Alternatively, 1 mg/kg daily may be given in divided doses, to a maximum of 2.5 mg/kg daily in children aged 1 to 6 years, and to a maximum of 2 mg/kg daily in those aged 6 years and over. The pre- or postoperative sedative dose in children is 600 micrograms/kg. Dosage should be reduced in patients with hepatic or renal impairment, see below.

Hydroxyzine hydrochloride may also be given by deep intramuscular injection. For prompt control of anxiety or agitation in adults 50 to 100 mg is injected intramuscularly initially, and the dose may be repeated every four to six hours as required. For other indications when oral dosage is not practical, the intramuscular dose is 25 to 100 mg for adults and 1.1 mg/kg for children. Hydroxyzine should not be given by intravenous injection since haemolysis may result.

Administration in hepatic or renal impairment. In patients with hepatic impairment, UK licensed product information recommends a 33% reduction in the total oral daily dose of hydroxyzine. In patients with moderate or severe renal impairment, a dose reduction of 50% is recommended.

Anxiety disorders. Although hydroxyzine is used in the management of anxiety, there is little evidence to support its efficacy in anxious patients,[1] and the *BNF* considers that use of antihistamines solely for their sedative effect in anxiety is not appropriate.

1. Ballenger JC, *et al.* Consensus statement on generalized anxiety disorder from the International Consensus Group on Depression and Anxiety. *J Clin Psychiatry* 2001; **62** (suppl 11): 53–8. Available at: http://www.psychiatrist.com/private/supplenet/v62s11/v62s1108.pdf (accessed 15/08/08)

Preparations

USP 31: Hydroxyzine Hydrochloride Injection; Hydroxyzine Hydrochloride Syrup; Hydroxyzine Hydrochloride Tablets; Hydroxyzine Pamoate Capsules; Hydroxyzine Pamoate Oral Suspension.

Proprietary Preparations (details are given in Part 3)

Arg.: Ataraxone; Hidroxina†; Hyderax; ***Austria:*** Atarax; ***Belg.:*** Atarax; ***Braz.:*** Hixizine; Prurizin; ***Canad.:*** Atarax; ***Chile:*** Dalun; Fasarax; Nexit†; ***Cz.:*** Atarax; ***Denm.:*** Atarax; ***Fin.:*** Atarax; ***Fr.:*** Atarax; ***Ger.:*** AH 3 N; Atarax; Elroquil N; ***Gr.:*** Atarax; Iremofar; ***Hong Kong:*** Atarax; Qualidrozine; ***Hung.:*** Atarax; ***India:*** Atarax; ***Indon.:*** Bestalin; Iterax; ***Israel:*** Otarex; ***Ital.:*** Atarax; ***Malaysia:*** Atarax; ***Mex.:*** Atarax; ***Neth.:*** Atarax; Navicalm†; ***Norw.:*** Atarax; ***NZ:*** Serecid; ***Philipp.:*** Iterax; ***Pol.:*** Atarax; ***Port.:*** Atarax; Coraphene; ***Rus.:*** Atarax (Атаракс); ***S.Afr.:*** Aterax; Neurax; ***Singapore:*** Atarax; Hizin; Phymorax†; ***Spain:*** Atarax; ***Swed.:*** Atarax; ***Switz.:*** Atarax; ***Thai.:*** Abacus; Allerax; Antizine; Atano; Atarax; Cerax; Darax†; Drazine; Hadarax; Histan; Hizin; Honsa; Hydroxin†; Katrax; Masarax†; Med-Xyzarax†; Polizine†; Postarax†; R-Rax; Taraxin; Trandrozine; Unamine; ***Turk.:*** Atarax; Validol; ***UK:*** Atarax; Ucerax; ***USA:*** Atarax†; Vistaril; Vistazine†.

Multi-ingredient: ***Austria:*** Diligan; ***Braz.:*** Marax; ***Ger.:*** Diligan†; ***India:*** Marax; ***Port.:*** Diligan†; Vesparax†; ***S.Afr.:*** Geratar; ***Spain:*** Calmoplex; Dolodens; ***USA:*** Hydrophed; Marax; Theomax DF; ***Venez.:*** Marax†.

Isothipendyl Hydrochloride *(BANM, rINNM)*

Hidrocloruro de isotipendil; Isothipendyl, Chlorhydrate d'; Isothipendyli Hydrochloridum. *NN*-Dimethyl-1-(pyrido[3,2-*b*][1,4]benzothiazin-10-ylmethyl)ethylamine hydrochloride.

