Preparations

BP 2008: Cocaine Eye Drops;
USP 31: Cocaine and Tetracaine Hydrochlorides and Epinephrine Topical Solution; Cocaine Hydrochloride Tablets for Topical Solution.

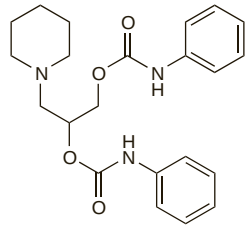
Diperodon Hydrochloride *(BANM, rINNM)*

Diperocaine Hydrochloride; Dipérodon, Chlorhydrate de; Diperodoni Hydrochloridum; Hidrocloruro de diperodón. 3-Piperidinopropylene bis(phenylcarbamate) hydrochloride.

Диперодона Гидрохлорид

$C_{22}H_{27}N_3O_4$,HCl = 433.9.

CAS — 101-08-6 (anhydrous diperodon); 51552-99-9 (diperodon monohydrate); 537-12-2 (diperodon hydrochloride).



(diperodon)

Profile

Diperodon is a local anaesthetic (p.1850) that has been used as the base or the hydrochloride for surface anaesthesia.

Dyclonine Hydrochloride *(BANM, rINNM)*

Dyclocaine Hydrochloride; Dyclocaini Chloridum; Dyclonine, Chlorhydrate de; Dyclonini Hydrochloridum; Hidrocloruro de diclonina. 4′-Butoxy-3-piperidinopropiophenone hydrochloride.

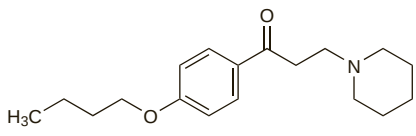
Диклонина Гидрохлорид

$C_{18}H_{27}NO_2$,HCl = 325.9.

CAS — 586-60-7 (dyclonine); 536-43-6 (dyclonine hydrochloride).

ATC — N01BX02; R02AD04.

ATC Vet — QN01BX02; QR02AD04.



(dyclonine)

Pharmacopoeias. In *US*.
USP 31 (Dyclonine Hydrochloride). White crystals or white crystalline powder, with a slight odour. Soluble 1 in 60 of water, 1 in 24 of alcohol, and 1 in 2.3 of chloroform; soluble in acetone; practically insoluble in ether and in hexane. A 1% solution in water has a pH of 4.0 to 7.0. Store in airtight containers. Protect from light.

Profile

Dyclonine hydrochloride is a local anaesthetic (p.1850) used topically for surface anaesthesia of the skin and mucous membranes. Lozenges containing up to 3 mg and throat sprays containing 0.1% of dyclonine hydrochloride have been used for the temporary relief of pain associated with sore throats or mouth irritation; a 1% gel has also been used. A concentration of 0.75% has been used on the skin. It may cause irritation at the site of application.

Preparations

USP 31: Dyclonine Hydrochloride Gel; Dyclonine Hydrochloride Topical Solution.

Proprietary Preparations (details are given in Part 3)

Canad.: Cepacol Spray; Sucrets; Sucrets for Kids; ***Israel:*** Childrens Cherry Sucrets†; Sucrets Children's Formula†; Sucrets Maximum Strength†; ***USA:*** Dyclone†; Sucrets Childrens Formula; Sucrets Original Formula Sore Throat Wild Cherry; Sucrets Throat Spray.

Multi-ingredient: ***Canad.:*** Tanac†; ***USA:*** Cepacol Maximum Strength Sore Throat; Skin Shield; Sucrets Complete; Sucrets Maximum Strength Sore Throat; Tanac.

Ethyl Chloride

Aethylium Chloratum; Chlorethyl; Cloruro de etilo; Ethyli Chloridum; Ethylis Chloridum; Etylklorid; Etylu chlorek; Etyylikloridi; Hydrochloric Ether; Monochlorethane. Chloroethane.

C_2H_5Cl = 64.51.

