr* 2001; **41:** 251–86.

Preparations

Proprietary Preparations (details are given in Part 3)
Mex.: Viviolax†.

Multi-ingredient: ***Arg.:*** Cirulaxia; Mermelax; ***Austral.:*** Neo-Cleanse; Prolax†; ***Canad.:*** Fruitatives†; ***Chile:*** Tamarine; ***Fr.:*** Carres Parapsyllium; Laxarine; ***Mex.:*** Ciruelax Jalea; Laxacaps.

Rabeprazole Sodium *(BANM, USAN, rINNM)*

E-3810; LY-307640; Natrii Rabeprazolum; Rabeprazol sódico; Rabeprazol Sodyum; Rabéprazole sodique; Rabeprazolum natricum; Sodium Pariprazole. 2-({[4-(3-Methoxypropoxy)-3-methyl-2-pyridyl]methyl}sulfinyl)-1*H*-benzimidazole sodium.

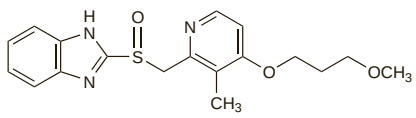
Натрий Рабепразол

$C_{18}H_{20}N_3NaO_3S$ = 381.4.

CAS — 117976-89-3 (rabeprazole); 117976-90-6 (rabeprazole sodium).

ATC — A02BC04.

ATC Vet — QA02BC04.



(rabeprazole)

Adverse Effects and Precautions

As for Omeprazole, p.1753.

Effects on the endocrine system. For cases of gynaecomastia associated with rabeprazole see p.1753.

Effects on the kidneys. For reports of interstitial nephritis associated with rabeprazole see p.1753.

Effects on the nervous system. For a report of neuropsychiatric symptoms associated with rabeprazole, see under Omeprazole, p.1754.

Interactions

As for Omeprazole (p.1755) but clinically significant interactions with diazepam, phenytoin, theophylline, or warfarin have not been found in healthy subjects.

Pharmacokinetics

Rabeprazole is rapidly absorbed and peak plasma concentrations are reached about 3.5 hours after an oral dose. The oral bioavailability is about 52% with the enteric-coated tablet formulation, because of first-pass metabolism, and does not appear to vary after single or repeated doses. Rabeprazole is about 97% bound to plasma proteins. It is extensively metabolised in the liver by cytochrome P450 isoenzymes CYP2C19 and CYP3A4 to the thioether, thioether carboxylic acid, sulfone, and desmethylthioether. Metabolites are excreted principally in the urine (about 90%) with the remainder in the faeces. The plasma half-life is about 1 hour, increased two to threefold in hepatic impairment, 1.6 times in CYP2C19 slow metabolisers (see also Metabolism under Omeprazole, p.1755), and by 30% in the elderly.

◊ References.

1. Yasuda S, *et al.* Comparison of the kinetic disposition and metabolism of E3810, a new proton pump inhibitor, and omeprazole in relation to S-mephenytoin 4-hydroxylation status. *Clin Pharmacol Ther* 1995; **58:** 143–54.
2. Keane WF, *et al.* Rabeprazole: pharmacokinetics and tolerability in patients with stable, end-stage renal failure. *J Clin Pharmacol* 1999; **39:** 927–33.

Uses and Administration

Rabeprazole is a proton pump inhibitor with actions and uses similar to those of omeprazole (p.1755). It is given orally as rabeprazole sodium in the form of enteric-coated tablets. It is normally taken in the morning.

In the treatment of severe (erosive or ulcerative) **gastro-oesophageal reflux disease** (p.1696), the usual dose of rabeprazole sodium is 20 mg once daily for 4 to 8 weeks; in the USA, a further 8-week course is permitted for healing of erosive oesophagitis. Thereafter, maintenance therapy can be continued with 10 or 20 mg daily depending on the response. For symptomatic disease without erosive or ulcerative oesophagitis a dose of 10 or 20 mg may be given once daily for 4 weeks; in the USA, a further 4-week course is permitted. Once symptoms have resolved, a dose of 10 mg once daily may be given as necessary.