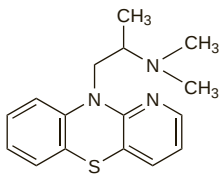
Изотипендила Гидрохлорид

$C_{16}H_{19}N_3S,HCl$ = 321.9.

CAS — 482-15-5 (isothipendyl); 1225-60-1 (isothipendyl hydrochloride).

ATC — D04AA22; R06AD09.

ATC Vet — QD04AA22; QR06AD09.



(isothipendyl)

Profile

Isothipendyl hydrochloride, an azaphenothiazine derivative, is an antihistamine (p.561) that has been applied topically for hypersensitivity and pruritic skin disorders although as with any antihistamine there is a risk of sensitisation. It has also been given orally and by the rectal route.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Actapront; ***Braz.:*** Andantol; ***Fr.:*** Sedermyl; ***Indon.:*** Andantol; ***Israel:*** Thiodantol; ***Ital.:*** Calmogel; ***Mex.:*** Andantol.

Ketotifen Fumarate *(BANM, USAN, rINNM)*

Fumarato de ketotifeno; HC-20511 (ketotifen); Ketotifeenivetyfumaraatti; Ketotifen Hydrogen Fumarate; Kétotifène, Fumarate de; Kétotifène, hydrogénofumarate de; Ketotifen-fumarát; Ketotifén-hidrogén-fumarát; Ketotifeni Fumaras; Ketotifeni hydrogenofumaras; Ketotifeno-vandenilio fumaratas; Ketotifenvätefumarat. 4-(1-Methylpiperidin-4-ylidene)-4*H*-benzo[4,5]cyclohepta-[1,2-*b*]thiophen-10(9*H*)-one hydrogen fumarate.

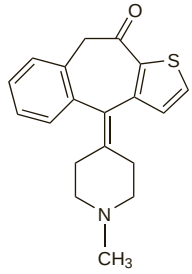
Кетотифена Фумарат

$C_{19}H_{19}NOS,C_4H_4O_4$ = 425.5.

CAS — 34580-13-7 (ketotifen); 34580-14-8 (ketotifen fumarate).

ATC — R06AX17; S01GX08.

ATC Vet — QR06AX17; QS01GX08.



(ketotifen)

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

Ph. Eur. 6.2 (Ketotifen Hydrogen Fumarate; Ketotifen Fumarate BP 2008). A white to brownish-yellow, fine crystalline powder. Sparingly soluble in water; very slightly soluble in acetonitrile; slightly soluble in methyl alcohol.

Adverse Effects and Precautions

As for the antihistamines in general, p.561; drowsiness may be a problem, and dry mouth and dizziness may occur at the beginning of treatment but usually resolve with continued use. Weight gain and CNS stimulation have been reported. Isolated cases of severe skin reactions, cystitis, and hepatitis have been reported. Irritation, pain, and punctate keratitis are commonly reported after topical application to the eye.

For precautions to be observed in asthmatic patients, see Sodium Cromoglicate, p.1136. Ketotifen may take several weeks to exert its full effect; existing anti-asthma treatment should not be abruptly withdrawn after starting ketotifen therapy. It should not be used for the treatment of acute asthma attacks.

Overdosage. Overdoses of ketotifen ranging from 10 to 120 mg were reported in 8 patients.[1] Symptoms included drowsiness, confusion, dyspnoea, bradycardia or tachycardia, disorientation, and convulsions. Gastric lavage was performed in 6 patients, and all 8 recovered within 12 hours after supportive treatment.

In an overview of 21 cases of overdosage (including those reported above) the manufacturers stated that no serious signs or symptoms had been reported with doses below 20 mg, and there had been no fatalities.[2] The most serious effects reported had included unconsciousness, convulsions, bradycardia and tachycardia, and a severe hypotensive reaction. Management is essentially supportive and symptomatic.

1. Jefferys DB, Volans GN. Ketotifen overdose: surveillance of the toxicity of a new drug. *BMJ* 1981; **282:** 1755–6.
2. Le Blaye I, *et al.* Acute ketotifen overdosage: a review of present clinical experience. *Drug Safety* 1992; **7:** 387–92.

Interactions

As for the sedating antihistamines in general, p.563.

A reversible fall in the platelet count has been seen in a few patients receiving ketotifen with oral antidiabetics and it has been suggested that this combination should therefore be avoided.