CAS — 75-00-3.

ATC — N01BX01.

ATC Vet — QN01BX01.

Pharmacopoeias. In *Pol.* and *US*.
USP 31 (Ethyl Chloride). A colourless, mobile, very volatile liquid at low temperatures or under pressure, with a characteristic ethereal odour. B.p. 12° to 13°. Slightly soluble in water; freely soluble in alcohol and in ether. Store in airtight containers, preferably hermetically sealed.

Stability. Ethyl chloride is highly flammable and mixtures of the gas with 5 to 15% of air are explosive.

Adverse Effects and Precautions

As for Chloroform, p.1781.

Cutaneous sensitisation can occur rarely. Thawing of frozen tissue following surgery may be painful and prolonged spraying onto the skin can cause chemical frostbite. Freezing may also distort the histological structure of biopsy specimens. Ethyl chloride should not be applied to broken skin or mucous membranes.

Uses and Administration

Owing to its low boiling-point and the intense cold produced by evaporation, ethyl chloride has been used as a local anaesthetic in minor surgery but such use is not generally recommended. It has also been used topically for the relief of pain and to test the effectiveness of regional anaesthesia. Ethyl chloride was formerly used as an inhalational anaesthetic but has no place in modern anaesthetic practice.

Preparations

Proprietary Preparations (details are given in Part 3)
Ger.: Chloraethyl Dr Henning; WariActiv; ***Hong Kong:*** WariActiv; ***Hung.:*** Chloraethyl†; ***Israel:*** Chloraethyl Dr Henning; ***Mex.:*** Traumazol; ***Spain:*** Cloretilo Chemirosa; ***Switz.:*** Chlorethyl; ***UK:*** Cryogesic.

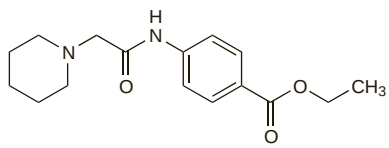
Multi-ingredient: ***USA:*** Fluro-Ethyl.

Ethyl *p*-Piperidinoacetylaminobenzoate

EPAB; *p*-Piperidinoacetilaminobenzoato de etilo; SA-7. 4-[(1-Piperidinylacetyl)amino]benzoic acid ethyl ester.

$C_{16}H_{22}N_2O_3$ = 290.4.

CAS — 41653-21-8.



Profile

Ethyl *p*-piperidinoacetylaminobenzoate is an amide local anaesthetic (p.1850) that has been given orally for the symptomatic relief of gastritis.

Preparations

Proprietary Preparations (details are given in Part 3)
Jpn: Sulcain.

Multi-ingredient: ***Hong Kong:*** Sulcain†; ***Singapore:*** Sulcain†; ***Thai.:*** Sulcain†.

Etidocaine *(BAN, USAN, rINN)*

Etidocaína; Étidocaïne; Etidocainum; Etidokaiini; Etidokain. (±)-2-(*N*-Ethylpropylamino)-butyro-2′,6′-xylidide.

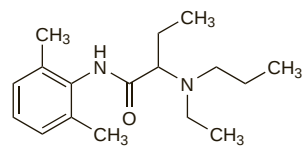
Этидокаин

$C_{17}H_{28}N_2O$ = 276.4.

CAS — 36637-18-0.

ATC — N01BB07.

ATC Vet — QN01BB07.



Etidocaine Hydrochloride *(BANM, rINNM)*

Étidocaïne, Chlorhydrate d'; Etidocaini Hydrochloridum; Hidrocloruro de etidocaína; W-19053.

Этидокаина Гидрохлорид

$C_{17}H_{28}N_2O$,HCl = 312.9.

CAS — 36637-19-1.

ATC — N01BB07.

ATC Vet — QN01BB07.

Adverse Effects, Treatment, and Precautions

As for Local Anaesthetics in general, p.1850.