For the treatment of active **peptic ulcer disease** (p.1702), 20 mg daily is given for 4 to 8 weeks for duodenal ulcer and 6 to 12 weeks for gastric ulcer. For the eradication of *Helicobacter pylori* rabeprazole sodium may be combined with two antibacterials in a 1-week **triple therapy** regimen. Effective regimens include 20 mg twice daily combined with clarithromycin 500 mg twice daily and amoxicillin 1 g twice daily, or combined with clarithromycin 250 mg twice daily and metronidazole 400 mg twice daily.

For **Zollinger-Ellison syndrome** (p.1704), the starting dose is 60 mg once daily, adjusted according to response. Doses up to 120 mg daily have been given; when the daily dose is more than 100 mg it should be given in 2 divided doses.

◊ Reviews.

1. Prakash A, Faulds D. Rabeprazole. *Drugs* 1998; **55:** 261–7.
2. Anonymous. Rabeprazole. *Med Lett Drug Ther* 1999; **41:** 110–12.
3. Carswell CI, Goa KL. Rabeprazole: an update of its use in acid-related disorders. *Drugs* 2001; **61:** 2327–2356.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Pariet; Rabec; ***Austral.:*** Pariet; ***Austria:*** Pariet; ***Belg.:*** Pariet; ***Braz.:*** Pariet; ***Canad.:*** Pariet; ***Chile:*** Gastrodine; ***Denm.:*** Pariet; ***Fin.:*** Pariet; ***Fr.:*** Pariet; ***Ger.:*** Pariet; ***Gr.:*** Pariet; ***Hong Kong:*** Pariet; ***Hung.:*** Pariet; ***India:*** Odirab; Rabeloc; Rabicip; ***Indon.:*** Pariet; ***Irl.:*** Pariet; ***Ital.:*** Pariet; ***Jpn:*** Pariet; ***Malaysia:*** Pariet; ***Mex.:*** Pariet; ***Neth.:*** Pariet; ***Philipp.:*** Pariet; ***Pol.:*** Pariet; ***Port.:*** Pariet; ***Rus.:*** Pariet (Париет); ***S.Afr.:*** Pariet; ***Singapore:*** Pariet; ***Spain:*** Aciphex; Pariet; ***Swed.:*** Pariet; ***Switz.:*** Pariet; ***Thai.:*** Pariet; ***Turk.:*** Pariet; ***UK:*** Pariet; ***USA:*** Aciphex; ***Venez.:*** Pariet.

Racecadotril *(rINN)*

Acetorphan; Racécadotril; Racecadotrilo; Racecadotrilum. (±)-*N*-{2-[(Acetylthio)methyl]-1-oxo-3-phenylpropyl}glycine phenylmethyl ester; *N*-[(*R,S*)-3-acetylthio-2-benzylpropanoyl]glycine benzyl ester; (±)-*N*-[α-(Mercaptomethyl)hydrocinnamoyl]glycine benzyl ester acetate.

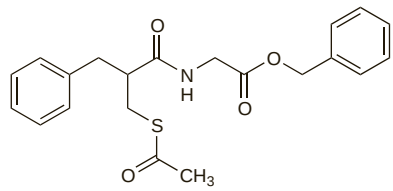
Рацекадотрил

$C_{21}H_{23}NO_4S$ = 385.5.

CAS — 81110-73-8.

ATC — A07XA04.

ATC Vet — QA07XA04.



Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Racecadotril). A white or almost white powder. Practically insoluble in water; freely soluble in methyl alcohol and in dichloromethane.

Profile

Racecadotril is an enkephalinase inhibitor that inhibits the breakdown of endogenous opioids, thus reducing intestinal secretions. It is given orally in doses of 100 mg three times daily before meals for up to 7 days for the symptomatic management of acute diarrhoea (p.1694).

