Enoxolone Aluminium *(BANM, rINNM)*

Aluminii Enoxolonum; Aluminium Glycyrrhetate; Aluminium Glycyrrhetinate; Enoxolona de aluminio; Enoxolone Aluminum; Énoxolone d'Aluminium. 3β-Hydroxy-11-oxo-olean-12-en-30-oic acid, aluminium salt.

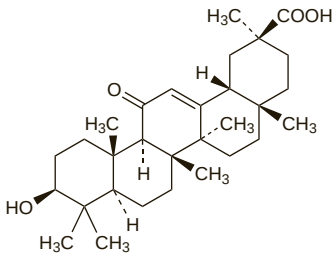
Алюминий Эноксолон

$(C_{30}H_{46}O_4)_3.Al$ = 1439.0.

CAS — 4598-66-7.

ATC — D03AX10.

ATC Vet — QD03AX10.



(enoxolone)

Profile

Enoxolone aluminium is an analogue of carbenoxolone (p.1714) that has been used in preparations for the treatment of peptic ulcer disease and other gastrointestinal disorders. It has also been used in preparations for skin disorders and mouth and throat disorders.

Primary pulmonary hypertension. *In-utero* exposure to enoxolone was implicated in a fatal case of neonatal primary pulmonary hypertension; the mother had used a lotion for prurigo that contained enoxolone and the authors supposed it had contributed at least in part to the pulmonary hypertension.[1]

1. Navarre-Belhassen C, *et al.* An unexpected case of primary pulmonary hypertension of the neonate (PPHN): potential role of topical administration of enoxolone. *J Perinat Med* 2002; **30:** 437–9.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Spain:*** Gastroalgine.

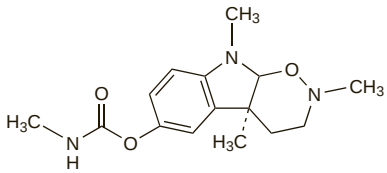
Eseridine Salicylate *(rINNM)*

Éséridine, Salicylate d'; Eseridini Salicylas; Eserine Aminoxide Salicylate; Eserine Oxide Salicylate; Physostigmine Aminoxide Salicylate; Physostigmine *N*-Oxide Salicylate; Salicilato de eseridina. (4a*S*,9a*S*)-2,3,4,4a,9,9a-Hexahydro-2,4a,9-trimethyl-1,2-oxazino[6,5-*b*]indol-6-ylmethylcarbamate salicylate.

Эзеридина Салицилат

$C_{15}H_{21}N_3O_3.C_7H_6O_3$ = 429.5.

CAS — 25573-43-7 (eseridine); 5995-96-0 (eseridine salicylate).



(eseridine)

Profile

Eseridine salicylate, a derivative of physostigmine, is an inhibitor of cholinesterase activity that has been given orally for dyspepsia in doses of up to 4.5 mg 3 times daily, taken 30 minutes before meals.

Preparations

Proprietary Preparations (details are given in Part 3)

Fr.: Geneserine.

Esomeprazole *(BAN, rINN)*

Esomepratsoli; Esomeprazol; Ésoméprazole; Esomeprazolum; H-199/18; Perprazole. 5-Methoxy-2-{(*S*)-[(4-methoxy-3,5-dimethyl-2-pyridyl)methyl]sulfinyl}benzimidazole.

Эзомепразол

$C_{17}H_{19}N_3O_3S$ = 345.4.

CAS — 119141-88-7.

ATC — A02BC05.

ATC Vet — QA02BC05.

Esomeprazole Magnesium *(BANM, USAN, rINNM)*

Esomeprazol; Esomeprazol magnésico; Ésoméprazole magnésique; Ésoméprazole Magnesique; Esomeprazolum magnesicum; H199/18 (esomeprazole); Magnesii Esomeprazolum; Perprazole (esomeprazole). 5-Methoxy-2-{(*S*)-[(4-methoxy-3,5-dimethyl-2-pyridyl)methyl]sulfinyl}benzimidazole magnesium (2:1) trihydrate.

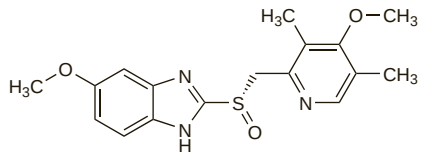
Магния Эзомепразол

$C_{34}H_{36}MgN_6O_6S_2.3H_2O$ = 767.2.

CAS — 217087-09-7.

ATC — A02BC05.

ATC Vet — QA02BC05.



(esomeprazole)

Pharmacopoeias. In *US.*

USP 31 (Esomeprazole Magnesium). A white to slightly coloured powder. Slightly soluble in water; soluble in methyl alcohol; practically insoluble in heptane. Store in airtight containers. Protect from light.

Esomeprazole Sodium *(BANM, USAN, rINNM)*

Esomeprazol sódico; Ésoméprazole Sodique; Natrii Esomeprazolum.

Натрий Эзомепразол

$C_{17}H_{19}N_3NaO_3S$ = 368.4.

CAS — 161796-78-7.

ATC — A02BC05.

ATC Vet — QA02BC05.

Adverse Effects and Precautions

As for Omeprazole, p.1753.

◊ General references.

1. Davies M, *et al.* Safety profile of esomeprazole: results of a prescription-event monitoring study of 11 595 patients in England. *Drug Safety* 2008; **31:** 313–23.

Effects on the cardiovascular system. For discussion of cardiac effects ostensibly seen with esomeprazole, see under Omeprazole, p.1753.

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

Effects on the skin. For mention of exacerbation of vitiligo with esomeprazole, see p.1754.

