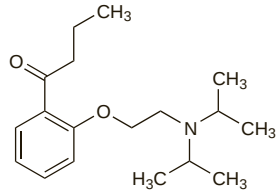
Ketocaine Hydrochloride *(rINNM)*

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.

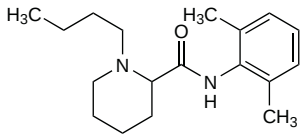
Левобупивакаин

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

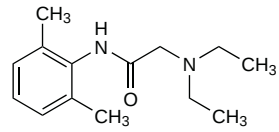
Лидокаин

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