The *S*-form of racecadotril (sinorphan, ecadotril—see Natriuretic Peptides, p.1347) has been investigated for hypertension and heart failure.

◊ References.

1. Baumer P, *et al.* Effects of acetorphan, an enkephalinase inhibitor, on experimental and acute diarrhoea. *Gut* 1992; **33:** 753–8.
2. Roge J, *et al.* The enkephalinase inhibitor, acetorphan, in acute diarrhoea: a double-blind, controlled clinical trial versus Loperamide. *Scand J Gastroenterol* 1993; **28:** 352–4.
3. Beaugerie L, *et al.* Treatment of refractory diarrhoea in AIDS with acetorphan and octreotide: a randomized crossover study. *Eur J Gastroenterol Hepatol* 1996; **8:** 485–9.
4. Salazar-Lindo E, *et al.* Racecadotril in the treatment of acute watery diarrhea in children. *N Engl J Med* 2000; **343:** 463–7.
5. Matheson AJ, Noble S. Racecadotril. *Drugs* 2000; **59:** 829–35.
6. Alam NH, *et al.* Efficacy and tolerability of racecadotril in the treatment of cholera in adults: a double blind, randomised, controlled clinical trial. *Gut* 2003; **52:** 1419–23.
7. Wang H-H, *et al.* A blind, randomized comparison of racecadotril and loperamide for stopping acute diarrhea in adults. *World J Gastroenterol* 2005; **11:** 1540–3.
8. Szajewska H, *et al.* Systematic review: racecadotril in the treatment of acute diarrhoea in children. *Aliment Pharmacol Ther* 2007; **26:** 807–13.

Preparations

Proprietary Preparations (details are given in Part 3)
Braz.: Tiorfan; ***Fr.:*** Tiorfan; ***Ger.:*** Tiorfan; ***Gr.:*** Hidrasec; ***Indon.:*** Hidrasec; ***Mex.:*** Hidrasec; ***Port.:*** Tiorfan; ***Spain:*** Tiorfan; ***Thai.:*** Hidrasec†; ***Venez.:*** Hidrasec.

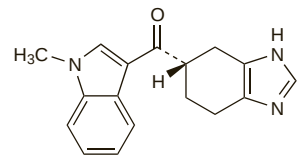
Ramosetron Hydrochloride *(rINNM)*

Hidrocloruro de ramosetrón; Ramosétron, Chlorhydrate de; Ramosetroni Hydrochloridum; YM-060. (–)-(*R*)-1-Methylindol-3-yl 4,5,6,7-tetrahydro-5-benzimidazolyl ketone hydrochloride.

Рамосетрона Гидрохлорид

$C_{17}H_{17}N_3O,HCl$ = 315.8.

CAS — 132036-88-5 (ramosetron); 132907-72-3 (ramosetron hydrochloride).



(ramosetron)

Profile

Ramosetron is a 5-HT_3 antagonist with general properties similar to those of ondansetron (p.1756). Ramosetron hydrochloride is given for its antiemetic properties in the management of nausea and vomiting induced by cancer chemotherapy in usual doses of 300 micrograms once daily intravenously, or 100 micrograms once daily by mouth. Ramosetron is also under investigation in the management of diarrhoea-predominant irritable bowel syndrome.

Preparations

Proprietary Preparations (details are given in Part 3)
Indon.: Nasea; ***Jpn:*** Nasea; ***Philipp.:*** Nasea; ***Thai.:*** Nasea.

Ranitidine *(BAN, USAN, rINN)*

AH-19065; Ranitidiini; Ranitidin; Ranitidina; Ranitidinum. *NN*-Dimethyl-5-[2-(1-methylamino-2-nitrovinylamino)ethylthiomethyl]furfurylamine.

