

ing to creatinine clearance (CC). Licensed product information recommends the following oral doses in renal impairment:

- CC 20 to 50 mL/minute: doses should be reduced by 50%, or where the standard dose would be 150 mg daily, 150 mg may be given on alternate days
- CC less than 20 mL/minute: doses should be reduced by 75%, or where the standard dose would be 300 mg daily, 150 mg may be given on alternate days, and where the standard dose would be 150 mg daily, 150 mg may be given every third day

## Preparations

**BP 2008:** Nizatidine Intravenous Infusion;  
**USP 31:** Nizatidine Capsules.

**Proprietary Preparations** (details are given in Part 3)

**Austral.:** Nizac; Tacidine; Tazac; **Austria:** Ulixit; **Belg.:** Panaxid†; **Braz.:** Axid; **Canad.:** Axid; **Chile:** Nizaxid; **Denm.:** Izatart; **Nizax;** **Fin.:** Nizax; **Fr.:** Nizaxid; **Ger.:** Gastrax†; **Nizax;** **Gr.:** Axid†; Flectart†; Flexidon†; Ozeltart†; Ulcogastin†; **Hong Kong:** Axid; **Hung.:** Naxidin; **Indon.:** Axid; **Irl.:** Axid; **Ital.:** Cronizat; Nizax; Zanizal†; **Malaysia:** Axid†; **Mex.:** Axid; Uldadin†; **Neth.:** Axid; **Philipp.:** Axid; **Port.:** Nizaxid; Prospaxid; **S.Afr.:** Antizid; **Spain:** Distaxid; **Swed.:** Nizax†; **Switz.:** Calmaxid†; **Thai.:** Axid†; **Turk.:** Axid; **UK:** Axid; **USA:** Axid; **Venez.:** Axid†.

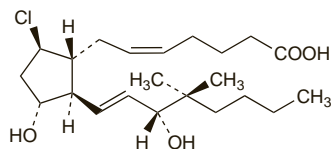
## Nocloprost (rINN)

Nocloprostum. (Z)-7-[(1R,2R,3R,5R)-5-Chloro-3-hydroxy-2-[(E)-(3R)-3-hydroxy-4,4-dimethyl-1-octenyl]cyclopentyl]-5-heptenoic acid.

Ноклопрост

$C_{22}H_{37}ClO_4 = 401.0$ .

CAS — 79360-43-3.



## Profile

Nocloprost is a synthetic analogue of dinoprostone (prostaglandin  $E_2$ ) that has been investigated in the treatment of peptic ulcer disease.

## References.

1. Täuber U, *et al.* Pharmacokinetics of nocloprost in human volunteers and its relation to dose. *Eur J Clin Pharmacol* 1993; **44**: 497–500.
2. Konturek JW, *et al.* Epidermal growth factor in gastric ulcer healing by nocloprost, a stable prostaglandin  $E_2$  derivative. *Scand J Gastroenterol* 1997; **32**: 980–4.

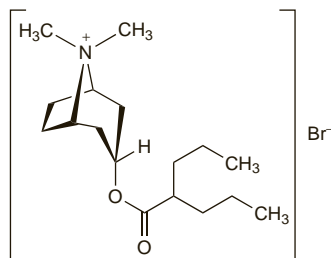
## Octatropine Methylbromide (BAN, rINN)

Anisotropine Methobromide; Anisotropine Methylbromide (USAN); Metilbromuro de octatropina; Octatropine, Méthylbromure d'; Octatropini Methylbromidum. (1R,3r,5S)-8-Methyl-3-(2-propylvaleryl-oxy)tropanium bromide.

Октатропина Метилбромид

$C_{17}H_{32}BrNO_2 = 362.3$ .

CAS — 80-50-2.



**Pharmacopoeias.** In *It*.

## Profile

Octatropine methylbromide is a quaternary ammonium antimuscarinic with peripheral actions similar to those of atropine (p.1219). It has been used as an adjunct in the treatment of peptic ulcer disease and to relieve visceral spasms.

