Analysis of data collected by the Swedish Medical Birth Registry between 1994 and 2001 revealed 15 cases of hypospadias among a cohort of 2780 newborns exposed to loratadine during the first trimester of pregnancy.[1] The authors noted that the individual risk for having an infant with hypospadias after loratadine use is small (less than 1%) and the attributive risk of extra cases in the population is low. The US CDC has also analysed data from the National Birth Defects Prevention study;[2] they found no increase in the risk of second- or third-degree hypospadias in the infants of women who used loratadine in early pregnancy. In addition, an earlier prospective multicentre study[3] in 161 women taking a median dose of loratadine 10 mg daily in the first trimester of pregnancy suggested that its use was not associated with a significant risk of major congenital malformations.

1. Källén B, Olausson PO. Monitoring of maternal drug use and infant congenital malformations: does loratadine cause hypospadias? *Int J Risk Safety Med* 2001; **14:** 115–19.
2. CDC. Evaluation of an association between loratadine and hypospadias — United States, 1997-2001. *MMWR* 2004; **53:** 219–21. Also available at: http://www.cdc.gov/mmwr/PDF/wk/mm5310.pdf (accessed 11/05/04)
3. Moretti ME, *et al.* Fetal safety of loratadine use in the first trimester of pregnancy: a multicenter study. *J Allergy Clin Immunol* 2003; **111:** 479–83.

Sedation. For discussion of the sedative effects of antihistamines see p.562.

Interactions

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

Loratadine is metabolised by cytochrome P450 isoenzymes CYP3A4 and CYP2D6. Therefore use with other drugs that inhibit or are metabolised by these hepatic enzymes may result in changes in plasma concentrations of either drug and, possibly, adverse effects. Drugs known to inhibit one or other of these enzymes include cimetidine, erythromycin, ketoconazole, quinidine, fluconazole, and fluoxetine.

Antibacterials. Data held on file by the manufacturer show that *erythromycin* can inhibit the metabolism of loratadine. However, even when given in large doses loratadine does not appear to cause the cardiac conduction disorders associated with the non-sedating antihistamines astemizole (see p.567) and terfenadine (see p.590).[1] Similarly, *clarithromycin* seemed to inhibit the metabolism of loratadine and its active metabolite desloratadine.[2]

1. Affrime MB, *et al.* Three month evaluation of electrocardiographic effects of loratadine in humans. *J Allergy Clin Immunol* 1993; **91:** 259.
2. Carr RA, *et al.* Steady-state pharmacokinetics and electrocardiographic pharmacodynamics of clarithromycin and loratadine after individual or concomitant administration. *Antimicrob Agents Chemother* 1998; **42:** 1176–80.

Antifungals. *Ketoconazole* also appears to be able to inhibit the metabolism of loratadine and at therapeutic doses, is about 3 times more inhibitory than erythromycin.[1] However, the concentrations of ketoconazole required are reported to be much higher than those required to inhibit the metabolism of astemizole or terfenadine. Clearance of the active metabolite desloratadine is also reduced.

1. Brannan MD, *et al.* Effects of various cytochrome P450 inhibitors on the metabolism of loratadine. *Clin Pharmacol Ther* 1995; **57:** 193.

Gastrointestinal drugs. *Cimetidine* appears to have an inhibitory effect on the metabolism of loratadine and also attenuates the clearance of its active metabolite desloratadine although no clinically significant consequences have been seen.[1]

1. Brannan MD, *et al.* Effects of various cytochrome P450 inhibitors on the metabolism of loratadine. *Clin Pharmacol Ther* 1995; **57:** 193.

Pharmacokinetics

Loratadine is rapidly absorbed from the gastrointestinal tract after oral doses, peak plasma concentrations being attained in about 1 hour. Bioavailability is increased and time to peak plasma concentrations is delayed when taken with food. Loratadine undergoes extensive metabolism. The major metabolite, desloratadine (p.576), has potent antihistaminic activity. Reported mean elimination half-lives for loratadine and desloratadine are 8.4 and 28 hours, respectively. Loratadine is about 98% bound to plasma proteins; desloratadine is less extensively bound. Loratadine and its metabolites have been detected in breast milk, but do not appear to cross the blood-brain barrier to a significant extent. Most of a dose is excreted equally in the urine and faeces, mainly in the form of metabolites.

Renal impairment. The disposition of loratadine does not appear to be significantly altered in patients with severe renal impairment and haemodialysis does not appear to be an effective means of removing loratadine or its metabolite desloratadine from the body.[1]

1. Matzke GR, *et al.* Pharmacokinetics of loratadine in patients with renal insufficiency. *J Clin Pharmacol* 1990; **30:** 364–71.