Pharmacokinetics

Ketotifen fumarate is almost completely absorbed from the gastrointestinal tract after oral doses, but bioavailability is reported to be only about 50% due to hepatic first-pass metabolism. Peak plasma concentrations occur 2 to 4 hours after an oral dose. It is mainly excreted in the urine as inactive metabolites with a small amount of unchanged drug; the terminal elimination half-life is about 21 hours.

Uses and Administration

Ketotifen is a sedating antihistamine (p.563) that also has a stabilising action on mast cells analogous to that of sodium cromoglicate (p.1137). It is used in the treatment of allergic conditions such as rhinitis (p.565) and conjunctivitis (p.564). Ketotifen has also been used in the prophylactic management of asthma, when it may take several weeks to exert its full effect; it should not be used to treat acute asthma attacks.

Ketotifen is given as the fumarate, but doses are expressed in terms of the base; ketotifen fumarate 1.38 mg is equivalent to about 1 mg of ketotifen.

Ketotifen fumarate is taken in oral doses equivalent to 1 mg of ketotifen twice daily with food, increased if necessary to 2 mg twice daily; 0.5 to 1 mg at night may be preferable for the first few days of treatment if drowsiness is likely to be a problem.

Ketotifen fumarate has also been applied topically, as eye drops equivalent to 0.025% ketotifen, used twice daily.

For children's doses, see below.

Action. It has been suggested that the anti-allergic action of ketotifen was independent of its antihistaminic properties.[1] This might be due to its effect on responses to platelet-activating factor (PAF).[2] However, the significance of PAF in the pathogenesis of asthma has been questioned.

1. Greenwood C. The pharmacology of ketotifen. *Chest* 1982; **82** (suppl): 45S–8S.
2. Morley J, *et al.* Effects of ketotifen upon responses to platelet activating factor: a basis for asthma prophylaxis. *Ann Allergy* 1986; **56:** 335–40.

Administration in children. Ketotifen fumarate can be given to children for the treatment of allergic conditions such as rhinitis (p.565) or conjunctivitis (p.564), and has been used in the prophylactic management of asthma. Oral doses equivalent to 1 mg of ketotifen twice daily with food may be used from 3 years of age. A dose equivalent to 500 micrograms ketotifen twice daily has been suggested in children between 6 months and 3 years of age.

Ketotifen fumarate has also been applied topically twice daily, as eye drops equivalent to 0.025% ketotifen, in children from 3 years of age.

Asthma. Results of studies on the effectiveness of ketotifen in the treatment of asthma (p.1108) have been conflicting; although some have found it effective in reducing symptoms[1-4] and in enabling a reduction in use of other anti-asthmatic drugs,[2,4] others have reported no significant benefits,[5,6] and UK guidelines on the management of asthma consider ketotifen to be ineffective.[7] A systematic review[8] found that it was of benefit in improving control of asthma and wheezing in children with mild to moderate disease, but noted that the high prevalence of atopy in several of the studies reviewed meant that the results might not be generalisable to children with asthma in general. A study in children described as 'preasthmatic' (that is, being at high risk of developing asthma) suggested that long-term therapy with ketotifen decreased the risk of asthma onset.[9]

1. Paterson JW, *et al.* Evaluation of ketotifen (HC20-511) in bronchial asthma. *Eur J Clin Pharmacol* 1983; **25:** 187–93.
2. Tinkelman DG, *et al.* A multicenter trial of the prophylactic effect of ketotifen, theophylline, and placebo in atopic asthma. *J Allergy Clin Immunol* 1985; **76:** 487–97.
3. Miraglia Del Giudice M, *et al.* Study of the efficacy of ketotifen treatment in asthmatic children under 3 years of age. *Curr Ther Res* 1986; **40:** 685–93.
4. Rackham A, *et al.* A Canadian multicenter study with Zaditen (ketotifen) in the treatment of bronchial asthma in children aged 5 to 17 years. *J Allergy Clin Immunol* 1989; **84:** 286–96.
5. White MP, *et al.* Ketotifen in the young asthmatic—a double-blind placebo-controlled trial. *J Int Med Res* 1988; **16:** 107–13.
6. Volovitz B, *et al.* Efficacy and safety of ketotifen in young children with asthma. *J Allergy Clin Immunol* 1988; **81:** 526–30.
7. Scottish Intercollegiate Guidelines Network/British Thoracic Society. British guideline on the management of asthma: a national clinical guideline. Revised edition May 2008. Available at: http://www.sign.ac.uk/pdf/sign101.pdf (accessed 23/06/08)
8. Bassler D, *et al.* Ketotifen alone or as additional medication for long-term control of asthma and wheeze in children. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2004 (accessed 14/04/08).
9. Bustos GJ, *et al.* Prevention of asthma with ketotifen in preasthmatic children: a three-year follow-up study. *Clin Exp Allergy* 1995; **25:** 568–73.