## Preparations

**Proprietary Preparations** (details are given in Part 3)

**Multi-ingredient:** **Arg.:** Espasmo Dioxadol; **Chile:** Bufacyl; Valpin; **Ital.:** Valpinax.

## Olsalazine Sodium (BANM, USAN, rINN)

Azodisal Sodium; Cl Mordant Yellow 5; Cj-91B; Colour Index No. 14130; Natrii Olsalazinum; Olsalatsiininatrium; Olsalazin disodná sůl; Olsalazin Sodyum; Olsalazina sodica; Olsalazine sodique; Olsalazinnatrium; Olsalazino natrio druska; Olsalazinum Dinatrium; Olsalazinum natrium; Olsalazin-nátrium; Sodium Azodisalicylate. Disodium 5,5'-azodisalicylate.

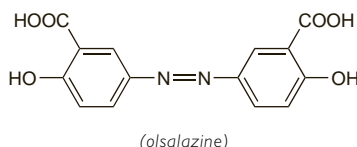
Натрий Олсалазин

$C_{14}H_8N_2Na_2O_6 = 346.2$ .

CAS — 6054-98-4.

ATC — A07EC03.

ATC Vet — QA07EC03.



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

**Ph. Eur. 6.2** (Olsalazine Sodium). A yellow, fine, crystalline powder; it exhibits polymorphism. Sparingly soluble in water; soluble in dimethyl sulfoxide; very slightly soluble in methyl alcohol.

## Adverse Effects and Precautions

As for Mesalazine, p.1745. The most common adverse effects associated with olsalazine sodium are diarrhoea, arthralgia, and skin rashes. Diarrhoea may be watery in some patients; it may resolve with dosage reduction but can be severe enough to require withdrawal of treatment. Diarrhoea is less likely if the drug is taken after meals. There have been a few reports of blood dyscrasias. If a blood dyscrasia is suspected treatment should be stopped immediately and a blood count performed. Patients or their carers should be told how to recognise signs of haematotoxicity and should be advised to seek immediate medical attention if symptoms such as fever, sore throat, mouth ulcers, bruising, or bleeding develop.

**Incidence of adverse effects.** In an open study<sup>1</sup> of olsalazine 1 g daily by mouth involving 160 patients with active ulcerative colitis and a history of sulfasalazine intolerance, 103 (64.4%) patients had no adverse effects; 29 patients reported only minor adverse effects: gastrointestinal disturbances in 22 patients, transient skin rash in 3, and headache, increased salivation, cough, and irritability each in one patient. The most common adverse effect was frequent loose stools which affected 25 patients, 20 of whom had to stop treatment. This adverse effect occurred early in treatment, within 10 hours of the first dose in 13 patients. Severe diarrhoea was more frequent in patients with widespread disease, but the incidence of diarrhoea did not correlate with disease severity.

A subsequent study<sup>2</sup> in healthy subjects has shown that olsalazine has a significant inhibitory effect on water and electrolyte absorption in the small intestine, which may account, at least in part, for the induction of diarrhoea. Patients with extensive colitis have reduced colonic absorptive function and may be less able to assimilate the increased colonic inflow volumes.

1. Sandberg-Gertzén H, *et al.* Azodisal sodium in the treatment of ulcerative colitis: a study of tolerance and relapse-prevention properties. *Gastroenterology* 1986; **90**: 1024–30.
2. Raimundo AH, *et al.* Effects of olsalazine and sulphasalazine on jejunal and ileal water and electrolyte absorption in normal human subjects. *Gut* 1991; **32**: 270–4.

**Breast feeding.** A study<sup>1</sup> involving a 39-year-old woman with Crohn's disease found that olsalazine did not appear to present a clinically significant risk to the breast-fed infant. Olsalazine was undetectable in the breast milk for 48 hours after a single oral 500-mg dose, and although small amounts of the metabolite acetylated 5-aminosalicylic acid were detected in breast milk the infant showed no adverse effects during the 3 weeks afterwards in which the mother continued taking olsalazine.

