been withdrawn from the market in most countries because of the risk of adverse effects.

Astemizole has been given in an oral dose of 10 mg once daily, or 5 mg daily in children aged 6 to 12 years. These doses must not be exceeded because of the risk of cardiac arrhythmias with higher doses.

The active metabolite of astemizole, tecastemizole (norastemizole) has been investigated for the treatment of allergic rhinitis.

Preparations

USP 31: Astemizole Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Alermizol†; Astezol†; Cezane†; Mudantil†; ***Cz.:*** Hismanal†; ***Gr.:*** Mibiron†; Tulipe-R†; Tyrenol†; Waruzol†; ***India:*** Astizole; Stemiz†; ***Mex.:*** Adistan†; Alerfur; Alerken; Alermi; Aleztem; Anerzol; Antagon 1; Astemina; Astesen; Aztemin; Aztil; Aztrolen; Biostan; Dexodin; Emdar; Emizol; Farmidal S; Fustermizol; Ginomizol†; Histalino; Histaser; Novasten; Practizol; Ulcoid-Zol†; Urtigen; ***Port.:*** Perifer H1†; ***Spain:*** Alermizol†; Esmacen†; Hubermizol†; Narvizol†; Rifedot†; Simprox†; Urdrim†; ***Venez.:*** Asemin†; Corexan†; Histalong†; Prevan†.

Multi-ingredient: ***Arg.:*** Bio Cabal†; Bronco Biotaer†; Dallamizol-D†; Gentiabron†; Muco Cortos†; Predual Descongestivo†; Wilpan C†.

Azatadine Maleate *(BANM, USAN, rINNM)*

Atsatadiinimaleaatti; Azatadine, Maléate d'; Azatadini Maleas; Azatadinmaleat; Maleato de azatadina; Sch-10649. 6,11-Dihydro-11-(1-methyl-4-piperidylidene)-5*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridine dimaleate.

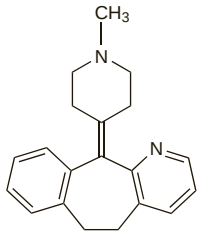
Азатадина Малеат

$C_{20}H_{22}N_2,2C_4H_4O_4$ = 522.5.

CAS — 3964-81-6 (azatadine); 3978-86-7 (azatadine maleate).

ATC — R06AX09.

ATC Vet — QR06AX09.



(azatadine)

Pharmacopoeias. In *US.*

USP 31 (Azatadine Maleate). A white to light cream-coloured, odourless powder. Freely soluble in water, in alcohol, in chloroform, and in methyl alcohol; practically insoluble in ether and in benzene.

Adverse Effects and Precautions

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

Extrapyramidal effects. An acute dystonic reaction was reported in a patient who had taken azatadine maleate 20 to 30 mg orally over a 24-hour period.[1] The condition was reversed by intravenous injection of benzatropine 2 mg.

1. Joske DJL. Dystonic reaction to azatadine. *Med J Aust* 1984; **141:** 449.

Interactions

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

Pharmacokinetics

Azatadine maleate is readily absorbed from the gastrointestinal tract and is partly metabolised. Peak plasma concentrations are achieved in about 4 hours. The elimination half-life has been reported to be 9 to 12 hours. Excretion of unchanged drug and metabolites is via the urine.

Uses and Administration

Azatadine maleate is a piperidine derivative closely related to cyproheptadine. It is a sedating antihistamine with a long duration of action; it also has antimuscarinic and antiserotonin properties.

Azatadine maleate is used for the symptomatic relief of allergic conditions including rhinitis (p.565) and urticaria (p.565); it is also used for other pruritic skin disorders as well as reactions to insect bites and stings. It is given in usual oral doses of 1 mg twice daily; if necessary 2 mg twice daily may be given. Children aged 6 to 12 years may be given 0.5 to 1 mg twice daily.

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

Preparations

USP 31: Azatadine Maleate Tablets.

Proprietary Preparations (details are given in Part 3)

Austral.: Zadine; ***Canad.:*** Optimine; ***Hong Kong:*** Zadine†; ***Malaysia:*** Zadine†; ***Mex.:*** Idulamine†; ***NZ:*** Zadine†; ***Singapore:*** Zadine†; ***Spain:*** Lergocil.

