Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Austria:*** Coldadolin; Dolmix; Helopyrin; Nisicur; Seltoc; ***Cz.:*** Cephyl†; ***Ger.:*** Glutisal†; Kolton grippale N†; ***Indon.:*** Farapon; Neo Novapon Plus; ***Jpn:*** Sin Colgen Kowa Kaze; ***Pol.:*** Erka; Etomar; Etopiryna; ***Port.:*** Cephyl; ***Rus.:*** Nextrim Aktiv (Нектрим Актив); ***Switz.:*** Nicaphlogyl†; Seranex sans codeine†.

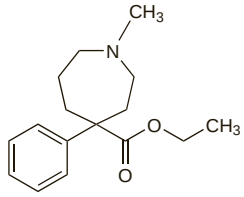
Ethoheptazine Citrate *(BANM, rINNM)*

Citrato de etoheptacina; Éthoheptazine, Citrate d'; Ethoheptazini Citras; Wy-401. Ethyl 1-methyl-4-phenylperhydroazepine-4-carboxylate dihydrogen citrate.

Этогептазина Цитрат

$C_{16}H_{23}NO_2,C_6H_8O_7$ = 453.5.

CAS — 77-15-6 (ethoheptazine); 6700-56-7 (ethoheptazine citrate); 2085-42-9 ((±)-ethoheptazine citrate).



(ethoheptazine)

Profile

Ethoheptazine citrate is an opioid analgesic (p.101) structurally related to pethidine (p.113). It has been used as an analgesic in the short-term treatment of mild to moderate pain, usually with other drugs such as aspirin and meprobamate.

Preparations

Proprietary Preparations (details are given in Part 3)

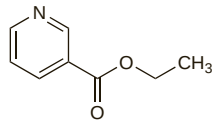
Multi-ingredient: ***India:*** Equagesic; ***S.Afr.:*** Equagesic.

Ethyl Nicotinate

Nicotinato de etilo.

$C_8H_9NO_2$ = 151.2.

CAS — 614-18-6.



Profile

Ethyl nicotinate is used in concentrations of up to 2% in topical rubefacient preparations for the relief of pain in musculoskeletal, joint, and soft-tissue disorders. It has also been used as suppositories in anorectal disorders.

Preparations

Proprietary Preparations (details are given in Part 3)

Austria: Mucotherm.

Multi-ingredient: ***Austria:*** Percucor†; Thermal; ***Belg.:*** Transvane; ***Hung.:*** Nicoflex; ***Irl.:*** Transvasin; ***Norw.:*** Thermal†; ***Switz.:*** Baume Esco Forte; Frixo-Dragon Vert†; Knobel Huile N; Thermocutan†; Ziegella; ***UK:*** PR Heat Spray; Transvasin Heat Rub.

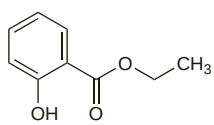
Ethyl Salicylate

Salicilato de etilo. Ethyl 2-hydroxybenzoate.

Этилсалицилат

$C_9H_{10}O_3$ = 166.2.

CAS — 118-61-6.



Profile

Ethyl salicylate is a salicylic acid derivative that is used similarly to methyl salicylate (p.85) in concentrations of up to 5% in topical rubefacient preparations for the relief of pain in musculoskeletal, joint, and soft-tissue disorders.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Austral.:*** Deep Heat; Radian-B†; ***Belg.:*** Rado-Salil; ***Israel:*** Deep Heat Spray; ***Ital.:*** Remy; ***Pol.:*** Deep Heat; ***S.Afr.:*** Deep Heat Spray; ***Singapore:*** Deep Heating Spray†; ***Switz.:*** Alginex†; ***UK:*** Deep Heat Spray; Dubam; Numark Muscle Spray; Ralgex.