1. Miller LG, *et al.* Disposition of olsalazine and metabolites in breast milk. *J Clin Pharmacol* 1993; **33**: 703–6.

**Effects on the blood.** As of July 1995, the UK CSM had received 4 reports of blood dyscrasias associated with olsalazine, none of them fatal.<sup>1</sup> It was recommended that a blood count be performed and the drug stopped immediately if there was suspicion of a dyscrasia. See also under Mesalazine, p.1745.

1. Committee on Safety of Medicines/Medicines Control Agency. Blood dyscrasias and mesalazine. *Current Problems* 1995; **21**: 5–6. Also available at: [http://www.mhra.gov.uk/home/idcplg?IdcService=GET\\_FILE&DocName=CON2015619&RevisionSelectionMethod=LatestReleased](http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&DocName=CON2015619&RevisionSelectionMethod=LatestReleased) (accessed 15/06/06)

**Effects on the kidneys.** A report of nephrotoxicity, characterised by interstitial nephritis, was associated with the use of olsalazine.<sup>1</sup> Symptoms resolved on stopping of the drug. See also under Mesalazine, p.1745.

1. Wilcox GM, *et al.* Nephrotoxicity associated with olsalazine. *Am J Med* 1996; **100**: 238–40.

## Interactions

**Antineoplastics.** For mention of 5-aminosalicylates such as olsalazine inhibiting the metabolism of thiopurine antineoplastics, and increasing their toxicity, see Mercaptopurine, p.1744.

## Pharmacokinetics

Very little of an oral dose of olsalazine is absorbed via the upper gastrointestinal tract, and almost the entire dose reaches its site of action in the colon intact. It is broken down by the colonic bacterial flora into 2 molecules of 5-aminosalicylic acid (mesalazine). Some mesalazine is absorbed and acetylated (see p.1746) but systemic concentrations of mesalazine and its metabolite are lower than after comparable oral doses of mesalazine, perhaps because there is less release of mesalazine in the small intestine, where absorption is better. Mesalazine concentrations in the colon after a dose of olsalazine are stated to be about 1000 times greater than systemic concentrations.

The small amounts (1 to 2% of the dose or less) of intact olsalazine that are absorbed are excreted mainly in urine; the elimination half-life after an intravenous dose has been calculated at about 1 hour. Some olsalazine is metabolised by sulfate conjugation in the liver: the elimination half-life of the metabolite is reported to be about 7 days.

## References.

1. Ryde EM. Pharmacokinetic aspects of drugs targeted for the colon, with special reference to olsalazine. *Acta Pharm Suec* 1988; **25**: 327–8.
2. Laursen LS, *et al.* Disposition of 5-aminosalicylic acid by olsalazine and three mesalazine preparations in patients with ulcerative colitis: comparison of intraluminal colonic concentrations, serum values, and urinary excretion. *Gut* 1990; **31**: 1271–6.

## Uses and Administration

Olsalazine consists of two molecules of mesalazine (p.1745) linked with an azo bond. It is activated in the colon where the active mesalazine is released. It is used as the sodium salt in the management of acute mild ulcerative colitis and for the maintenance of remission (see Inflammatory Bowel Disease, p.1697). The usual initial dose of olsalazine sodium is 1 g by mouth daily in divided doses and this is gradually increased, if necessary, over one week, to a maximum dose of 3 g daily. The usual dose for the maintenance of remission is 500 mg twice daily. Doses should be taken after meals and a single dose should not exceed 1 g. Although not licensed for use in children, the *BNFC* includes a dose for children aged 2 years and over; the adult dose may be given for management of an acute attack of mild ulcerative colitis, and a dose of 250 to 500 mg twice daily may be used for maintenance.

## Preparations

**Proprietary Preparations** (details are given in Part 3)

**Arg.:** Dipentum†; **Austral.:** Dipentum; **Austria:** Dipentum; **Canad.:** Dipentum; **Chile:** Dipentum; **Denm.:** Dipentum; **Fin.:** Dipentum; **Fr.:** Dipentum; **Ger.:** Dipentum; **Gr.:** Dipentum†; **Hong Kong:** Dipentum; **Hung.:** Dipentum†; **Irl.:** Dipentum; **Israel:** Dipentum†; **Ital.:** Dipentum†; **Neth.:** Dipentum; **Norw.:** Dipentum; **NZ:** Dipentum; **S.Afr.:** Dipentum; **Spain:** Rasalf; **Swed.:** Dipentum; **Switz.:** Dipentum; **Turk.:** Dipentum; **UK:** Dipentum; **USA:** Dipentum.