Effects on the cardiovascular system. For a discussion of the cardiotoxicity of etidocaine, see under the Adverse Effects of Bupivacaine Hydrochloride, p.1855.

Porphyria. Etidocaine is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *animals*.

Interactions

For interactions associated with local anaesthetics, see p.1851.

Pharmacokinetics

Etidocaine is rapidly absorbed into the circulation after parenteral injection and is about 95% bound to plasma proteins. It crosses the placenta but the ratio of fetal to maternal concentrations is relatively low. It also diffuses across the blood-brain barrier. Etidocaine is metabolised in the liver and its numerous metabolites are excreted in the urine; less than 10% of the drug is excreted unchanged. The plasma elimination half-life of etidocaine is 2 to 3 hours in adults.

See also under Local Anaesthetics, p.1852.

Pregnancy. After maternal injection etidocaine rapidly crosses the placenta[1] but the degree of transfer is less than for other local anaesthetics including bupivacaine.[2] The ratio of fetal to maternal concentrations of etidocaine varies but values up to about 0.35 are usual.[1,2] Some metabolites appear to be transferred to a greater degree than the parent compound[1]. Etidocaine is highly protein bound but the fraction of unbound drug in plasma increases in pregnant women during delivery.[1] Protein binding of etidocaine is also reduced in fetal plasma.[3] Although neonates are able to metabolise etidocaine it appears that they are less able to do so than adults; a mean elimination half-life of 6.42 hours has been reported in neonates.[3]

1. Morgan DJ, *et al*. Disposition and placental transfer of etidocaine in pregnancy. *Eur J Clin Pharmacol* 1977; **12:** 359–65.
2. Poppers PJ. Evaluation of local anaesthetic agents for regional anaesthesia in obstetrics. *Br J Anaesth* 1975; **47:** 322–7.
3. Morgan D, *et al*. Pharmacokinetics and metabolism of the anilide local anaesthetics in neonates: 11: etidocaine. *Eur J Clin Pharmacol* 1978; **13:** 365–71.

Uses and Administration

Etidocaine hydrochloride is a local anaesthetic of the amide type with actions and uses similar to those described on p.1852. It has a rapid onset and a long duration of action. Etidocaine has been used for infiltration anaesthesia, peripheral nerve block, and epidural block, usually with adrenaline 1 in 200 000. (Local anaesthetic techniques are discussed on p.1853.)

Preparations

Proprietary Preparations (details are given in Part 3)
USA: Duranest†.

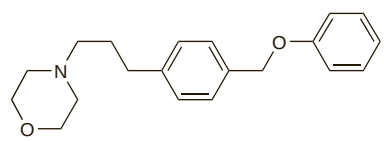
Fomocaine Hydrochloride *(BANM, rINNM)*

Fomocaïne, Chlorhydrate de; Fomocaini Hydrochloridum; Hidrocloruro de fomocaína. 4-[3-(α-Phenoxy-*p*-tolyl)propyl]morpholine hydrochloride.

Фомокаина Гидрохлорид

$C_{20}H_{25}NO_2$,HCl = 347.9.

CAS — 17692-39-6 (fomocaine); 56583-43-8 (fomocaine hydrochloride).



(fomocaine)

Profile

Fomocaine is a local anaesthetic that has been included, as the hydrochloride, in mixed products intended for use in infected skin conditions.

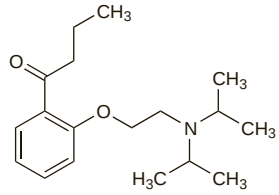
Ketocaine Hydrochloride *(rINNM)*

Chetocaina Cloridrata; Hidrocloruro de ketocaína; Kétocaïne, Chlorhydrate de; Ketocaini Hydrochloridum. 2′-(2-Di-isopropylaminoethoxy)butyrophenone hydrochloride.

Кетокаина Гидрохлорид

$C_{18}H_{29}NO_2,HCl$ = 327.9.

