

- Morgner A, *et al.* Esomeprazole: prevention and treatment of NSAID-induced symptoms and ulcers. *Expert Opin Pharmacother* 2007; **8**: 975–88.
- Blandizzi C, *et al.* Clinical efficacy of esomeprazole in the prevention and healing of gastrointestinal toxicity associated with NSAIDs in elderly patients. *Drugs Aging* 2008; **25**: 197–208.

Administration. *In-vitro* studies found that almost the entire contents of an esomeprazole capsule is deliverable through small calibre and standard sizes of nasogastric and gastrostomy tubes.^{1,2}

- White CM, *et al.* Delivery of esomeprazole magnesium enteric-coated pellets through small calibre and standard nasogastric tubes and gastrostomy tubes in vitro. *Am J Health-Syst Pharm* 2002; **59**: 2085–8.
- Shah SA, *et al.* Delivery of esomeprazole magnesium through nasogastric and gastrostomy tubes using an oral liquid vehicle as a suspending agent in vitro. *Am J Health-Syst Pharm* 2006; **63**: 1882–7.

Administration in children. UK licensed product information allows for the use of adult doses of esomeprazole (see Uses and Administration, above) in children over 12 years.

In the USA licensed doses, which may be given once daily for up to 8 weeks for the treatment of gastro-oesophageal reflux in children, are:

- 1 to 11 years: 10 mg
- 12 to 17 years: 20 or 40 mg

For healing erosive oesophagitis in children, the following doses based on body-weight are licensed in the USA to be given once daily for up to 8 weeks:

- less than 20 kg: 10 mg
- 20 kg or over: 10 or 20 mg

Administration in hepatic impairment. No dosage adjustment of esomeprazole is considered necessary for patients with mild to moderate hepatic impairment (Child-Pugh Classes A and B, respectively). For patients with severe hepatic impairment (Child-Pugh Class C), a daily dose of 20 mg should not be exceeded.

Administration in renal impairment. Although no dosage adjustment is considered necessary in patients with renal impairment, UK licensed product information advises caution in those with severe renal impairment, as experience in these patients is limited.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Esomac; **Nexium; Austral.:** Nexium; **Austria:** Nexium; **Belg.:** Nexiam; **Braz.:** Nexium; **Canad.:** Nexium; **Chile:** Nexium; **Ulcratex; Cz.:** Nexium; **Denm.:** Nexium; **Fin.:** Nexium; **Fr.:** Nexium; **Ger.:** Nexium; **Gr.:** Nexium; **Hong Kong:** Nexium; **Hung.:** Nexium; **India:** Esomac; **Esoz; Sompraz; Indon.:** Nexium; **Israel:** Nexium; **Ital.:** Axagon; **Esopral; Lucen.:** Nexium; **Malaysia:** Nexium; **Mex.:** Nexium; **Neth.:** Esopral; **Nexium; Norw.:** Nexium; **Philipp.:** Nexium; **Pol.:** Nexium; **Port.:** Nexium; **Rus.:** Nexium (Нексиум); **S.Afr.:** Nexium; **Singapore:** Nexium; **Spain:** Axago; **Nexium; Swed.:** Nexium; **Switz.:** Nexium; **Thai.:** Nexium; **Turk.:** Nexium; **UK:** Nexium; **USA:** Nexium; **Venez.:** Esos; **Nexium; Multi-ingredient: Austral.:** Nexium Hp; **India:** Esos-D; **Swed.:** Nexium Hp.

Euonymus

Evónimo; Fusain Noir Pourpré; Spindle Tree Bark; Wahoo Bark. Бересклетова Кора

Profile

Euonymus is the dried root-bark of *Euonymus atropurpureus* (= *Euonymus atropurpurea*) (Celastraceae). It is reported to have laxative, choleric, and diuretic activity.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: Fr.: Jecopeptol; **UK:** Acidosis; GB Tablets; Indigestion Mixture.

Famotidine (BAN, USAN, rINN)

Famotidini; Famotidin; Famotidina; Famotidinas; Famotidinum; L-643341; MK-208; YM-11170. 3-[2-(Diaminomethyleneamino)-thiazol-4-ylmethylthio]-N-sulphamoylpropionamide.

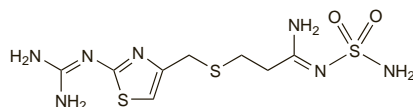
Фамотидин

C₈H₁₅N₇O₂S₃ = 337.4.

CAS — 76824-35-6.

ATC — A02BA03.

ATC Vet — QA02BA03.



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

Ph. Eur. 6.2 (Famotidine). A white or yellowish-white, crystalline powder or crystals. It exhibits polymorphism. Very slightly soluble in water and in dehydrated alcohol; freely soluble in glacial acetic acid; practically insoluble in ethyl acetate. It dissolves in dilute mineral acids. Protect from light.