## Omeprazole (BAN, USAN, rINN)

H-168/68; Omepratsoli; Omeprazol; Omeprazolas; Oméprazole; Omeprazolium. (R<sub>S</sub>)-5-Methoxy-2-(4-methoxy-3,5-dimethyl-2-pyridylmethylsulphonyl)benzimidazole.

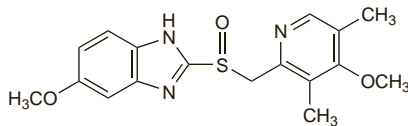
Омепразол

C<sub>17</sub>H<sub>19</sub>N<sub>3</sub>O<sub>5</sub>S = 345.4.

CAS — 73590-58-6.

ATC — A02BC01.

ATC Vet — QA02BC01.



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

**Ph. Eur. 6.2** (Omeprazole). A white or almost white powder. It exhibits polymorphism. Very slightly soluble in water; sparingly soluble in alcohol and in methyl alcohol; soluble in dichloromethane. It dissolves in dilute solutions of alkali hydroxides. Store in airtight containers at a temperature between 2° and 8°. Protect from light.

**USP 31** (Omeprazole). A white to off-white powder. Very slightly soluble in water; sparingly soluble in alcohol and in methyl alcohol; soluble in dichloromethane. Store in airtight containers at a temperature not exceeding 8°. Protect from moisture.

## Omeprazole Magnesium (BANM, USAN, rINN)

Magnesi Omeprazolium; Omeprazol magnésico; Oméprazole magnésique; Oméprazole Magnésique; Omeprazolium magnesium.

Магния Омепразол

C<sub>34</sub>H<sub>36</sub>MgN<sub>6</sub>O<sub>10</sub>S<sub>2</sub> = 713.1.

CAS — 95382-33-5.

ATC — A02BC01.

ATC Vet — QA02BC01.

**Pharmacopoeias.** In *US*.

**USP 31** (Omeprazole Magnesium). A white to off-white powder. Very soluble in water and in dichloromethane; slightly soluble in alcohol; sparingly soluble in methyl alcohol. Store in airtight containers. Protect from light.

## Omeprazole Sodium (BANM, USAN, rINN)

Natrii Omeprazolium; Omepratsolinatrium; Omeprazol sódico; Omeprazol sodná sůl monohydrát; Oméprazole sodique; Omeprazolnatrium; Omeprazol-nátrium; Omeprazol natrio druska; Omeprazolium natrium; Omeprazolium Natrium Monohydricum.

Натрий Омепразол

C<sub>17</sub>H<sub>18</sub>N<sub>3</sub>NaO<sub>5</sub>S = 367.4.

CAS — 95510-70-6.

ATC — A02BC01.

ATC Vet — QA02BC01.

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

**Ph. Eur. 6.2** (Omeprazole Sodium). A white or almost white, hygroscopic powder. Freely soluble in water and in alcohol; very slightly soluble in dichloromethane; soluble in propylene glycol. The pH of a 2% solution in water is 10.3 to 11.3. Store in airtight containers. Protect from light.

## Adverse Effects

Proton pump inhibitors are generally well tolerated, and adverse effects are relatively infrequent. The adverse effects reported most often with omeprazole and other proton pump inhibitors have been headache, diarrhoea, and skin rashes; they have sometimes been severe enough to require stopping treatment. Other effects include pruritus, dizziness, fatigue, constipation, nausea and vomiting, flatulence, abdominal pain, arthralgia and myalgia, urticaria, and dry mouth. Isolated cases of photosensitivity, bullous eruption, erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis have occurred. Hypersensitivity reactions, including fever, bronchospasm, angioedema, and anaphylaxis have been reported. Effects on the CNS include occasional insomnia, somnolence, and vertigo; reversible confusional states, agitation, depression, and hallucinations have occurred in severely ill patients. Raised liver enzymes, and isolated cases of hepatitis, jaundice, hepatic failure, and hepatic encephalopathy, have been reported. Other adverse effects reported rarely include paraesthesia, blurred vision, alopecia, stomatitis, increased sweating, taste

disturbances, peripheral oedema, malaise, hyponatraemia, blood disorders (including agranulocytosis, leucopenia, and thrombocytopenia), gynaecomastia, impotence, and interstitial nephritis.