Multi-ingredient: ***Braz.:*** Cedrin; ***Canad.:*** Trinalin; ***Mex.:*** Trinalin†; ***Spain:*** Atiramin; Idulanex; ***USA:*** Rynatan†; Trinalin†.

Azelastine Hydrochloride

(BANM, USAN, rINNM)

A-5610 (azelastine or azelastine hydrochloride); Atselastiinihydrokloridi; Azelastin Hidroklorür; Azélastine, chlorhydrate d'; Azelastin-hydrochlorid; Azelastinhydroklorid; Azelastini hydrochloridum; Azelastino hidrochloridas; E-0659 (azelastine or azelastine hydrochloride); Hidrocloruro de azelastina; W-2979M (azelastine or azelastine hydrochloride). 4-(*p*-Chlorobenzyl)-2-(hexahydro-1-methyl-1*H*-azepin-4-yl)-1(2*H*)-phthalazinone monohydrochloride.

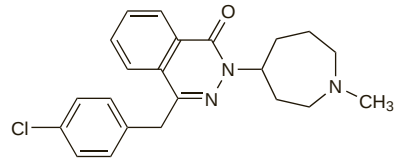
Азеластина Гидрохлорид

$C_{22}H_{24}ClN_3O,HCl$ = 418.4.

CAS — 58581-89-8 (azelastine); 79307-93-0 (azelastine hydrochloride).

ATC — R01AC03; R06AX19; S01GX07.

ATC Vet — QR01AC03; QR06AX19; QS01GX07.



(azelastine)

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

Ph. Eur. 6.2 (Azelastine Hydrochloride). A white or almost white, crystalline powder. Sparingly soluble in water; soluble in dehydrated alcohol and in dichloromethane.

Adverse Effects and Precautions

As for the antihistamines in general, p.561.

When given intranasally, irritation of the nasal mucosa and taste disturbances have been reported; somnolence, headache, and dry mouth have also been noted in some patients. Taste disturbance can occur after use in the eye.

Pharmacokinetics

About 40% of an intranasal dose of azelastine reaches the systemic circulation. Elimination is via hepatic metabolism with excretion mainly in the faeces.

◊ Azelastine is rapidly and almost completely absorbed when given *orally,* peak plasma concentrations being achieved in 4 to 5 hours. Azelastine undergoes hepatic metabolism; the major metabolite, demethylazelastine, has antihistamine activity. The elimination half-life of azelastine is about 25 hours, increasing to 35.5 hours after multiple oral doses, possibly as a result of accumulation of the demethyl metabolite. Azelastine and its metabolites are excreted predominantly in the faeces and also in urine.

Uses and Administration

Azelastine hydrochloride is an antihistamine that, in addition to its histamine H_1-receptor-blocking activity, appears to inhibit the release of inflammatory mediators from mast cells. It is used topically in the symptomatic relief of allergic conditions including rhinitis (p.565) and conjunctivitis (p.564). It is also used in the treatment of non-allergic rhinitis.

In the treatment of allergic **rhinitis** in adults and children aged 5 years and over, the usual dose in the UK is 140 micrograms by nasal spray into each nostril twice daily. In the USA, however, 2 sprays of a similar preparation (supplying 137 micrograms per spray) may be given into each nostril twice daily; children aged 5 years and over may be given 1 spray into each nostril twice daily. In the USA, azelastine is also used in the treatment of non-allergic rhinitis in adults and children aged 12 years and over. The dose is 2 sprays into each nostril twice daily. In the treatment of **conjunctivitis**, azelastine is licensed in the UK for the treatment of seasonal allergic conjunctivitis in adults and children aged 4 years and over and for the treatment of perennial allergic conjunctivitis in adults and children aged 12 years and over. In the USA, it is licensed for the treatment of allergic conjunctivitis in adults and children aged 3 years and over. Regardless of the age and indication, a 0.05% solution is instilled into each eye twice daily; this may be increased to four times daily in severe conditions.

