

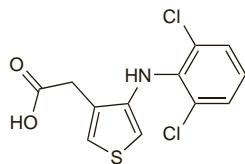
Maxigan (Максиган); Nebalgan (Небалган); Pentalgin-N (Пенталгин-Н); Revalgin (Ревалгин); Sedal-M (Седал-М); Sedalgin-Neo (Седальгин-Нео); Spasgan (Спазган); Spasmalgon (Спазмалгон); Spasmalin (Спазмалин); Tempalgin (Темпалгин); Tempanginol (Темпангинол); **S.Afr.:** Baralgan; Buscopan Compositum; Norfortan; Scopex Co. **Spain:** Buscapina Compositum; Nolotil Compositum; **Thai:** Butanion; Novapam. **Turk:** Buscopan Compositum; Peralgin; Scopolin. **Venez.:** Bortil; Buscapina Compositum; Butilamina Compuesta; Cotaril; Diezol Compuesto; Flemibar; Hioscinol Compuesto; Praxona; Sarfan Compuesto; Sistolcin Compositum.

### Eltenac (rINN)

Elténac; Eltenaco; Eltenacum. 4-(2,6-Dichloroanilino)-3-thiophe-neoic acid.

Эльтенак

$C_{12}H_9Cl_2NO_2S = 302.2$ .  
CAS — 72895-88-6.



### Profile

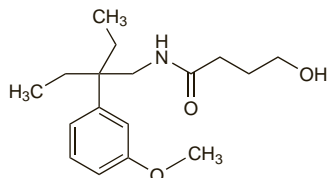
Elténac is an NSAID (p.96) used in veterinary medicine.

### Embutramide (BAN, USAN, rINN)

Embutramida; Embutramidum; Hoe-18-680. N-(β,β-Diethyl-methoxyphenethyl)-4-hydroxybutyramide.

Эмбутрамида

$C_{17}H_{27}NO_3 = 293.4$ .  
CAS — 15687-14-6.



### Profile

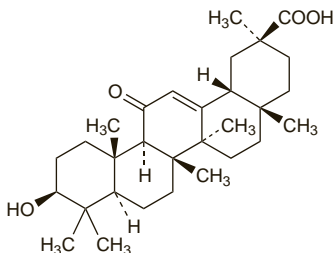
Embutramide is an opioid analgesic used in veterinary medicine for euthanasia.

### Enoxolone (BAN, rINN)

Enoksolonas; Enoksoloni; Enoxolon; Enoxolona; Énoxolone; Enoxolonum; Glycyrrhetic Acid; Glycyrrhetic Acid; Kwas glicyryzowy; 3β-Hydroxy-11-oxo-olean-12-en-30-oic acid.

ЭНОКСОЛОН

$C_{30}H_{46}O_4 = 470.7$ .  
CAS — 471-53-4.  
ATC — D03AX10.  
ATC Vet — QD03AX10.



NOTE. Do not confuse with glycyrrhizic acid (p.2316).

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

**Ph. Eur. 6.2** (Enoxolone). A white or almost white, crystalline powder. It exhibits polymorphism. Practically insoluble in water; soluble in dehydrated alcohol; sparingly soluble in dichloromethane. Protect from light.

### Profile

Enoxolone is a complex triterpene prepared from glycyrrhetic acid (p.2316), a constituent of liquorice (p.1740). Enoxolone is used locally in preparations for the treatment of non-infective in-

flammatory disorders of the skin, mouth, throat, and rectum. Enoxolone potassium (potassium glycyrrhetinate) has been used similarly.

Derivatives of enoxolone, including its aluminium salt (p.1729) and carbenoxolone (p.1714) have been used in the treatment of benign peptic ulcer disease and other gastrointestinal disorders.

◇ Enoxolone is a potent inhibitor of the enzyme 11β-hydroxysteroid dehydrogenase, which inactivates cortisol, and use with hydrocortisone has been shown in *animal* studies to potentiate the activity of hydrocortisone in skin.<sup>1</sup> Whether this also increased the systemic absorption and toxicity of hydrocortisone was unclear.<sup>2</sup> However, for reference to adverse effects attributed to systemic inhibition of cortisol when enoxolone (glycyrrhetic acid) is produced during metabolism of ingested liquorice, see Effects on Fluid and Electrolyte Homeostasis, p.1740.