Proton pump inhibitors may increase the risk of gastrointestinal infections because of their acid suppressive effects.

Early toxicological studies identified carcinoid-like tumours of the gastric mucosa in *rats* given very high doses of omeprazole over long periods; this is reviewed in more detail under Gastrointestinal Tumours, below.

**Incidence of adverse effects.** Prescription-event monitoring for 16 205 patients prescribed omeprazole, 17 329 prescribed lansoprazole, and 11 541 prescribed pantoprazole indicated that adverse events were reported infrequently, with the most common being gastrointestinal disturbances and headache. The incidences of diarrhoea, the most commonly reported event, per 1000 days of exposure, were 0.18 for omeprazole, 0.39 for lansoprazole, and 0.23 for pantoprazole. Despite the inherent biases of such a cohort study, there did seem to be some evidence that lansoprazole might be associated with a somewhat greater risk of diarrhoea, particularly in the elderly.<sup>1</sup>

1. Martin RM, *et al.* The rates of common adverse events reported during treatment with proton pump inhibitors used in general practice in England: cohort studies. *Br J Clin Pharmacol* 2000; **50**: 366–72.

**Effects on the blood.** There have been rare cases of leucopenia, agranulocytosis, thrombocytopenia, and pancytopenia, with omeprazole and other proton pump inhibitors such as lansoprazole and pantoprazole.<sup>1,3</sup> Auto-immune haemolytic anaemia has also been reported with omeprazole.<sup>4</sup>

1. Holt TL, *et al.* Neutropenia associated with omeprazole. *Med J Aust* 1999; **170**: 141–2.  
2. Zlabek JA, Anderson CG. Lansoprazole-induced thrombocytopenia. *Ann Pharmacother* 2002; **36**: 809–11.  
3. Watson TD, *et al.* Pantoprazole-induced thrombocytopenia. *Ann Pharmacother* 2006; **40**: 758–61.  
4. Butt ML, *et al.* Autoimmune haemolytic anaemia associated with use of omeprazole. *Br J Hosp Med* 2007; **68**: 108.

**Effects on the cardiovascular system.** Results and preliminary analyses from 2 studies raised concerns about a possible increased risk of myocardial infarction, cardiac failure, and cardiac-related sudden death in patients taking omeprazole or esomeprazole compared with patients who received surgery for gastro-oesophageal reflux disease.<sup>1,2</sup> However, an FDA safety review found that patients who underwent surgery tended to be younger and less likely to have a history of cardiac problems or cardiac risk factors than those treated with one of the drugs.<sup>2</sup> The FDA concluded that long-term use of these drugs is not likely to be associated with an increased risk of cardiac problems.<sup>3</sup> However, while Health Canada<sup>4</sup> considered that there was no evidence to support such an increased risk with long-term use of esomeprazole they were unable to make such a definitive conclusion for omeprazole.

1. FDA. Early communication about an ongoing safety review: omeprazole (Prilosec) esomeprazole (Nexium) (issued 9th August 2007). Available at: [http://www.fda.gov/cder/drug/early\\_comm/omeprazole\\_esomeprazole.htm](http://www.fda.gov/cder/drug/early_comm/omeprazole_esomeprazole.htm) (accessed 28/01/08)  
2. FDA. Follow-up to the August 9, 2007, communication about the ongoing safety review of omeprazole and esomeprazole (issued 10th December 2007). Available at: [http://www.fda.gov/cder/drug/early\\_comm/omeprazole\\_esomeprazole\\_update.htm](http://www.fda.gov/cder/drug/early_comm/omeprazole_esomeprazole_update.htm) (accessed 28/01/08)  
3. FDA. FDA's safety reviews of Prilosec and Nexium find no evidence of increased rates of cardiac events (issued 10th December 2007). Available at: <http://www.fda.gov/bbs/topics/NEWS/2007/NEW01754.html> (accessed 28/01/08)  
4. Health Canada. Health Canada completes safety review of Losec (omeprazole) and Nexium (esomeprazole) (issued 27 February 2008). Available at: [http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/\\_2008/2008\\_34-eng.php](http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/_2008/2008_34-eng.php) (accessed 09/07/08)