Fever. For a report of hyperpyrexia associated with esomeprazole, see under Omeprazole, p.1754.

Interactions

As for Omeprazole, p.1755.

◊ References.

1. Andersson T, *et al.* Drug interaction studies with esomeprazole, the (S)-isomer of omeprazole. *Clin Pharmacokinet* 2001; **40:** 523–37.

Pharmacokinetics

Esomeprazole is rapidly absorbed after oral doses, with peak plasma levels occurring after about 1 to 2 hours. It is acid labile and an enteric-coated formulation has been developed. Bioavailability of esomeprazole increases with both dose and repeated administration to about 68 and 89% for doses of 20 and 40 mg respectively. Food delays and decreases the absorption of esomeprazole, but this does not significantly change its effect on intragastric acidity. Esomeprazole is about 97% bound to plasma proteins. It is extensively metabolised in the liver by the cytochrome P450 isoenzyme CYP2C19 to hydroxy and desmethyl metabolites, which have no effect on gastric acid secretion. The remainder is metabolised by the cytochrome P450 isoenzyme CYP3A4 to esomeprazole sulfone. With repeated dosage, there is a decrease in first-pass metabolism and systemic clearance, probably caused by an inhibition of the CYP2C19 isoenzyme. However, there is no accumulation during once daily use. The plasma elimination half-life is about 1.3 hours. Almost 80% of an oral dose is eliminated as metabolites in the urine, the remainder in the faeces.

◊ References.

1. Andersson T, *et al.* Pharmacokinetic studies with esomeprazole, the (S)-isomer of omeprazole. *Clin Pharmacokinet* 2001; **40:** 411–26.
2. Sostek MB, *et al.* Effect of timing of dosing in relation to food intake on the pharmacokinetics of esomeprazole. *Br J Clin Pharmacol* 2007; **64:** 386–90.

Metabolism. As for omeprazole (p.1755), the cytochrome P450 isoenzyme CYP2C19 is involved in the metabolism of esomeprazole, and individuals who are deficient in this enzyme are poor metabolisers of esomeprazole. However, there is some suggestion that the metabolism of esomeprazole is less dependent on this genotype, as there may be a metabolic shift towards the CYP3A4-mediated pathway.[1]

1. Schwab M, *et al.* Esomeprazole-induced healing of gastro-esophageal reflux disease is unrelated to the genotype of CYP2C19: evidence from clinical and pharmacokinetic data. *Clin Pharmacol Ther* 2005; **78:** 627–34.

Uses and Administration

Esomeprazole is the *S*-isomer of the proton pump inhibitor omeprazole (p.1753) and is used similarly in the treatment of peptic ulcer disease and NSAID-associated ulceration (p.1702), in gastro-oesophageal reflux disease (p.1696), and the Zollinger-Ellison syndrome (p.1704). It is given as the magnesium or sodium salt but doses are calculated in terms of esomeprazole. Esomeprazole magnesium 22.2 mg and esomeprazole sodium 21.3 mg are each equivalent to about 20 mg of esomeprazole.

Usual doses for **peptic ulcer disease**, as a component of a triple therapy regimen with amoxicillin and clarithromycin, are the equivalent of 20 mg esomeprazole orally twice daily for 7 days, or 40 mg once daily for 10 days.

Oral doses of 20 mg daily, for 4 to 8 weeks, are used in the treatment of **NSAID-associated ulceration**; a dose of 20 mg daily may also be used for prophylaxis in patients at risk of such lesions who require continued NSAID treatment.

In the UK, the dose for treatment of severe (erosive) **gastro-oesophageal reflux disease** is 40 mg once daily for 4 weeks, extended for a further 4 weeks if necessary; in the USA, where doses of 20 or 40 mg daily are permitted for initial treatment, a further 4 to 8 weeks of treatment may be considered for patients who do not heal after 4 to 8 weeks. For maintenance, or for symptomatic disease without erosive oesophagitis, doses equivalent to 20 mg of esomeprazole daily may be used in both countries.

For the treatment of **Zollinger-Ellison syndrome**, the recommended initial oral dose of esomeprazole is 40 mg twice daily, which is then adjusted as needed. The majority of patients can be controlled on doses between 80 and 160 mg daily, although doses of 240 mg have been given. Doses above 80 mg daily should be given in 2 divided doses.

PARENTERAL DOSAGE.

Similar doses to the above may be given intravenously for gastro-oesophageal reflux disease and NSAID-associated ulceration. Esomeprazole is given as the sodium salt by slow intravenous injection over at least 3 minutes or by intravenous infusion over 10 to 30 minutes.

Doses of esomeprazole may need to be reduced in patients with hepatic impairment (see below).

◊ References.

1. Maton PN, *et al.* Safety and efficacy of long term esomeprazole therapy in patients with healed erosive oesophagitis. *Drug Safety* 2001; **24:** 625–35.
2. Scott LJ, *et al.* Esomeprazole: a review of its use in the management of acid-related disorders. *Drugs* 2002; **62:** 1503–38.
3. Keating GM, Figgitt DP. Intravenous esomeprazole. *Drugs* 2004; **64:** 875–82.
4. Metz DC, *et al.* Comparison of the effects of intravenously and orally administered esomeprazole on acid output in patients with symptoms of gastro-oesophageal reflux disease. *Aliment Pharmacol Ther* 2005; **22:** 813–21.
5. Edwards SJ, *et al.* Systematic review: proton pump inhibitors (PPIs) for the healing of reflux oesophagitis - a comparison of esomeprazole with other PPIs. *Aliment Pharmacol Ther* 2006; **24:** 743–50.