CAS — 1092-46-2 (ketocaine); 1092-47-3 (ketocaine hydrochloride).



(ketocaine)

Profile

Ketocaine hydrochloride is a local anaesthetic (p.1850) that has been used as a surface anaesthetic in suppositories or ointments for anorectal disorders.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Ital.:*** Proctolyn.

Levobupivacaine *(BAN, rINN)*

S(−)-Bupivacaine; Levobupivacaína; Lévobupivacaïne; Levobupivacainum; Levobupivakaiini; Levobupivakain. (*S*)-1-Butyl-2-piperidylformo-2′,6′-xylidide.

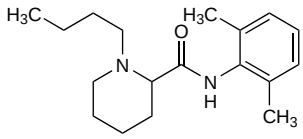
Левобупивакаин

$C_{18}H_{28}N_2O$ = 288.4.

CAS — 27262-47-1.

ATC — N01BB10.

ATC Vet — QN01BB10.



Levobupivacaine Hydrochloride

(BANM, USAN, rINNM)

Hidrocloruro de levobupivacaína; Lévobupivacaïne, Chlorhydrate de; Levobupivacaini Hydrochloridum; Levobupivakain Hidroklorür.

Левобупивакаина Гидрохлорид

$C_{18}H_{28}N_2O,HCl$ = 324.9.

CAS — 27262-48-2.

ATC — N01BB10.

ATC Vet — QN01BB10.

Adverse Effects, Treatment, and Precautions

As for Local Anaesthetics in general, p.1850.

Levobupivacaine is contra-indicated for use in intravenous regional anaesthesia (Bier's block) and for paracervical block in obstetrics. The 0.75% solution is also contra-indicated for epidural block in obstetrics.

Effects on the cardiovascular system. It has been suggested[1] that levobupivacaine may have a lower risk of causing cardiotoxicity than bupivacaine (for the effects of bupivacaine on the cardiovascular system see p.1855).

1. Mather LE, Chang DH. Cardiotoxicity with modern local anaesthetics: is there a safer choice? *Drugs* 2001; **61:** 333–42.

Interactions

For interactions associated with local anaesthetics, see p.1851. Plasma concentrations of levobupivacaine may be reduced by enzyme-inducing drugs such as rifampicin. Levobupivacaine is metabolised by the cytochrome P450 isoenzymes CYP3A4 and CYP1A2 and there is a theoretical possibility that substrates for or inhibitors of these isoenzymes may adversely alter plasma concentrations of levobupivacaine.

Pharmacokinetics

The pharmacokinetics of levobupivacaine are similar to those of the racemic form, bupivacaine (p.1855). Levobupivacaine is at least 97% bound to plasma proteins. After intravenous doses the mean half-life is about 80 minutes. Levobupivacaine is extensively metabolised and excreted as its metabolites mainly in the urine, with smaller amounts appearing in the faeces. 3-Hydroxylevobupivacaine is a major metabolite and its formation is mediated by the cytochrome P450 isoenzyme CYP1A2; the isoenzyme CYP3A4 is also involved in the metabolism of levobupivacaine.

Uses and Administration

Levobupivacaine is a local anaesthetic of the amide type with actions and uses similar to those described on p.1852. It is the S-enantiomer of bupivacaine (p.1854). Levobupivacaine is given as the hydrochloride for infiltration anaesthesia and regional nerve blocks including epidural block; however it is contra-indicated for obstetric paracervical block and for use in intravenous regional anaesthesia (Bier's block). The 0.75% solution is also contra-indicated for epidural blocks in obstetrics. (Local anaesthetic techniques are discussed on p.1853.)

Levobupivacaine hydrochloride is available in solutions containing the equivalent of 0.25 to 0.75% of levobupivacaine. The dosage depends on the site of injection and the procedure used as well as the status of the patient. The recommended **maximum single dose** is 150 mg. The total daily dose should not exceed 400 mg. A test dose of a suitable local anaesthetic, preferably with adrenaline, should be given before commencing epidural block with levobupivacaine to detect inadvertent intravascular injection. Subsequent doses of levobupivacaine should be given in small increments. Levobupivacaine should be given in reduced doses to elderly, debilitated, or acutely ill patients.