A cream containing enoxolone with hyaluronic acid, telmesteine, and a grape extract, has been investigated with apparent benefit in the management of mild to moderate eczema.<sup>3,4</sup> However, topical application of enoxolone has been associated with contact dermatitis.<sup>5</sup>

- Teelucksingh S, *et al.* Potentiation of hydrocortisone activity in skin by glycyrrhetic acid. *Lancet* 1990; **335**: 1060-3.
- Greaves MW. Potentiation of hydrocortisone activity in skin by glycyrrhetic acid. *Lancet* 1990; **336**: 876.
- Belloni G, *et al.* A randomised, double-blind, vehicle-controlled study to evaluate the efficacy and safety of MAS063D (Atopiclair) in the treatment of mild to moderate atopic dermatitis. *Eur J Dermatol* 2005; **15**: 31-6.
- Abramovits W, Boguniewicz M. Adult Atopiclair Study Group. A multicenter, randomized, vehicle-controlled clinical study to examine the efficacy and safety of MAS063DP (Atopiclair) in the management of mild to moderate atopic dermatitis in adults. *J Drugs Dermatol* 2006; **5**: 236-44.
- Tanaka S, *et al.* Allergic contact dermatitis from enoxolone. *Contact Dermatitis* 2001; **44**: 192.

### Preparations

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

**Belg.:** Dermanox; **Fr.:** Arthrodont; Moustidose; PO 12; **S.Afr.:** Arthrodont.

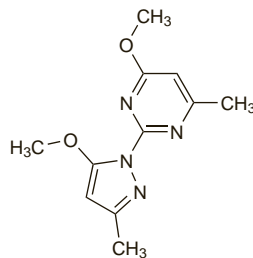
**Multi-ingredient:** **Arg.:** Anastim con RTH; Empecid Pie; **Chile:** Ginglacert; Ruboni; Sebiom AKN; Suavigel; **Fr.:** Apaisance; Erygine; Fluocanil dents sensibles; Hexalyse; Hyseke; Hyseke Solaire; Mousticoligne; Moustidose Bebe-Nourrison; Night Peel; Novophane; Novophane S; Photoderm Flush; Photoderm Laser; Pyreflor; Sebiom AKN; Sedorrohoide; Tiq'Aouta; Vocady; **Hong Kong:** Hexalyse; **Indon.:** Polik; **Israel:** Aphantone; Aphantax; Gelclair; **Ital.:** Acnesant; Bactilene; Benodent Gel Gengivale; Biothymus DS; Eudent con Glysant; Fluocanil; Lenipasta; Lenirose; Lisomucl Gola; Neo-Stomygen; Pastiglie Valda; Prurex; Skab 2; Viderm; **Mex.:** Angenovag; Periodenty; **Port.:** Despigmantante; **Rus.:** Hexalyse (Гексальза); **Spain:** Angileptol; Anginovag; Roberfanin; **UK:** Atopiclair; Geldair; Xclair; **USA:** Atopiclair; Geldair; **Venez.:** Sebiom AKN; Sensibio DS.

### Epirizole (USAN, pINN)

DA-398; Epirizol; Épirizole; Epirizolum; Mepirizole. 4-Methoxy-2-(5-methoxy-3-methylpyrazol-1-yl)-6-methylpyrimidine.

ЭПИРИЗОЛ

$C_{11}H_{14}N_4O_2 = 234.3$ .  
CAS — 18694-40-1.



**Pharmacopoeias.** In *Jpn.*

### Profile

Epirizole is an NSAID (p.96) that has been given in a usual oral dose of 150 to 450 mg daily in divided doses; larger doses of up to 600 mg daily have been used in patients with rheumatoid arthritis.

### Preparations

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

**Braz.:** Mebront; **Jpn.:** Mebront; **Venez.:** Dalex.

### Etanercept (BAN, USAN, rINN)

Étanercept; Etanerceptum; Etanersept; Etanersepti; rhu-TNFRFc; TNR-001. A dimer of 1-235 tumour necrosis factor receptor (human) fusion protein with 236-467-immunoglobulin G1 (human γ1-chain Fc fragment).