Uses and Administration

Loratadine, a piperidine derivative related to azatadine, is a long-acting, non-sedating antihistamine with no significant antimuscarinic activity. It is used for the symptomatic relief of allergic conditions including rhinitis (p.565) and chronic urticaria (p.565).

Loratadine is given in an oral dose of 10 mg once daily. Children aged 2 to 5 years may be given 5 mg once daily and those aged 6 to 12 years may be given 10 mg once daily for seasonal allergic rhinitis and chronic idiopathic urticaria.

It is also used with a decongestant such as pseudoephedrine sulfate.

For dosage in hepatic or renal impairment, see below.

◊ References.

1. Haria M, *et al.* Loratadine: a reappraisal of its pharmacological properties and therapeutic use in allergic disorders. *Drugs* 1994; **48:** 617–37.

Administration in hepatic or renal impairment. US product information recommends that patients with hepatic failure or renal impairment (glomerular filtration rate less than 30 mL/minute) should be given an initial oral dose of loratadine 10 mg on alternate days.

Preparations

USP 31: Loratadine Oral Solution; Loratadine Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Aerotina; Alergipan; Alermuc; Alerpriv; Algistop; Aseptobron Descongestivo; Bedix; Benadryl 24; Biloina; Bioaler†; Clarityne; Devedryl; Hisplex; Lertamine†; Lisaler; Loisan; Loratex†; Loratine; Loremex Antialergico; Nastizol Antialergico†; Negalerg L†; Niltro; Novo Vagran†; Nularef; Omega 100 L; Pulmosan Aller; Sinaler; Tabcin Alergia; Vagran; Vixidone L; ***Austral.:*** Alledine; AllerEze; Claratyne; Lorano; Lorastyne†; ***Austria:*** Allernon; Clarityn; Lictyn; Lorano; Loratyn; ***Belg.:*** Claritine; Rupton; Sanelor; ***Braz.:*** Alergaliv; Atinac†; Clarilerg†; Claritin; Clistin†; Histadin; Histamix†; Loradine; Loralerg; Loranil; Lorasc†; Loratamed; Loremix; Loritil; Neo Loratadin; ***Canad.:*** Claritin; ***Chile:*** Alergan; Alledryl; Clarityne; Frenaler; Histaplus†; Hysticlar; Larmax†; Lontadex; ***Cz.:*** Claritine; Erolin; Flonidan; Loranol; Roletra; ***Denm.:*** Claritynn; Geklimon†; Loritin; Mildin; Oratyn; Versal†; ***Fin.:*** Claritynn; Geklimon†; Tuulix; ***Fr.:*** Clarityne; ***Ger.:*** Lisino; Livotab†; Lobeta; Lora; Lora-Lich; Lora-Puren; Loraclar†; Loraderm; Loragalen; Loralerg†; Lorano; Loratadura; Loratagamma; Loravis; Vividrin Loratadin†; ***Gr.:*** Allerdrug; Allergofact; Biliranin†; Bollinol; Clarityne; Difmedol; Helporigin; Horestyl; Igir; Latoren; Lora; Loratab; Novacloxab; Ralinet; Ristotadin; Tirlor; Utel; Zelmar; ***Hong Kong:*** Allertyn; Ambrace; Carin; Claritync CP-Loradine; Erolin; Ezede; Loradin; Loraton; Lotadine; Lotin; Marlora; Rinityn; Rotifar; Voratadine; ***Hung.:*** Claritine; Erolin; Flonidan; Lorano; Roletra; ***India:*** Awayke†; Loratin; Lorfast; Loridin; Lorin; ***Indon.:*** Alernitis; Allohex; Alloris; Anhissen; Anlos; Clarihis; Claritin; Clatatin; Cronitin; Folerin; Hislorex; Histaritin; Imunex; Inclarin; Klinset; Lergia; Lesidas; Lolergi; Loran; Lorapharm; Lorihis; Nosedin; Prohistin; Pylor; Rahistin; Rihest; Safetin; Sohotin; Tinnic; Winatin; ***Irl.:*** Claritynt; Histaclar; ***Israel:*** Lorastine; Loratrim; ***Ital.:*** Alorint; Claritynt; Fristamin; ***Jpn:*** Claritin; ***Malaysia:*** Carin; Clarityne; Ezede†; Loradine; Lorastyne†; Loratyn†; Ridamin; Roletra; Tirlor; ***Mex.:*** Alerfin; Aludix; Antilergal; Biolorat; Claritync; Curyken; Dimegan; Dissen; Ditana; Doralan; Dotagil; Dymaten; Efectine; Fartadin; Grimeral; Histina; Histox; Inigrin; Laritol; Lertamine; Lictyn; Liferamin; Lotan; Lovarin; Neoalexil; Nidatar; Quimtadine; Rodakin; Rokadin†; Sensibit; Serralsina; Sitinir; Vincidal; ***Neth.:*** Allerfre; Claritine; Kruidvat Hooikoortstabletten; Lorastad; Otrivin neusallergie loratadine; Sanelor; ***Norw.:*** Clarityn; Versal†; ***NZ:*** Claratyne; Lora-Tabs; ***Philipp.:*** Allerta; Claritin; Lergicyl; Loradex; Lorahist; Lorano; Loratyne; Lordam; Lordane; Onemin; Rinityn; Zylohist; ***Pol.:*** Alerfan; Aleric; Claritine; Flonidan; Lorahexal; Loram; Loratan; Loratine; Nalergine; Rotadin; ***Port.:*** Alertrin; Claritine; Evertine; Histadin; Profenox; Zolargene; ***Rus.:*** Alerpriv (Алерприв); Clargotil (Кларготил); Clarisens (Кларисенс); Claritine (Кларитин); Clarotadine (Кларотадин); Erolin (Эролин); Klallergine (Клаллергин); Klarfast (Кларфаст); Klaridol (Кларидол); Lomilan (Ломилан); Lorahexal (Лорагексал); Lorid (Лорид); Loridin (Лоридин); ***S.Afr.:*** Clarinese; Clarityne; Demazin Anti-Allergy†; Laura; Lorahist; Lorano; Loratyne†; Polaratyne†; Pollentyme; Rhinigine; ***Singapore:*** Allertyn; Ardin; Carin; Claritync; Ezede; Histalor; Lorfast; Loridin; Lotadine; Ridamin; Rinityn; Roletra; Tirlor; ***Spain:*** Civeran; Claritync; Fadina†; Optimin†; Velodan; ***Swed.:*** Claritync; Versal; ***Switz.:*** Claritine; ***Thai.:*** Aller-Tab; Allerdine; Allersil; Caradine; Carinose†; Clalodine; Clarid; Clarityne; Halodin; Hisracon; Klaryne; Lindine; Loracine; Loradine; Loranox; Lordin; Lorin; Lorita; Lorityne†; Lorsedin; Lortadine; Ridamin; Rityne; Roletra; Tiradine; Tirlor; ***Turk.:*** Alarin; Claritine; Histadin; Loradif; Lorantis; Loritine; Ritin; ***UAE:*** Loratin; ***UK:*** Claritynn; ***USA:*** Alavert; Claritin; Clear-Atadine; Non-Drowsy Allergy; Tavist ND; ***Venez.:*** Alerdina; Alertidine†; Biolorat; Claritync; Loradin†; Lorat; Loraval; Lorex; Loriden; Lotal; Polaramine Reformulado; Proactin†; Tirlor.

