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:*** Ulxit; ***Belg.:*** Panaxid†; ***Braz.:*** Axid; ***Canad.:*** Axid; ***Chile:*** Nizaxid; ***Denm.:*** Izatax; Nizax; ***Fin.:*** Nizax; ***Fr.:*** Nizaxid; ***Ger.:*** Gastrax†; Nizax; ***Gr.:*** Axid†; Flectar†; Flexidon†; Ozeltan†; Ulcogastrin†; ***Hong Kong:*** Axid; ***Hung.:*** Naxidin; ***Indon.:*** Axid; ***Irl.:*** Axid; ***Ital.:*** Cronizat; Nizax; Zaniza†; ***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†.

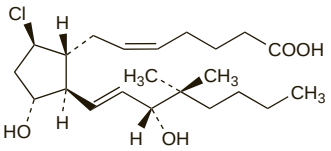
Nocloprost *(rINN)*

Nocloprostum. (*Z*)-7-[(1*R*,2*R*,3*R*,5*R*)-5-Chloro-3-hydroxy-2-[(*E*)-(3*R*)-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 E2 derivative. *Scand J Gastroenterol* 1997; **32:** 980–4.

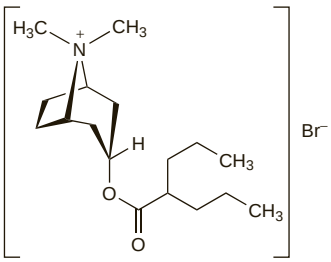
Octatropine Methylbromide *(BAN, rINN)*

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

Azodisal Sodium; CI Mordant Yellow 5; CJ-91B; Colour Index No. 11130; Natrii Olsalazinum; Olsalatsiininatrium; Olsalazin disodná sůl; Olsalazin Sodyum; Olsalazina sódica; Olsalazine sodique; Olsalazinnatrium; Olsalazino natrio druska; Olsalazinum Dinatricum; Olsalazinum natricum; Olszalazin-nátrium; Sodium Azodisalicylate. Disodium 5,5′-azodisalicylate.

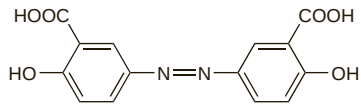
Натрий Ольсалазин

$C_{14}H_8N_2Na_2O_6$ = 346.2.

CAS — 6054-98-4.

ATC — A07EC03.

ATC Vet — QA07EC03.



(olsalazine)

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[1] 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[2] 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[1] 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.[1] 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&dDocName=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.[1] 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.744.

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:*** Rasal†; ***Swed.:*** Dipentum; ***Switz.:*** Dipentum; ***Turk.:*** Dipentum; ***UK:*** Dipentum; ***USA:*** Dipentum.