***NZ:*** Asmafen; Zaditen; ***Philipp.:*** Zadec; Zaditen; ***Pol.:*** Zaditen; ***Port.:*** Bentifen; Cipanfeno; Quefeno†; Zaditen; ***Rus.:*** Zaditen (Задитен); Zetifen (Зетифен); ***S.Afr.:*** Ketohexal; Zaditen; Zetofen; ***Singapore:*** Asmafen†; Asumalife; Beatifen; Dhatifen; Erliten†; Tofen†; Zaditen; ***Spain:*** Ketasma†; Zaditen; Zasten; ***Swed.:*** Zaditen; ***Switz.:*** Zaditen; ***Thai.:*** Asmanoc†; Denerel†; Ibis; Katifen; Kenefen; Keten; Ketifen; Keto; Ketofen; Medkofen; Medotifen†; Politifen; Sykofen; Xidanef†; Zadino; Zaditen; Zytofen; ***Turk.:*** Astafen; Zaditen; ***UAE:*** Asmafort; ***UK:*** Zaditen; ***USA:*** Alaway; Zaditor; ***Venez.:*** Cosolve; Ketoptic; Ketotisin; Musibon†; Zaditen.

**Multi-ingredient:** ***Arg.:*** Airbronal†; Fatigan Bronquial†; Hyalcrom NF; Inastmol†; ***Mex.:*** Hyalcrom NF.

## Levocabastine Hydrochloride

*(BANM, USAN, rINNM)*

Hidrocloruro de levocabastina; Lévocabastine, chlorhydrate de; Levocabastini hydrochloridum; Levokabastiinihydrokloridi; Levokabastin-hydrochlorid; Levokabastinhydroklorid; Levokabastino hidrochloridas; Levokabasztin-hidroklorid; R-50547. (−)-*trans*-1-[*cis*-4-Cyano-4-(*p*-fluorophenyl)cyclohexyl]-3-methyl-4-phenylisonipecotic acid hydrochloride.

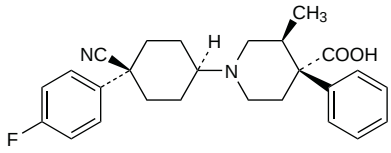
Левокабастина Гидрохлорид

$C_{26}H_{29}FN_2O_2$,HCl = 457.0.

*CAS — 79516-68-0 (levocabastine); 79547-78-7 (levocabastine hydrochloride); 79449-98-2 (cabastine).*

*ATC — R01AC02; S01GX02.*

*ATC Vet — QR01AC02; QS01GX02.*



*(levocabastine)*

NOTE. Cabastine *(rINN)* is the racemate of levocabastine.

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

**Ph. Eur. 6.2** (Levocabastine Hydrochloride). A white or almost white powder. Practically insoluble in water; slightly soluble in alcohol and in a 0.2% solution of sodium hydroxide; sparingly soluble in methyl alcohol. Protect from light.

**USP 31** (Levocabastine Hydrochloride). Protect from light.

### Adverse Effects and Precautions

As for the antihistamines in general, p.561. The most common adverse effects reported with levocabastine eye drops are transient stinging and burning of the eyes, urticaria, dyspnoea, drowsiness, and headache. With nasal use headache, nasal irritation, somnolence, and fatigue have been noted. The use of levocabastine nasal spray is not recommended in those with significant renal impairment.

### Pharmacokinetics

Levocabastine is absorbed after both nasal and ocular use. Systemic availability has been estimated at 60 to 80% after nasal doses and 30 to 60% after ocular use. However absolute peak plasma concentrations are low. Plasma protein binding is about 55%. An elimination half-life of 35 to 40 hours has been reported for all routes of delivery. Elimination of levocabastine is primarily renal with 70% excreted as unchanged drug and 10% as an inactive acetylglucuronide metabolite; the remaining 20% is excreted unchanged in the faeces.

Trace amounts of levocabastine have been found in breast milk after ocular and nasal use.

◊ References.

1. Heykants J, *et al.* The pharmacokinetic properties of topical levocabastine: a review. *Clin Pharmacokinet* 1995; **29:** 221–30.

### Uses and Administration

Levocabastine, a piperidine derivative, is a long-acting and potent antihistamine with a rapid onset of action. Levocabastine hydrochloride equivalent to 0.05% levocabastine is used topically twice daily as eye drops or as a nasal spray in the treatment of allergic conjunctivitis (p.564) and rhinitis (p.565), respectively, in adults and children aged 9 years and over. The frequency of the dose in both conditions may be increased to 3 or 4 times daily if necessary. In conjunctivitis it is recommended that treatment should be stopped if there is no improvement within 3 days.

◊ References.