**Effects on the endocrine system.** Up to December 1991, WHO had received 30 reports of impotence or gynaecomastia which might have been due to omeprazole;<sup>1</sup> of these reports 15 were of impotence, 13 of gynaecomastia in men, and 2 of breast enlargement in women. The Spanish Pharmacovigilance System reported 24 cases of gynaecomastia in association with use of proton pump inhibitors, including lansoprazole and rabeprazole, between January 1982 and July 2006. In most of the cases, gynaecomastia improved after stopping the drug.<sup>2</sup> For reference to a case-control study showing no statistical link between gynaecomastia and omeprazole, see under Cimetidine, p.1717.

1. Lindquist M, Edwards IR. Endocrine adverse effects of omeprazole. *BMJ* 1992; **305**: 451–2.  
2. Carvajal A, *et al.* Gynaecomastia associated with proton pump inhibitors: a case series from the Spanish Pharmacovigilance System. *Drug Safety* 2007; **30**: 527–31.

**Effects on the eyes.** Visual disturbances associated with the use of omeprazole have included 6 cases of irreversible blindness or visual impairment in severely ill patients given the drug intravenously, and 13 cases of visual disturbances associated with oral use.<sup>1</sup> As a result of concern about these effects the availability of intravenous omeprazole was restricted in Germany; however, the consensus appears to be that a causal link has not been

established between omeprazole and these ocular effects. Suggestions that visual (and also auditory<sup>2</sup>) impairment could follow drug-induced vasculitis<sup>2,4</sup> appear to be contentious.<sup>1,5,7</sup> A cohort study involving 140 128 patients receiving antiseecretory therapy, 33 988 of whom received omeprazole, found no evidence that any of the drugs used was associated with a major increase in risk of vascular or inflammatory disorders of the eye;<sup>8</sup> however, the statistical power of this study was not high.<sup>9</sup>

1. Creutzfeldt WC, Blum AL. Safety of omeprazole. *Lancet* 1994; **343**: 1098.  
2. Schönhöfer PS. Intravenous omeprazole and blindness. *Lancet* 1994; **343**: 665.  
3. Schönhöfer PS. Safety of omeprazole and lansoprazole. *Lancet* 1994; **343**: 1369–70.  
4. Schönhöfer PS, *et al.* Ocular damage associated with proton pump inhibitors. *BMJ* 1997; **314**: 1805.  
5. Colin-Jones D. Safety of omeprazole and lansoprazole. *Lancet* 1994; **343**: 1369.  
6. Lessell S. Omeprazole and ocular damage. *BMJ* 1998; **316**: 67.  
7. Sachs G. Omeprazole and ocular damage. *BMJ* 1998; **316**: 67–8.  
8. García Rodríguez LA, *et al.* A cohort study of the ocular safety of anti-ulcer drugs. *Br J Clin Pharmacol* 1996; **42**: 213–16.  
9. Merlo J, Ransam J. Ocular safety of anti-ulcer drugs. *Br J Clin Pharmacol* 1997; **43**: 449.