- For **surgical anaesthesia** doses of levobupivacaine for *epidural block* are 50 to 100 mg (10 to 20 mL) as a 0.5% solution, or 75 to 150 mg (10 to 20 mL) as a 0.75% solution; for caesarean section, doses are 75 to 150 mg (15 to 30 mL) as a 0.5% solution. The dose for *spinal block* is 15 mg (3 mL) as a 0.5% solution.
- For *peripheral nerve blocks*, doses are 2.5 to 150 mg as a 0.25 or 0.5% solution; a volume of 40 mL should not be exceeded. Alternatively doses for peripheral block have been expressed on the basis of body-weight: 1 to 2 mg/kg (0.4 mL/kg) as a 0.25 or 0.5% solution.
- For *infiltration anaesthesia* up to 150 mg (60 mL) as a 0.25% solution may be used. For peribulbar block in *ophthalmic* procedures 37.5 to 112.5 mg (5 to 15 mL) as a 0.75% solution may be given. For ilioinguinal or iliohypogastric blocks in **children** under 12 years, doses of levobupivacaine are 0.625 to 2.5 mg/kg (0.25 to 0.5 mL/kg) as a 0.25 or 0.5% solution.
- In the management of **acute pain** levobupivacaine may be given as an epidural bolus or by continuous infusion. For pain relief during *labour* 15 to 50 mg (6 to 20 mL) as a 0.25% solution is given as a bolus. Alternatively, a 0.125% solution may be given as an infusion in a dose of 5 to 12.5 mg (4 to 10 mL) per hour, or a 0.0625% solution may be given in a dose of 5 to 12.5 mg (8 to 20 mL) per hour. For *postoperative pain* 10 to 25 mg (4 to 10 mL) per hour as a 0.25% solution, 12.5 to 18.75 mg (10 to 15 mL) per hour as a 0.125% solution, or 12.5 to 18.75 mg (20 to 30 mL) per hour as a 0.0625% solution may be given as an epidural infusion.

In some countries such as the UK, licensed product information recommends that a lower concentration such as the 0.125% solution should be used if other analgesics are also given for pain relief; in other countries product information has specifically stated that the 0.125% solution should only be used for adjunctive therapy with fentanyl or clonidine. When necessary, dilutions should be made with sodium chloride 0.9%.

◊ Reviews

1. Foster RH, Markham A. Levobupivacaine: a review of its pharmacology and use as a local anaesthetic. *Drugs* 2000; **59:** 551–79.

Action. A comparison[1] of epidural bupivacaine with levobupivacaine in women in labour found that levobupivacaine had 98% of the potency of the racemate, a clinically insignificant difference. However it was pointed out that whereas the concentration of bupivacaine solutions was expressed in terms of the hydrochloride, solutions of levobupivacaine had their strength expressed in terms of the free base. When calculations were made in terms of molar equivalents levobupivacaine appeared to be 13% less potent than racemic bupivacaine. The difference in expression should be borne in mind when evaluating comparative studies.

1. Lyons G, *et al.* Epidural pain relief in labour: potencies of levobupivacaine and racemic bupivacaine. *Br J Anaesth* 1998; **81:** 899–901.