Conjunctivitis. References.

1. Martín AP, *et al.* The effect of ketotifen on inflammatory markers in allergic conjunctivitis: an open, uncontrolled study. *BMC Ophthalmol* 2003; **3:** 2. Available at: http://www.biomedcentral.com/1471-2415/3/2 (accessed 14/04/08)
2. Kidd M, *et al.* Efficacy and safety of ketotifen eye drops in the treatment of seasonal allergic conjunctivitis. *Br J Ophthalmol* 2003; **87:** 1206–11.
3. Ganz M, *et al.* Ketotifen fumarate and olopatadine hydrochloride in the treatment of allergic conjunctivitis: a real-world comparison of efficacy and ocular comfort. *Adv Therapy* 2003; **20:** 79–91.
4. Abelson MB, *et al.* Efficacy and safety of single- and multiple-dose ketotifen fumarate 0.025% ophthalmic solution in a pediatric population. *Pediatr Allergy Immunol* 2004; **15:** 551–7.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Antilerg; Bilozen; Biomira; Ketocev; Ketokid†; Respimex; Zaditen; ***Austral.:*** Zaditen; ***Austria:*** Ketotisan; Zaditen; ***Belg.:*** Zaditen; ***Braz.:*** Asdron; Asmalergin; Asmanon; Asmax; Asmen; Asmifen; Asmofen; Biatos; Broncoten†; Profilasmim-Ped†; Uni Cetotifen†; Zaditen; Zetitec†; ***Canad.:*** Zaditen; Zaditor; ***Chile:*** Ketotisin; Oftaler; Zaditen; ***Cz.:*** Ketof; Zaditen; ***Denm.:*** Zaditen; ***Fin.:*** Zaditen; ***Fr.:*** Zaditen; ***Ger.:*** Astifat†; Ketof; Padiatifen†; Zaditen; Zatofug†; ***Gr.:*** Dovidin; Ecradin; Eucycline; Fental; Frenasma; Isocaren; K-Drops; Kathricol; Klevistamin; Labelphen; Lavoptik; Nostimex†; Noxtor; Orpidix; Pellexeme; Urpem; Zaditen; Zeoklamin; Zethrinal; Zidofen; ***Hong Kong:*** Amitone; Asmafen; Asmaten; Astifen; Dhatifen; Ketifen; Vidatifen; Zaditen; ***Hung.:*** Zaditen; ***India:*** Ketasma; ***Indon.:*** Astifen; Intifen; Nortifen; Prevas; Profilas; Scanditen; Zaditen; ***Irl.:*** Zaditen; ***Israel:*** Profiten; Zaditen; ***Ital.:*** Alleal; Allerket; Bentifen; Chetofen; Ketoftil; Sosefen; Stamifen; Zaditen; ***Malaysia:*** Asmafen; Asumalife; Denerel; Dhatifen; Ketifen; Licoften; Xidanef†; Zaden†; Zaditen; ***Mex.:*** Asmaral-K; Biotifen; Cantel; Kasmal; Kedrop; Keraffler; Ketaxal†; Nemodine; Nomotec; Osaten; Pretifen; Saluket-H1; Ventisol; Zaditen; ***Neth.:*** Bentifen; Zaditen; ***Norw.:*** Zaditen;

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.

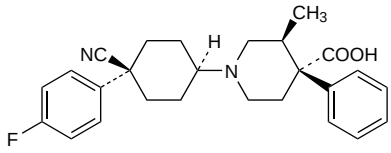
Левокабастина Гидрохлорид

$C_{26}H_{29}FN_2O_2$,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.

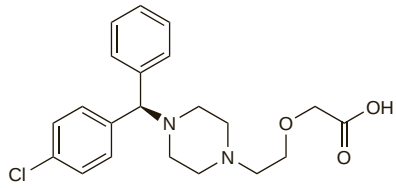
Левоцетиризин

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

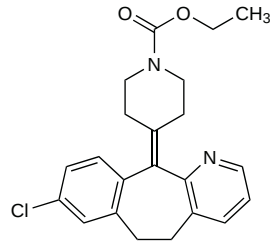
Лоратадин

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