1. Noble S, McTavish D. Levocabastine: an update of its pharmacology, clinically efficacy and tolerability in the topical treatment of allergic rhinitis and conjunctivitis. *Drugs* 1995; **50:** 1032–49.
2. Doughty MJ. Levocabastine, a topical ocular antihistamine available as a pharmacy medicine – a literature review. *Pharm J* 2002; **268:** 367–70.

### Preparations

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

***Arg.:*** Histimet; ***Austral.:*** Livostin; ***Austria:*** Livostin; ***Belg.:*** Livostin; ***Braz.:*** Livostin; ***Canad.:*** Livostin; ***Cz.:*** Livostin; ***Denm.:*** Livostin; ***Fin.:*** Livostin; ***Fr.:*** Levophta; ***Ger.:*** Levophta†; Livocab; ***Gr.:*** Livostin; ***Hung.:*** Livostin†; ***Israel:*** Livostin; ***Ital.:*** Levostab; Livocab; Livostin; ***Jpn:*** Livostin; ***Mex.:*** Livostin; ***Neth.:*** Livocab; ***Norw.:*** Livostin; ***NZ:*** Livostin; ***Port.:*** Livostin; ***S.Afr.:*** Livostin; ***Spain:*** Bilina; Livocab; ***Swed.:*** Livostin; ***Switz.:*** Livostin; ***Thai.:*** Livostin†; ***Turk.:*** Livostin; ***UK:*** Livostin; ***USA:*** Livostin†; ***Venez.:*** Livostin.

**Multi-ingredient:** ***Chile:*** Livostin.

## Levocetirizine *(BAN, USAN, rINN)*

Levocetirizina; Lévocétirizine; Levocetirizinum. (2-{4-[(*R*)-*p*-Chloro-α-phenylbenzyl]-1-piperazinyl}ethoxy)acetic acid.

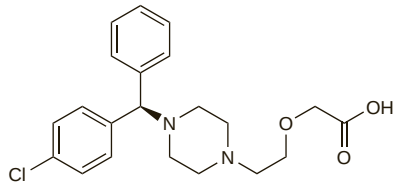
Левоцетиризин

$C_{21}H_{25}ClN_2O_3$ = 388.9.

*CAS — 130018-77-8.*

*ATC — R06AE09.*

*ATC Vet — QR06AE09.*



## Levocetirizine Hydrochloride *(BANM, rINNM)*

Hidrocloruro de levocetirizina; Lévocétirizine, Chlorhydrate de; Levocetirizine Dihydrochloride *(USAN)*; Levocetirizini Hydrochloridum; UCB-28556.

Левоцетиризина Гидрохлорид

$C_{21}H_{25}ClN_2O_3$,2HCl = 461.8.

*CAS — 130018-87-0.*

*ATC — R06AE09.*

*ATC Vet — QR06AE09.*

### Profile

Levocetirizine is the *R*-enantiomer of cetirizine (p.570) and is used similarly, as the hydrochloride, for the symptomatic relief of allergic conditions including rhinitis (p.565) and chronic urticaria (p.565). The usual oral dose of levocetirizine hydrochloride is 5 mg once daily. US licensed product information suggests that the dose should be given in the evening, and that a dose of 2.5 mg may be adequate in some patients.

For doses in children or in patients with renal impairment, see below.

◊ References.

1. Scheinfeld N. The new antihistamines—desloratadine and levocetirizine: a review. *J Drugs Dermatol* 2002; **1:** 311–16.
2. Tillement JP, *et al.* Compared pharmacological characteristics in humans of racemic cetirizine and levocetirizine, two histamine H1-receptor antagonists. *Biochem Pharmacol* 2003; **66:** 1123–6.
3. Horak F, *et al.* Levocetirizine has a longer duration of action on improving total nasal symptoms score than fexofenadine after single administration. *Br J Clin Pharmacol* 2005; **60:** 24–31.
4. Nettis E, *et al.* Levocetirizine in the treatment of chronic idiopathic urticaria: a randomized, double-blind, placebo-controlled study. *Br J Dermatol* 2006; **154:** 533–8.
5. Hair PI, Scott LJ. Levocetirizine: a review of its use in the management of allergic rhinitis and skin allergies. *Drugs* 2006; **66:** 973–96.

**Administration in children.** Levocetirizine hydrochloride may be given orally to children for the symptomatic relief of allergic rhinitis and chronic idiopathic urticaria, although licensed doses may vary between countries. In the UK, children aged 2 to 6 years may be given a dose of 2.5 mg daily in 2 divided doses, and those older than 6 years may be given the adult dose of 5 mg daily. In the USA, however, levocetirizine hydrochloride is not recommended for children under 6 years of age. In those aged 6 to 11 years, a dose of 2.5 mg once daily in the evening may be given, and the adult dose of 5 mg daily only given to children aged 12 years and older.