Preparations

Proprietary Preparations (details are given in Part 3)

Austral.: Chirocaine; ***Austria:*** Chirocaine; ***Belg.:*** Chirocaine; ***Braz.:*** Novabupi; ***Chile:*** Chirocaina; ***Cz.:*** Chirocaine; ***Fin.:*** Chirocaine; ***Fr.:*** Chirocaine; ***Gr.:*** Chirocaine; ***Hong Kong:*** Chirocaine; ***Hung.:*** Chirocaine; ***Irl.:*** Chirocaine; ***Ital.:*** Chirocaine; ***Mex.:*** Quirocaine; ***Neth.:*** Chirocaine; ***Norw.:*** Chirocaine; ***NZ:*** Chirocaine†; ***Philipp.:*** SensiBloq; ***Port.:*** Chirocaine; ***S.Afr.:*** Chirocaine; ***Singapore:*** Chirocaine; ***Spain:*** Chirocaine; ***Swed.:*** Chirocaine; ***Switz.:*** Chirocaine; ***Turk.:*** Chirocaine; ***UK:*** Chirocaine; ***USA:*** Chirocaine†; ***Venez.:*** Chirocaina.

Lidocaine *(BAN, rINN)*

Lidocaína; Lidocaïne; Lidocainum; Lidokaiini; Lidokain; Lidokaina; Lidokainas; Lignocaine. 2-Diethylaminoaceto-2′,6′-xylidide.

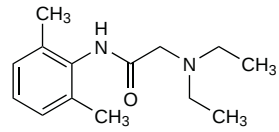
Лидокаин

$C_{14}H_{22}N_2O$ = 234.3.

CAS — 137-58-6.

ATC — C01BB01; C05AD01; D04AB01; N01BB02; R02AD02; S01HA07; S02DA01.

ATC Vet — QC01BB01; QC05AD01; QD04AB01; QN01BB02; QR02AD02; QS01HA07; QS02DA01.



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

Ph. Eur. 6.2 (Lidocaine). A white or almost white, crystalline powder. M.p. 66° to 70°. Practically insoluble in water; very soluble in alcohol and in dichloromethane.

USP 31 (Lidocaine). A white to slightly yellow crystalline powder with a characteristic odour. M.p. 66° to 69°. Practically insoluble in water; very soluble in alcohol and in chloroform; freely soluble in ether and in benzene; dissolves in oils.

Eutectic mixture. Lidocaine forms a mixture with prilocaine that has a melting-point lower than that of either ingredient. This eutectic mixture is used in the preparation of topical dosage forms.

Lidocaine Hydrochloride *(BANM, rINNM)*

Hidrocloruro de lidocaína; Lidocaïne, chlorhydrate de; Lidocaini hydrochloridum; Lidocaini Hydrochloridum Monohydricum; Lidokaiinihydrokloridi; Lidokain Hidroklorür; Lidokain-hidroklorid; Lidokain-hydrochlorid monohydrát; Lidokainhydroklorid; Lidokaino hidrochloridas; Lidokainy chlorowodorek; Lignoc. Hydrochlor.; Lignocaine Hydrochloride; Lignokain Hidroklorür.

Лидокаина Гидрохлорид

$C_{14}H_{22}N_2O,HCl,H_2O$ = 288.8.

CAS — 73-78-9 (anhydrous lidocaine hydrochloride); 6108-05-0 (lidocaine hydrochloride monohydrate).

ATC — C01BB01; C05AD01; D04AB01; N01BB02; R02AD02; S01HA07; S02DA01.

ATC Vet — QC01BB01; QC05AD01; QD04AB01; QN01BB02; QR02AD02; QS01HA07; QS02DA01.

NOTE. LIDFLN is a code approved by the BP 2008 for use on single unit doses of eye drops containing lidocaine hydrochloride and fluorescein sodium where the individual container may be too small to bear all the appropriate labelling information.

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

Ph. Eur. 6.2 (Lidocaine Hydrochloride). A white, or almost white, crystalline powder. M.p. 74° to 79°. Very soluble in water; freely soluble in alcohol. A 0.5% solution in water has a pH of 4.0 to 5.5. Protect from light.

USP 31 (Lidocaine Hydrochloride). A white, odourless, crystalline powder. M.p. 74° to 79°. Very soluble in water and in alcohol; soluble in chloroform; insoluble in ether.