Этанерцепт

CAS — 185243-69-0.  
ATC — L04AB01.  
ATC Vet — QL04AB01.

### Adverse Effects and Precautions

As for Infliximab, p.69.

Mild to moderate injection site reactions with symptoms of erythema, itching, pain, or swelling are common with etanercept. Other common reactions include headache, dizziness, asthenia, nausea and vomiting, abdominal pain, dyspepsia, and allergic reactions. Antibodies to etanercept may develop.

Etanercept should be used with caution in patients with heart failure.

◇ References.

- Sánchez Carazo JL, *et al.* Safety of etanercept in psoriasis: a critical review. *Drug Safety* 2006; **29**: 675-85.

**Wegener's granulomatosis.** The addition of etanercept to standard therapy (including cyclophosphamide or methotrexate and corticosteroids) was not shown to be effective in patients with Wegener's granulomatosis and was associated with an increased incidence of various non-cutaneous malignancies.<sup>1</sup> Licensed product information recommends that etanercept should not be added to therapy in patients with Wegener's granulomatosis.

- Wegener's Granulomatosis Etanercept Trial (WGET) Research Group. Etanercept plus standard therapy for Wegener's granulomatosis. *N Engl J Med* 2005; **352**: 351-61.

### Interactions

As for Infliximab, p.71. The use of etanercept with sulfasalazine has resulted in decreased white blood cell counts; however, the clinical significance of this is unknown. For an increased incidence of malignancy when etanercept was added to standard immunosuppressive therapy in patients with Wegener's granulomatosis, see above.

### Pharmacokinetics

After a single subcutaneous dose of etanercept, UK licensed product information states that the mean half-life is about 70 hours, and the time to peak serum concentration 48 hours. In contrast, US information gives the half-life as 102 hours and the time to peak concentration as about 70 hours, although with a considerable range. Repeated dosing was noted to result in a two- to sevenfold increase in serum levels of etanercept in some patients.

◇ References.

- Korth-Bradley JM, *et al.* The pharmacokinetics of etanercept in healthy volunteers. *Ann Pharmacother* 2000; **34**: 161-4.
- Zhou H. Clinical pharmacokinetics of etanercept: a fully humanized soluble recombinant tumor necrosis factor receptor fusion protein. *J Clin Pharmacol* 2005; **45**: 490-7.
- Yim D-S, *et al.* Population pharmacokinetic analysis and simulation of the time-concentration profile of etanercept in pediatric patients with juvenile rheumatoid arthritis. *J Clin Pharmacol* 2005; **45**: 246-56.
- Don BR, *et al.* The pharmacokinetics of etanercept in patients with end-stage renal disease on haemodialysis. *J Pharm Pharmacol* 2005; **57**: 1407-13.
- Sullivan JT, *et al.* Bioequivalence of liquid and reconstituted lyophilized etanercept subcutaneous injections. *J Clin Pharmacol* 2006; **46**: 654-61.
- Nestorov I, *et al.* Pharmacokinetics of subcutaneously administered etanercept in subjects with psoriasis. *Br J Clin Pharmacol* 2006; **62**: 435-45.
- Elewski B, *et al.* Comparison of clinical and pharmacokinetic profiles of etanercept 25 mg twice weekly and 50 mg once weekly in patients with psoriasis. *Br J Dermatol* 2007; **156**: 138-42.

### Uses and Administration

Etanercept is a recombinant version of soluble human tumour necrosis factor (TNF) receptor that binds specifically to tumour necrosis factor (p.783) and blocks its interaction with endogenous cell-surface TNF receptors. This interaction prevents the important effect of TNF in the inflammatory processes of rheumatoid arthritis; elevated TNF levels are also found in psoriatic plaques, in the synovium of patients with psoriatic arthritis, and in the serum and synovium of patients with ankylosing spondylitis.

Etanercept is used in the treatment of moderately to severely active **rheumatoid arthritis** and active and progressive **psoriatic arthritis**. In the UK, it is licensed for use in patients who have had an inadequate response to standard disease-modifying antirheumatic drugs although, in severe rheumatoid arthritis, it may be used in patients not previously treated with methotrexate. In the USA, it is licensed to treat early rheumatoid arthritis or psoriatic arthritis, to reduce the signs