For doses in children with renal impairment, see below.

**Administration in renal impairment.** The dose of levocetirizine hydrochloride should be reduced in patients with renal impairment according to creatinine clearance (CC), although recommendations can vary between countries. The following oral doses have been suggested for adults in the UK and for adults and adolescents aged 12 years and over in the USA:

- CC 50 to 79 mL/minute: 5 mg once daily in the UK; 2.5 mg once daily in the USA
- CC 30 to 49 mL/minute: 5 mg every other day in the UK; 2.5 mg every other day in the USA
- CC 10 to 29 mL/minute: 5 mg once every 3 days in the UK; 2.5 mg once every 3 or 4 days in the USA
- CC less than 10 mL/minute and patients undergoing dialysis: contra-indicated in both the UK and USA

Data are lacking for the use of levocetirizine in children with renal impairment. UK licensed product information suggests that the dose should be adjusted on an individual basis, taking into account the patient's renal clearance and body-weight.

### Preparations

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

***Arg.:*** Levomine; Supraler; ***Austria:*** Xyzall; ***Belg.:*** Xyzall; ***Braz.:*** Zyxem; ***Chile:*** Degraler; Neo Alertop; ***Cz.:*** Xyzal; ***Denm.:*** Xyzal; ***Fin.:*** Xyzal; ***Fr.:*** Xyzall; ***Ger.:*** Xusal; ***Gr.:*** Xozal; ***Hong Kong:*** Xyzal; ***Hung.:*** Xyzal; ***India:*** L-Cetridoc†; Leset; Levorid; Teczine; ***Indon.:*** Xyzal; ***Irl.:*** Xyzal; ***Ital.:*** Xyzal; ***Malaysia:*** Xyzal; ***Mex.:*** Xuzal; Zyxem; ***Neth.:*** Sopras; Virdos; Xyzal; ***Norw.:*** Xyzal; ***Philipp.:*** Xyzal; ***Pol.:*** Xyzal; ***Port.:*** Levrix; Xyzal; ***Rus.:*** Xyzal (Ксизал); ***S.Afr.:*** Xyzal; ***Singapore:*** Xyzal; ***Spain:*** Muntel; Sopras; Xazal; ***Switz.:*** Xyzal; ***Thai.:*** Xyzal; ***UK:*** Xyzal; ***USA:*** Xyzal.

**Multi-ingredient:** ***India:*** Levorid D.

## Loratadine *(BAN, USAN, rINN)*

Loratadiini; Loratadin; Loratadina; Loratadinum; Loratadyna; Sch-29851. Ethyl 4-(8-chloro-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-ylidene)piperidine-1-carboxylate.

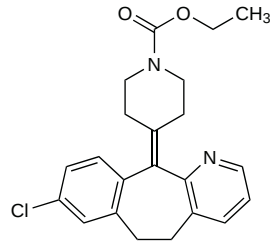
Лоратадин

$C_{22}H_{23}ClN_2O_2$ = 382.9.

*CAS — 79794-75-5.*

*ATC — R06AX13.*

*ATC Vet — QR06AX13.*



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

**Ph. Eur. 6.2** (Loratadine). A white or almost white, crystalline powder. It exhibits polymorphism. Practically insoluble in water; freely soluble in acetone and in methyl alcohol.

**USP 31** (Loratadine). A white to off-white powder. Insoluble in water; freely soluble in acetone, in chloroform, in methyl alcohol, and in toluene.

### Adverse Effects and Precautions

As for the non-sedating antihistamines in general, p.561.

**Breast feeding.** No adverse effects have been seen in breastfed infants whose mothers were receiving loratadine, and the American Academy of Pediatrics[1] considers that it is therefore usually compatible with breast feeding. However, UK licensed product information recommends that loratadine should not be used in breast-feeding mothers.

A study[2] in 6 women reported that about 0.03% of a single 40-mg oral dose of loratadine was distributed into breast milk over 48 hours as loratadine and its active metabolite, desloratadine.

1. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid.*; 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 08/04/04)
2. Hilbert J, *et al.* Excretion of loratadine in human breast milk. *J Clin Pharmacol* 1988; **28:** 234–9.

**Effects on the liver.** Two patients[1] developed severe necroinflammatory liver injury after receiving loratadine 10 mg daily for allergic rhinitis. Although both recovered after drug withdrawal, one patient required a liver transplantation and recovery was prolonged.

The product information notes that abnormal hepatic function including jaundice, hepatitis, and hepatic necrosis has been reported rarely.

1. Schiano TD, *et al.* Subfulminant liver failure and severe hepatotoxicity caused by loratadine use. *Ann Intern Med* 1996; **125:** 738–40.

**Pregnancy.** UK product information does not recommend the use of loratadine in pregnancy.