Multi-ingredient: ***Arg.:*** Alerpriv D; Bedix-D; Benadryl 24 D; Celestamine-L; Ciprocort D; Ciprocort L; Clarifriol; Clarityne Cort; Clarityne D; Cortistamin L; Decidex Plus; Dexaprof D; Histamino Corteroid L; Ideogrip; Lertamine D†; Lisaler Beta; Loisan-D; Loremex Descongestivo; Nastizol-L; Negalerg†; Novo Vagran D†; Novo-Nastizol†; Nularef Cort; Nularef-D; Paracetamol Grip NF; Pulmonix Grip; Pulmonix Plus; Sinaler B; Toraxan; Vagran D; Vixidone LB; ***Austral.:*** Clarinase; Sinease†; ***Austria:*** Clarinase; ***Belg.:*** Clarinase; ***Braz.:*** Claritin-D; Cloratadd D; Histadin D; Loralerg-D; Loranil D; Loremix D; Neofedrin; ***Canad.:*** Chlor-Tripolon ND; Claritin Allergy & Sinus; Claritin Extra†; Liberato; ***Chile:*** Alledryl D; Clarinase; Frenaler-D; Larmax D; Lertamine; Lertamine Extra; Lontadex D†; Rinomex; ***Cz.:*** Clarinase; ***Denm.:*** Clarinase; ***Fin.:*** Clarinase; ***Fr.:*** Clarinase; ***Gr.:*** Clarityne D; ***Hong Kong:*** Clariflu; Clarinase; Rhinos; ***Hung.:*** Clarinase; ***India:*** Loratin D; Lorfast-D; Loridin-D; ***Indon.:*** Aldisa; Clarinase; Glanos; Rhinos; ***Israel:*** Clarinase; ***Malaysia:*** Carinox; Clarinase; ***Mex.:*** Alerfin Ex; Alvium†; Alviumito†; Alviumthe†; Bisincof; Bramin; Bronar; Broquixol; Celestamine NS; Claricort†; Clariflu; Clarifriol; Clarinase†; Clarityne D; Coricidin Expec; Dimegan D; Doralan-Ax; Efectine D; Farmalor; Fluxibit; Gralddep; Laritol D; Laritol Ex; Laritol G; Lertamine D; Linfarden; Lovarin P†; Lyrsedin; Neoalexil P†; Quimtadine DSQ; Quimtafriol; Sensibit D; Sensibit XP; Sibilex; Tadinar-C; Tamex; Tavexyl; TheraFlu 24; TheraFlu N 12; TheraFlu TD; ***NZ:*** Clarinase†; Demazin Non-Drowsy†; ***Philipp.:*** Claricort; Clarinase; Rhinase; ***Pol.:*** Clarinase; ***Port.:*** Claridon; ***S.Afr.:*** Clarityne D; Demazin NS; Polaratyne D†; ***Singapore:*** Clarinase; ***Spain:*** Narine; ***Thai.:*** Clarinase; ***Turk.:*** Clarinase; ***USA:*** Alavert Allergy & Sinus D; Claritin-D; ***Venez.:*** Ambroclar; Celestamincort; Claricort; Claridex; Claridexultra; Clariflu; Clarigrip; Clarinase†; Fedyclar; Lokarin; Loracert; Rinase†.