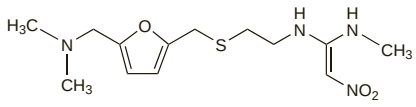
Ранитидин

$C_{13}H_{22}N_4O_3S$ = 314.4.

CAS — 66357-35-5.

ATC — A02BA02.

ATC Vet — QA02BA02.



Ranitidine Hydrochloride *(BANM, rINNM)*

AH-19065; Hidrocloruro de ranitidina; Ranitidiinihydrokloridi; Ranitidin Hidroklorür; Ranitidine, chlorhydrate de; Ranitidin-hidroklorid; Ranitidin-hydrochlorid; Ranitidinhydroklorid; Ranitidini hydrochloridum; Ranitidino hidrochloridas; Ranitydyny chlorowodorek.

Ранитидина Гидрохлорид

$C_{13}H_{22}N_4O_3S,HCl$ = 350.9.

CAS — 66357-59-3.

ATC — A02BA02.

ATC Vet — QA02BA02.

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

Ph. Eur. 6.2 (Ranitidine Hydrochloride). A white or pale yellow, crystalline powder. It exhibits polymorphism. Freely soluble in water; sparingly soluble or slightly soluble in dehydrated alcohol; very slightly soluble in dichloromethane. A 1% solution in water has a pH of 4.5 to 6.0. Store in airtight containers. Protect from light.

USP 31 (Ranitidine Hydrochloride). A white to pale yellow, practically odourless, crystalline powder. It is sensitive to light and to moisture. Very soluble in water; sparingly soluble in alcohol. A 1% solution in water has a pH of 4.5 to 6.0. Store in airtight containers. Protect from light.

Stability and incompatibility. References.

1. Chilvers MR, Lysne JM. Visual compatibility of ranitidine hydrochloride with commonly used critical-care medications. *Am J Hosp Pharm* 1989; **46:** 2057–8.
2. Wohlford JG, *et al.* More information on the visual compatibility of hetastarch with injectable critical-care drugs. *Am J Hosp Pharm* 1990; **47:** 297–8.
3. Williams MF, *et al.* In vitro evaluation of the stability of ranitidine hydrochloride in total parenteral nutrition mixtures. *Am J Hosp Pharm* 1990; **47:** 1574–9.
4. Galante LJ, *et al.* Stability of ranitidine hydrochloride at dilute concentration in intravenous infusion fluids at room temperature. *Am J Hosp Pharm* 1990; **47:** 1580–4.
5. Galante LJ, *et al.* Stability of ranitidine hydrochloride with eight medications in intravenous admixtures. *Am J Hosp Pharm* 1990; **47:** 1606–10.
6. Stewart JT, *et al.* Stability of ranitidine in intravenous admixtures stored frozen, refrigerated, and at room temperature. *Am J Hosp Pharm* 1990; **47:** 2043–6.
7. Montoro JB, Pou L. Comment on stability of ranitidine hydrochloride in total nutrient admixtures. *Am J Hosp Pharm* 1991; **48:** 2384.
8. Stewart JT, *et al.* Stability of ranitidine hydrochloride and seven medications. *Am J Hosp Pharm* 1994; **51:** 1802–7.
9. Crowther RS, *et al.* In vitro stability of ranitidine hydrochloride in enteral nutrient formulas. *Ann Pharmacother* 1995; **29:** 859–62.

Adverse Effects

As for Cimetidine, p.1716. Unlike cimetidine, ranitidine has little or no anti-androgenic effect, despite isolated reports of gynaecomastia and impotence.

◊ General references.

1. Wormsley KG. Safety profile of ranitidine: a review. *Drugs* 1993; **46:** 976–85.

Carcinogenicity. For a discussion of the possible association between histamine H_2-antagonists and cancer, including mention of a study with ranitidine, see Cimetidine, p.1717.

Effects on the blood. For a discussion of the adverse haematological effects of H_2-antagonists, see Cimetidine, p.1717.