Ethylmorphine Hydrochloride *(BANM)*

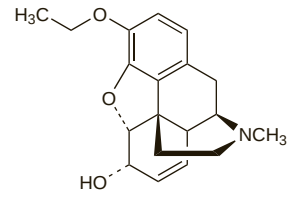
Aethylmorphinae Hydrochloridum; Aethylmorphini Hydrochloridum; Chlorhydrate de Codéthyline; Ethylmorfin-hydrochlorid dihydrát; Éthylmorphine, chlorhydrate d'; Ethylmorphini hydrochloridum; Ethylmorphini Hydrochloridum Dihydricum; Ethylmorphinium Chloride; Etilmorfina, hidrocloruro de; Etilmorfin-hidroklorid; Etilmorfino hidrochloridas; Etylmorfinhydroklorid; Etylomorfiny chlorowodorek; Etyylimorfiinihydrokloridi. 3-*O*-Ethylmorphine hydrochloride dihydrate; 7,8-Didehydro-4,5-epoxy-3-ethoxy-17-methylmorphinan-6-ol hydrochloride dihydrate.

$C_{19}H_{23}NO_3$,HCl,2H_2O = 385.9.

CAS — 76-58-4 (ethylmorphine); 125-30-4 (ethylmorphine hydrochloride).

ATC — R05DA01; S01XA06.

ATC Vet — QR05DA01; QS01XA06.



(ethylmorphine)

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

Ph. Eur. 6.2 (Ethylmorphine Hydrochloride). A white or almost white crystalline powder. Soluble in water and in alcohol. A 2% solution in water has a pH of 4.3 to 5.7. Protect from light.

Profile

Ethylmorphine hydrochloride is an opioid analgesic (p.101) and has properties similar to those of codeine (p.37). It is used mainly as a cough suppressant. It has also been used for its analgesic and antidiarrhoeal properties. It was formerly given in eye drops as a lymphagogue.

Ethylmorphine free base and the camphorate and camsilate have also been used.

◊ References.

1. Aasmundstad TA, *et al.* Biotransformation and pharmacokinetics of ethylmorphine after a single oral dose. *Br J Clin Pharmacol* 1995; **39:** 611–20.
2. Jonasson B, *et al.* Fatal poisonings where ethylmorphine from antitussive medications contributed to death. *Int J Legal Med* 1999; **112:** 299–302.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Dionina; ***Belg.:*** Codethyline; ***Cz.:*** Diolan; ***Fin.:*** Cocillana; ***Fr.:*** Dithiol†; ***UK:*** Collins Elixir.

Multi-ingredient: ***Austria:*** Modiscop; ***Belg.:*** Longbalsem; Saintbois; Tux†; ***Chile:*** Codelasa; ***Fin.:*** Indalgin; ***Fr.:*** Ephydion; Humex†; Tussipax; Vegetoserum; ***Hung.:*** Dolor; ***India:*** Bell Diono Resolvent; Bell Resolvent; ***Ital.:*** Mindol-Merck†; ***Norw.:*** Cosylan; Solvipect comp; ***Port.:*** Bronquiasmol†; Calmarum†; Xarope Antigripal†; ***Spain:*** Demusin; Sedalmerck†; ***Swed.:*** Cocillana-Etyfin; Lepheton; ***Switz.:*** Ipeca†; Phol-Tux; Saintbois; Sano Tuss; ***Turk.:*** Fenokodin; ***Venez.:*** Novacodin.

Etodolac *(BAN, USAN, rINN)*

AY-24236; Etodolaakki; Étodolac; Etodolaco; Etodolacum; Etodolák; Etodolak; Etodolakas; Etodolic Acid. 1,8-Diethyl-1,3,4,9-tetrahydropyrano[3,4-*b*]indol-1-ylacetic acid.

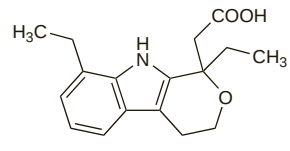
Этодолак

$C_{17}H_{21}NO_3$ = 287.4.

CAS — 41340-25-4.

ATC — M01AB08.

ATC Vet — QM01AB08.



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

Ph. Eur. 6.2 (Etodolac). A white or almost white crystalline powder. Practically insoluble in water; freely soluble in dehydrated alcohol and in acetone.

USP 31 (Etodolac). Store in airtight containers.

Adverse Effects, Treatment, and Precautions

As for NSAIDs in general, p.96.

The presence of phenolic metabolites of etodolac in the urine may give rise to a false-positive reaction for bilirubin.