USP 31 (Famotidine). A white to pale yellowish-white crystalline powder. Very slightly soluble in water; practically insoluble in alcohol, in acetone, in chloroform, in ether, and in ethyl acetate; freely soluble in dimethylformamide and in glacial acetic acid; slightly soluble in methyl alcohol. Protect from light.

Stability. References.

- Quercia RA, *et al.* Stability of famotidine in an extemporaneously prepared oral liquid. *Am J Hosp Pharm* 1993; **50**: 691–3.
- Dentinger PJ, *et al.* Stability of famotidine in an extemporaneously compounded oral liquid. *Am J Health-Syst Pharm* 2000; **1340**–2.

Adverse Effects

As for Cimetidine, p.1716. Unlike cimetidine, famotidine is reported to have little or no anti-androgenic effect, although there are isolated reports of gynecomastia and impotence.

General references.

- Howden CW, Tytgat GNJ. The tolerability and safety profile of famotidine. *Clin Ther* 1996; **18**: 36–54.

Effects on the blood. For reports of blood dyscrasias, some serious, occurring with famotidine, see under Cimetidine p.1717.

Effects on the cardiovascular system. Famotidine 40 mg daily by mouth reduced cardiac output and stroke volume, compared with placebo, cimetidine, or ranitidine in healthy subjects.¹ Similar effects seen in another study² were delayed by pretreatment with ranitidine. However, other workers have found that oral famotidine had no effect on exercise capacity or left ventricular systolic function in healthy subjects,³ and that famotidine 20 mg intravenously had no effect on any of the haemodynamic parameters measured in 11 critically ill patients.⁴ As with other H₂-antagonists (p.1717), bradycardia and AV block has been reported with famotidine,⁵ as has a case of QT prolongation.⁶

- Hinrichsen H, *et al.* Hemodynamic effects of different H₂-receptor antagonists. *Clin Pharmacol Ther* 1990; **48**: 302–8.
- 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.
- Hillermann DE, *et al.* Impact of chronic oral H₂-antagonist therapy of left ventricular systolic function and exercise capacity. *J Clin Pharmacol* 1992; **32**: 1033–7.
- Heiselmann DE, *et al.* Hemodynamic status during famotidine infusion. *DICP Ann Pharmacother* 1990; **24**: 1163–5.
- Schoenwald PK, *et al.* Complete atrioventricular block and cardiac arrest following intravenous famotidine administration. *Anesthesiology* 1999; **90**: 623–6.
- Endo T, *et al.* Famotidine and acquired long QT syndrome. *Am J Med* 2000; **108**: 438–9.

Effects on the endocrine system. Hyperprolactinaemia and breast engorgement occurred in a woman during the fourth month of treatment with famotidine 80 mg daily;¹ she had mistakenly been given twice the usual maximum dose. Recovery occurred when famotidine was withdrawn. Transient hyperprolactinaemia and galactorrhoea have also been reported in a woman after standard doses (40 mg daily) of famotidine.² There have been a few instances of impotence.³

- Delpre G, *et al.* Hyperprolactinaemia during famotidine therapy. *Lancet* 1993; **342**: 868.
- Güven K. Hyperprolactinemia and galactorrhea with standard-dose famotidine therapy. *Ann Pharmacother* 1995; **29**: 788.
- Kassianos GC. Impotence and nizatidine. *Lancet* 1989; **i**: 963.

Effects on the kidneys. For mention of acute interstitial nephritis associated with H₂-antagonists, including famotidine, see under Cimetidine, p.1717.

Effects on the liver. Mixed hepatocellular jaundice¹ and acute hepatitis² have been associated with use of famotidine; in the latter case hepatitis later recurred when the patient was given cimetidine.

- Ament PW, *et al.* Famotidine-induced mixed hepatocellular jaundice. *Ann Pharmacother* 1994; **28**: 40–2.
- Hashimoto F, *et al.* Hepatitis following treatments with famotidine and then cimetidine. *Ann Pharmacother* 1994; **28**: 37–9.

Effects on the nervous system. Similarly to other H₂-antagonists (p.1717), CNS reactions have occurred with famotidine, particularly in the elderly and those with renal failure.^{1–3} In one report,¹ convulsions and mental deterioration in 2 elderly patients with renal failure were associated with grossly elevated plasma and CSF concentrations of the drug; symptoms resolved within 3 days of withdrawing famotidine. In another elderly patient with renal impairment, delirium was associated with use of famotidine but did not occur with cimetidine.⁴

- Yoshimoto K, *et al.* Famotidine-associated central nervous system reactions and plasma and cerebrospinal drug concentrations in neurosurgical patients with renal failure. *Clin Pharmacol Ther* 1994; **55**: 693–700.
- Catalano G, *et al.* Famotidine-associated delirium: a series of six cases. *Psychosomatics* 1996; **37**: 349–55.