Effects on the cardiovascular system. Similarly to cimetidine (p.1717), bradycardia,[1,2] AV block,[2] and cardiac arrest[3] have been reported rarely during ranitidine therapy. A positive inotropic effect, without significant changes in heart rate or blood pressure, has also been reported in healthy subjects[4] and pretreatment with ranitidine has blocked the cardiac depressant effects seen in some subjects given famotidine or nizatidine.[5] Although studies in critically ill patients[6] and healthy subjects[7,8] have found no adverse haemodynamic effects associated with ranitidine, it is likely that a small proportion of patients are more susceptible to the cardiovascular effects of ranitidine. Caution is recommended when ranitidine is given intravenously, particularly in patients with cardiovascular disease.

1. Johnson WS, Miller DR. Ranitidine and bradycardia. *Ann Intern Med* 1988; **108:** 493.
2. Tanner LA, Arrowsmith JB. Bradycardia and H antagonists. *Ann Intern Med* 1988; **109:** 434–5.
3. Hart AM. Cardiac arrest associated with ranitidine. *BMJ* 1989; **299:** 519.
4. Meyer EC, *et al.* Inotropic effects of ranitidine. *Eur J Clin Pharmacol* 1990; **39:** 301–3.
5. Mescheder A, *et al.* Changes in the effects of nizatidine and famotidine on cardiac performance after pretreatment with ranitidine. *Eur J Clin Pharmacol* 1993; **45:** 151–6.
6. Vohra SB, *et al.* The haemodynamic effects of ranitidine injected centrally in optimally resuscitated patients. *Br J Hosp Med* 1989; **42:** 149.
7. Hughes DG, *et al.* Cardiovascular effects of H -receptor antagonists. *J Clin Pharmacol* 1989; **29:** 472–7.
8. Hilleman DE, *et al.* Impact of chronic oral H -antagonist therapy on left ventricular systolic function and exercise capacity. *J Clin Pharmacol* 1992; **32:** 1033–7.

Effects on the endocrine system. Unlike cimetidine (p.1717), ranitidine does not bind to androgen receptors and has little, if any, anti-androgenic effect. Studies in men taking ranitidine for the management of duodenal ulcer[1,2] reported no significant changes in the plasma concentrations of testosterone, luteinising hormone, follicle-stimulating hormone, or prolactin after up to 2 years of treatment; no significant changes in sperm concentration, motility, or morphology were noted.[1] There have been isolated reports of gynaecomastia,[3] loss of libido,[4] and impotence[5] associated with ranitidine, but in 9 patients with cimetidine-induced breast changes and impotence, transfer to ranitidine resulted in resolution of these symptoms.[6]

1. Wang C, *et al.* Ranitidine does not affect gonadal function in man. *Br J Clin Pharmacol* 1983; **16:** 430–2.
2. Knigge U, *et al.* Plasma concentrations of pituitary and peripheral hormones during ranitidine treatment for two years in men with duodenal ulcer. *Eur J Clin Pharmacol* 1989; **37:** 305–7.
3. Tosi S, Cagnoli M. Painful gynaecomastia with ranitidine. *Lancet* 1982; **i:** 160.
4. Smith RN, Elsdon-Dew RW. Alleged impotence with ranitidine. *Lancet* 1983; **ii:** 798.
5. Kassianos GC. Impotence and nizatidine. *Lancet* 1989; **i:** 963.
6. Jensen RT, *et al.* Cimetidine-induced impotence and breast changes in patients with gastric hypersecretory states. *N Engl J Med* 1983; **308:** 883–7.

Effects on the eyes. For a report of an increase in intra-ocular pressure associated with ranitidine, see under Cimetidine, p.1717. A cohort study involving 140 128 patients receiving anti-ulcer therapy, 70 389 of whom received ranitidine, found no evidence that any of the drugs studied were associated with a major increased risk of vascular or inflammatory disorders of the eye.[1]

For reference to loss of colour vision in a child receiving ranitidine see under Effects on the Nervous System, below.