Mebhydrolin *(BAN, rINN)*

Mebhidrolina; Mebhydroline; Mebhydrolinum. 5-Benzyl-1,2,3,4-tetrahydro-2-methyl-γ-carboline.

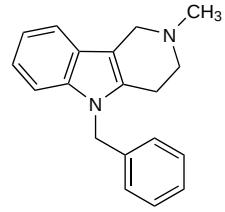
Мебгидролин

$C_{19}H_{20}N_2$ = 276.4.

CAS — 524-81-2.

ATC — R06AX15.

ATC Vet — QR06AX15.



Mebhydrolin Napadisilate *(BANM, rINNM)*

Diazolinum; Mebhydrolin Napadisylate; Mebhydrolin Naphthalenedisulphonate; Mebhydroline, Napadisilate de; Mebhydrolini Napadisilas; Napadisilato de mebhidrolina. Mebhydrolin naphthalene-1,5-disulphonate.

Мебгидролина Нападизилат

$(C_{19}H_{20}N_2)_2.C_{10}H_8O_6S_2$ = 841.0.

CAS — 6153-33-9.

ATC — R06AX15.

ATC Vet — QR06AX15.

Profile

Mebhydrolin, an ethylenediamine derivative, is a sedating antihistamine (p.561) with antimuscarinic and sedative properties. It has been given orally as the base or as the napadisilate salt for the symptomatic relief of allergic conditions including urticaria and rhinitis, and in pruritic skin disorders. Granulocytopenia and agranulocytosis have been reported.

Preparations

Proprietary Preparations (details are given in Part 3)

Indon.: Biolergy; Gabiten; Histapan; Incitin; Interhistin; Tralgi; Zoline; ***Israel:*** Cidalin; ***Rus.:*** Diazolin (Диазолин); ***S.Afr.:*** Fabahistin; ***Thai.:*** Dalhis; Dayhist; Manocidal; Manoeidai; Posidol.

Meclozine Hydrochloride

(BANM, pINNM)

Hidrocloruro de meclozina; Meclizine Hydrochloride; Meclizinium Chloride; Méclozine, chlorhydrate de; Meclozini Dihydrochloridum; Meclozini hydrochloridum; Meklotsiinihydrokloridi; Meklozin Hidroklorür; Meklozin-dihydrochlorid; Meklozin-hidroklorid; Meklozinhydroklorid; Meklozino hidrochloridas; Meklozyny chlorowodorek; Parachloramine Hydrochloride. 1-(4-Chlorobenzhydryl)-4-(3-methylbenzyl)piperazine dihydrochloride.

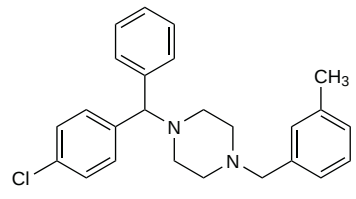
Меклозина Гидрохлорид

$C_{25}H_{27}ClN_2.2HCl$ = 463.9.

CAS — 569-65-3 (meclozine); 1104-22-9 (anhydrous meclozine hydrochloride); 31884-77-2 (meclozine hydrochloride monohydrate).

ATC — R06AE05.

ATC Vet — QR06AE05.



(meclozine)