- Odeh M, Oliven A. Central nervous system reactions associated with famotidine: report of five cases. *J Clin Gastroenterol* 1998; **27**: 253–4.

- Yuan R-Y, *et al.* Delirium following a switch from cimetidine to famotidine. *Ann Pharmacother* 2001; **35**: 1045–8.

Effects on the skin. Toxic epidermal necrolysis or erythema multiforme have been reported after use of famotidine;^{1,2} the second patient had a recurrence with cimetidine.

- Brunner M, *et al.* Toxic epidermal necrolysis (Lyell syndrome) following famotidine administration. *Br J Dermatol* 1995; **133**: 814–15.
- Horiuchi Y, Ikezawa K. Famotidine-induced erythema multiforme: cross-sensitivity with cimetidine. *Ann Intern Med* 1999; **131**: 795.

Fever. Famotidine 20 mg intravenously every 12 hours was associated with hyperpyrexia in a patient with facial and cranial trauma.¹ Rectal temperature in the 24 hours after starting famotidine was 40.5° and remained elevated for the 5 days of famotidine treatment, despite use of antipyretics. Withdrawal of famotidine resulted in a return to normal temperature within 24 hours.

- Norwood J, *et al.* Famotidine and hyperpyrexia. *Ann Intern Med* 1990; **112**: 632.

Precautions

As for Cimetidine, p.1718.

Hepatic impairment. For a report of increased resistance to H₂-antagonists in patients with liver cirrhosis, see Ranitidine, p.1766.

Renal impairment. In patients with renal impairment, famotidine clearance is reduced and the elimination half-life increased, resulting in increased serum-drug concentrations and in some cases clinical sequelae (see Effects on the Nervous System, above). The half-life of famotidine in healthy subjects is about 3 hours, but in patients with a creatinine clearance less than 38 mL/minute¹ or those with end-stage renal disease² it has been reported to be 19.3 hours and 27.2 hours respectively. A 50% reduction in the dose of famotidine in patients with renal impairment has therefore been recommended. However, it may not be sufficient to adjust the dose only on the basis of creatinine clearance since famotidine is partly eliminated by tubular secretion, which may also be diminished.¹ A chart review³ in patients with end-stage renal disease suggested that most patients would tolerate a dose of 20 mg daily, although a few might need further adjustment to prevent mental status changes.

Haemodialysis does not effectively remove famotidine from the systemic circulation. The proportion removed depends on the type of membrane used; with a high flux polysulfone membrane about 16% is reported to be removed, but only 6% with a cuprophane membrane.² Continuous ambulatory peritoneal dialysis is reported to remove about 5% of a dose.² Continuous haemofiltration may remove about 16% of a dose;² intermittent haemofiltration is reported to remove about 4%⁴ or 8%.² Dosage supplements of famotidine are not required during or after dialysis or filtration procedures.

- Inotsume N, *et al.* Pharmacokinetics of famotidine in elderly patients with and without renal insufficiency and in healthy young volunteers. *Eur J Clin Pharmacol* 1989; **36**: 517–20.
- Gładziwa U, *et al.* Pharmacokinetics and dynamics of famotidine in patients with renal failure. *Br J Clin Pharmacol* 1988; **26**: 315–21.
- Redmond AM, *et al.* Use of famotidine in adult patients with end-stage renal disease: assessment of dosing and mental status changes. *Am J Med Sci* 2005; **330**: 8–10.
- Saima S, *et al.* Hemofiltrability of H₂-receptor antagonist, famotidine, in renal failure patients. *J Clin Pharmacol* 1990; **30**: 159–62.

Interactions

Unlike cimetidine (see p.1718) famotidine does not inhibit cytochrome P450, and therefore is considered to have little effect on the metabolism of other drugs. However, like other H₂-antagonists its effects on gastric pH may affect the absorption of some other drugs.

Antacids. Giving famotidine 40 mg with a 10-mL dose of antacid containing 800 mg aluminium hydroxide with 800 mg magnesium hydroxide,¹ resulted in a decrease in the bioavailability of famotidine that was considered clinically insignificant. Giving famotidine with a 30-mL dose of the same antacid resulted in a greater reduction in the absorption of famotidine from the gastrointestinal tract, but the interaction could be minimised by separating ingestion by 2 hours.²

- Lin JH, *et al.* Effects of antacids and food on absorption of famotidine. *Br J Clin Pharmacol* 1987; **24**: 551–3.
- Barzaghi N, *et al.* Impaired bioavailability of famotidine given concurrently with a potent antacid. *J Clin Pharmacol* 1989; **29**: 670–2.

Probenecid. Probenecid in a total dose of 1500 mg had a significant effect on the pharmacokinetics of famotidine 20 mg in 8 healthy subjects.¹ The maximum serum concentration of famotidine and the area under the concentration/time curve were significantly increased and renal clearance significantly reduced.