1. García Rodríguez LA, *et al.* A cohort study of the ocular safety of anti-ulcer drugs. *Br J Clin Pharmacol* 1996; **42:** 213–16.

Effects on the kidneys. For reference to interstitial nephritis associated with H_2-antagonists including ranitidine, see under Cimetidine, p.1717.

Effects on the liver. There have been some case reports of ranitidine hepatotoxicity.[1-3] The increase in relative risk seen in a large cohort study involving 108 891 patients receiving antisecretory therapy was less for ranitidine (1.7:1) than for cimetidine (see p.1717).

1. Souza Lima MA. Ranitidine and hepatic injury. *Ann Intern Med* 1986; **105:** 140.
2. Ramrakhiani S, *et al.* Possible cholestatic injury from ranitidine with a review of the literature. *Am J Gastroenterol* 1998; **93:** 822–6.
3. Liberopoulos EN, *et al.* Possible ranitidine-induced cholestatic jaundice. *Ann Pharmacother* 2002; **36:** 172.

Effects on the nervous system. Ranitidine has been associated with adverse neurological effects including confusion,[1-8] loss of colour vision,[4] aggressiveness,[2,4,6] lethargy,[8] somnolence,[8] disorientation,[8] depression,[8] hallucinations,[1,7-9] and severe headache.[10] As with cimetidine (p.1717) these reactions occur mainly in the elderly, the severely ill, or patients with renal or hepatic impairment. Single-dose studies in young healthy subjects have found no adverse changes in performance, CNS function, or subjective assessment of mood after oral doses of ranitidine 150 or 300 mg.[11]

1. Hughes JD, *et al.* Mental confusion associated with ranitidine. *Med J Aust* 1983; **2:** 12–13.
2. Silverstone PH. Ranitidine and confusion. *Lancet* 1984; **i:** 1071.
3. Epstein CM. Ranitidine and confusion. *Lancet* 1984; **i:** 1071.
4. De Giacomo C, *et al.* Ranitidine and loss of colour vision in a child. *Lancet* 1984; **ii:** 47.
5. Mani RB, *et al.* H -receptor blockers and mental confusion. *Lancet* 1984; **ii:** 98.
6. Mandal SK. Psychiatric side effects of ranitidine. *Br J Clin Pract* 1986; **40:** 260.
7. MacDermott AJ, *et al.* Acute confusional episodes during treatment with ranitidine. *BMJ* 1987; **294:** 1616.
8. Slugg PH, *et al.* Ranitidine pharmacokinetics and adverse central nervous system reactions. *Arch Intern Med* 1992; **152:** 2325–9.
9. Price W, *et al.* Ranitidine-associated hallucinations. *Eur J Clin Pharmacol* 1985; **29:** 375–6.
10. Epstein CM. Ranitidine. *N Engl J Med* 1984; **310:** 1602.
11. Nicholson AN, Stone BM. The H -antagonists, cimetidine and ranitidine: studies on performance. *Eur J Clin Pharmacol* 1984; **26:** 579–82.

Effects on the skin. A report of vasculitic rash occurring in 3 patients undergoing ranitidine therapy.[1] In each case the rash cleared after withdrawal of the drug.

See also under Hypersensitivity, below, and also Cimetidine, p.1717.

1. Haboubi N, Asquith P. Rash mediated by immune complexes associated with ranitidine treatment. *BMJ* 1988; **296:** 897.

Fever. A report[1] of pyrexia associated with ranitidine. Apart from raised temperature the patient was otherwise well; fever resolved on stopping ranitidine and recurred on rechallenge.

1. Kavanagh GM, *et al.* Ranitidine fever. *Lancet* 1993; **341:** 1422.

Hypersensitivity. Respiratory stridor and an urticarial rash occurred in a patient shortly after taking the first dose of ranitidine;[1] the symptoms responded to adrenaline subcutaneously.