**Effects on the kidneys.** Acute interstitial nephritis developed in 2 elderly patients given omeprazole for the treatment of gastro-oesophageal reflux disease.<sup>1,2</sup> When the drug was stopped, renal function improved rapidly in 1 patient, but recurred upon rechallenge,<sup>1</sup> while in the other renal function remained severely affected for several months.<sup>2</sup> It was postulated that this adverse effect might have an allergic mechanism.<sup>2</sup> In these cases interstitial nephritis was associated with rash and eosinophilia; however, a further 2 cases of acute interstitial nephritis associated with omeprazole therapy in elderly patients<sup>3,4</sup> did not exhibit these symptoms. In another report, associated rash without eosinophilia was seen.<sup>5</sup>

The Australian Adverse Drug Reactions Advisory Committee (ADRAC)<sup>6</sup> stated in April 2003 that it had received 18 biopsy-confirmed reports of interstitial nephritis associated with the use of omeprazole. These patients had presented with symptoms including weight loss, malaise, fever, and nausea; polyuria and polydipsia occurred in one case. Most patients had raised plasma-urea and/or plasma-creatinine concentrations. ADRAC had also received 2 reports of interstitial nephritis associated with rabeprazole.<sup>6</sup> A case report (in March 2005) of 2 cases of interstitial nephritis associated with the omeprazole isomer *esomeprazole* noted that, by October 2004, the manufacturer had reported being aware of some 15 cases worldwide possibly associated with the drug, and at least 200 associated with omeprazole.<sup>7</sup> Acute interstitial nephritis has also been associated with the use of pantoprazole in an elderly woman for the treatment of gastro-oesophageal reflux disease.<sup>8</sup>

1. Ruffenach SJ, *et al.* Acute interstitial nephritis due to omeprazole. *Am J Med* 1992; **93**: 472–3.  
2. Christensen PB, *et al.* Renal failure after omeprazole. *Lancet* 1993; **341**: 55.  
3. Assouad M, *et al.* Recurrent acute interstitial nephritis on rechallenge with omeprazole. *Lancet* 1994; **344**: 549.  
4. Jones B, *et al.* Acute interstitial nephritis due to omeprazole. *Lancet* 1994; **344**: 1017–18.  
5. Kuiper JJ. Omeprazole-induced acute interstitial nephritis. *Am J Med* 1993; **95**: 248.  
6. Adverse Drug Reactions Advisory Committee (ADRAC). Interstitial nephritis with the proton pump inhibitors. *Aust Adverse Drug React Bull* 2003; **22**: 3. Also available at: <http://www.tga.health.gov.au/adra/aadr/aadr304.htm> (accessed 07/05/04)  
7. Geevasinga N, *et al.* Acute interstitial nephritis secondary to esomeprazole. *Med J Aust* 2005; **182**: 235–6.  
8. Ra A, Tobe SW. Acute interstitial nephritis due to pantoprazole. *Ann Pharmacother* 2004; **38**: 41–5.

**Effects on the liver.** Raised liver enzymes have occurred with omeprazole and other proton pump inhibitors, and there have been isolated cases of hepatotoxicity. For a study suggesting a relatively low incidence of acute liver injury in patients receiving omeprazole see Cimetidine, p.1717.

## References

1. Jochem V, *et al.* Fulminant hepatic failure related to omeprazole. *Am J Gastroenterol* 1992; **87**: 523–5.  
2. Kourg SI, *et al.* Omeprazole and the development of acute hepatitis. *Eur J Emerg Med* 1998; **5**: 467–9.

**Effects on the musculoskeletal system.** Progressive muscular weakness suggestive of myopathy developed in a 78-year-old patient given oral omeprazole.<sup>1</sup> After 4 weeks of treatment the patient required assistance in walking and rising from squatting. Weakness resolved on withdrawal of the drug, but returned on rechallenge. Acute myopathy has also been reported after a single infusion of omeprazole.<sup>2</sup> Analysis of the WHO adverse drug reaction database in March 2005 revealed 868 reports associating proton pump inhibitors with myalgia, of which 292 cases had symptoms indicative of muscle disorders including *polymyositis* and *rhabdomyolysis*.<sup>3</sup> Reports implicated omeprazole, pantoprazole, lansoprazole, esomeprazole, and rabeprazole, and it was suggested that myopathy was probably a class effect. The mechanism might involve induction of auto-immune antibodies. A report of 5 cases of arthralgia, sometimes associated with swelling of the affected joints, in patients receiving omeprazole,<sup>4</sup> also noted that some reported cases of omeprazole-associated headache were accompanied by arthralgia or myalgia. In another case<sup>5</sup> arthralgia in a patient with a hereditary myopathy receiving