Effects on the blood. Agranulocytosis has been reported in a patient receiving etodolac.[1] Coombs-positive haemolytic anaemia due to sensitivity to etodolac metabolites has also been reported.[2]

1. Cramer RL, *et al.* Agranulocytosis associated with etodolac. *Ann Pharmacother* 1994; **28:** 458–60.
2. Cunha PD, *et al.* Immune hemolytic anemia caused by sensitivity to a metabolite of etodolac, a nonsteroidal anti-inflammatory drug. *Transfusion* 2000; **40:** 663–8.

Effects on the gastrointestinal tract. Etodolac is reported to be a preferential inhibitor of cyclo-oxygenase 2 (COX-2) and consequently it may produce less gastric toxicity than the non-selective NSAIDs such as naproxen.[1-3]

1. Taha AS, *et al.* Effect of repeated therapeutic doses of naproxen and etodolac on gastric and duodenal mucosal prostaglandins (PGs) in rheumatoid arthritis (RA). *Gut* 1989; **30:** A751.
2. Bianchi Porro G, *et al.* A double-blind gastroscopic evaluation of the effects of etodolac and naproxen on the gastrointestinal mucosa of rheumatic patients. *J Intern Med* 1991; **229:** 5–8.
3. Weideman RA, *et al.* Risks of clinically significant upper gastrointestinal events with etodolac and naproxen: a historical cohort analysis. *Gastroenterology* 2004; **127:** 1322–8.

Interactions

For interactions associated with NSAIDs, see p.99.

Pharmacokinetics

Etodolac is a chiral compound given as the racemate. Peak plasma concentrations of the active (S)-enantiomer and of the inactive (R)-enantiomer are usually obtained within about 2 hours of a dose by mouth but plasma concentrations of the (R)-enantiomer have been reported to greatly exceed those of the (S)-enantiomer. Both enantiomers are highly bound to plasma proteins. Both are also distributed to the synovial fluid, although the difference in their concentrations may not be as marked as the difference in plasma concentrations. The plasma half-life of total etodolac has been reported to be about 7 hours; excretion is mainly in the urine as hydroxylated metabolites and glucuronide conjugates; some may be excreted in the bile.

◊ References.

1. Brocks DR, *et al.* Stereoselective disposition of etodolac enantiomers in synovial fluid. *J Clin Pharmacol* 1991; **31:** 741–6.
2. Brocks DR, *et al.* The stereoselective pharmacokinetics of etodolac in young and elderly subjects, and after cholecystectomy. *J Clin Pharmacol* 1992; **32:** 982–9.
3. Brocks DR, Jamali F. Etodolac clinical pharmacokinetics. *Clin Pharmacokinet* 1994; **26:** 259–74.
4. Boni J, *et al.* Pharmacokinetic and pharmacodynamic action of etodolac in patients after oral surgery. *J Clin Pharmacol* 1999; **39:** 729–37.
5. Boni JP, *et al.* Pharmacokinetics of etodolac in patients with stable juvenile rheumatoid arthritis. *Clin Ther* 1999; **21:** 1715–24.

Uses and Administration

Etodolac, a pyrano-indoleacetic acid derivative, is an NSAID (p.99) reported to be a preferential inhibitor of cyclo-oxygenase 2 (COX-2). It is used for rheumatoid arthritis, including juvenile idiopathic arthritis, and osteoarthritis and for the treatment of acute pain.

For the treatment of rheumatoid arthritis and osteoarthritis, the recommended oral dose is initially 600 to 1000 mg daily in divided doses adjusted according to response; single daily doses of up to 600 mg may also be given. Modified-release preparations are available for once-daily use in these conditions. For doses in children, see below.

For the treatment of acute pain, the recommended dose is 200 to 400 mg every 6 to 8 hours to a maximum of 1 g daily.

Administration in children. In the USA modified-release preparations of etodolac may be given for the oral treatment of juvenile idiopathic arthritis in children aged 6 to 16 years. Doses are given once daily according to body-weight as follows:

- 20 to 30 kg: 400 mg
- 31 to 45 kg: 600 mg
- 46 to 60 kg: 800 mg
- over 60 kg: 1 g