1. Brayko CM. Ranitidine. *N Engl J Med* 1984; **310:** 1601–2.

Meningitis. A 30-year-old man developed aseptic meningitis on 3 occasions after use of ranitidine.[1] In each case symptoms resolved rapidly on withdrawal of the drug.

1. Durand JM, *et al.* Ranitidine and aseptic meningitis. *BMJ* 1996; **312:** 886. Correction. *ibid.*; 1392.

Precautions

As for Cimetidine, p.1718.

Helicobacter pylori testing. For reference to the effect of ranitidine on the urea breath test for *Helicobacter pylori*, see p.1718.

Hepatic impairment. Sixteen of 27 patients with cirrhosis of the liver and indications for treatment with an H_2-antagonist (peptic ulcer, gastritis, or reflux oesophagitis) failed to respond to ranitidine 300 mg compared with 6 failures from 32 patients without cirrhosis. Famotidine 40 mg was given to 10 of the cirrhotic nonresponders and 8 still had no response; 7 of these patients were given cimetidine 800 mg and only 1 responded. In the control group, all 3 patients given famotidine did not respond and only 1 responded when given cimetidine. It was concluded that the incidence of non-response to H_2-antagonists is increased in patients with liver cirrhosis but no explanation could be given for this effect.[1] Interestingly there is an earlier report of patients with cirrhosis demonstrating increased bioavailability and decreased clearance of ranitidine.[2]

1. Walker S, *et al.* Frequent non-response to histamine H -receptor antagonists in cirrhotics. *Gut* 1989; **30:** 1105–9.
2. Young CJ, *et al.* Effects of cirrhosis and ageing on the elimination and bioavailability of ranitidine. *Gut* 1982; **23:** 819–23.

Porphyria. Ranitidine is considered to be unsafe in patients with porphyria although there is conflicting experimental evidence of porphyrinogenicity.

Renal impairment. For evidence of reduced clearance of ranitidine in patients with renal impairment see Administration in Renal Impairment, below.

Interactions

Unlike cimetidine (p.1718), ranitidine does not seem to affect cytochrome P450 to any great extent, and therefore is considered to have little effect on the metabolism of other drugs. However, as with other H_2-antagonists, its effects on gastric pH may alter the absorption of some other drugs.

◊ A review comparing the drug interactions of ranitidine with those of cimetidine.[1]

1. Smith SR, Kendall MJ. Ranitidine versus cimetidine: a comparison of their potential to cause clinically important drug interactions. *Clin Pharmacokinet* 1988; **15:** 44–56.

Cisapride. Peak plasma concentrations of ranitidine were achieved more rapidly in 12 healthy subjects who also took cisapride.[1] The clinical significance is questionable and such combinations have been used clinically, although the use of cisapride is now restricted in most countries.

1. Rowbotham DJ, *et al.* Effect of single doses of cisapride and ranitidine administered simultaneously on plasma concentrations of cisapride and ranitidine. *Br J Anaesth* 1991; **67:** 302–305.

Pharmacokinetics

Ranitidine is readily absorbed from the gastrointestinal tract with peak concentrations in plasma occurring about 2 to 3 hours after oral doses. Food does not significantly impair absorption. The bioavailability of ranitidine after oral doses is about 50%. Ranitidine is rapidly absorbed on intramuscular injection, with peak plasma concentrations occurring in about 15 minutes. It is weakly bound, about 15%, to plasma proteins.

The elimination half-life is about 2 to 3 hours and is increased in renal impairment. A small proportion of ranitidine is metabolised in the liver to the *N*-oxide, the *S*-oxide, and desmethylranitidine; the *N*-oxide is the major metabolite but accounts for only about 4 to 6% of a dose. About 30% of an oral dose and 70% of an intravenous dose is excreted unchanged in the urine in