Azelastine hydrochloride has also been given by mouth.

◊ References.

1. Wober W, *et al.* Efficacy and tolerability of azelastine nasal spray in the treatment of allergic rhinitis: large scale experience in community practice. *Curr Med Res Opin* 1997; **13:** 617–26.
2. McNeely W, Wiseman LR. Intranasal azelastine: a review of its efficacy in the management of allergic rhinitis. *Drugs* 1998; **56:** 91–114.
3. Lenhard G, *et al.* Double-blind, randomised, placebo-controlled study of two concentrations of azelastine eye drops in seasonal allergic conjunctivitis or rhinoconjunctivitis. *Curr Med Res Opin* 1997; **14:** 21–8.
4. Sabbah A, Marzetto M. Azelastine eye drops in the treatment of seasonal allergic conjunctivitis or rhinoconjunctivitis in young children. *Curr Med Res Opin* 1998; **14:** 161–70.
5. Duarte C, *et al.* Treatment of severe seasonal rhinoconjunctivitis by a combination of azelastine nasal spray and eye drops: a double-blind, double-placebo study. *J Investig Allergol Clin Immunol* 2001; **11:** 34–40.
6. Canonica GW, *et al.* Topical azelastine in perennial allergic conjunctivitis. *Curr Med Res Opin* 2003; **19:** 321–9.
7. Lee TA, Pickard AS. Meta-analysis of azelastine nasal spray for the treatment of allergic rhinitis. *Pharmacotherapy* 2007; **27:** 852–9.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Alager; Allergodil; Brixia; Xanaes; ***Austral.:*** Azep; ***Austria:*** Allergodil; Allergospray; Lasticom; Oculastin; ***Belg.:*** Allergodil; Otrivine Anti-Allergie; ***Braz.:*** Azelast†; Rino-Azetin†; Rino-Lastin; ***Chile:*** Allergodil†; Az Ofteno; Brixia; ***Cz.:*** Allergodil; ***Denm.:*** Allergodil; ***Fin.:*** Lastin; ***Fr.:*** Alerdual; Allergodil; Prorhinite; ***Ger.:*** Allergodil; Loxin; Vividrin akut Azelastin; ***Gr.:*** Afluon; ***Hong Kong:*** Azep; ***Hung.:*** Allergodil; ***India:*** Azep; ***Irl.:*** Rhinolast; ***Israel:*** Optilast; Rhinolast; ***Ital.:*** Allergodil; Lasticom; ***Malaysia:*** Azep†; ***Mex.:*** Astelin; AZ Ofteno; ***Neth.:*** Allergodil; Oculastin; Otrivin neusallergie azelastine; ***Norw.:*** Azelvin; Lastin; ***NZ:*** Eyezep; ***Philipp.:*** Azelone; Azep; ***Pol.:*** Allergodil; ***Port.:*** Allergodil; Azep; Oculastin; ***Rus.:*** Allergodil (Аллеродил); ***S.Afr.:*** Rhinolast; ***Singapore:*** Azep†; ***Spain:*** Afluon; Corifina; ***Swed.:*** Azelvin; Lastin; ***Switz.:*** Allergodil; Oculastin; Otrivin rhume des foins; ***Thai.:*** Azep†; ***Turk.:*** Allergodil; ***UK:*** Aller-Eze; Optilast; Rhinolast; ***USA:*** Astelin; Optivar; ***Venez.:*** Alergot; Allergodil; AZ; Brixia.

Multi-ingredient: ***India:*** Duonase.

Bamipine *(BAN, rINN)*

Bamipiini; Bamipin; Bamipina; Bamipinum. *N*-Benzyl-*N*-(1-methyl-4-piperidyl)aniline.

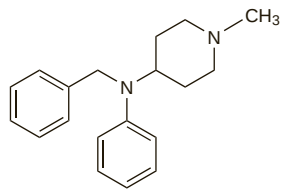
Бамипин

$C_{19}H_{24}N_2$ = 280.4.

CAS — 4945-47-5.

ATC — D04AA15; R06AX01.

ATC Vet — QD04AA15; QR06AX01.



Profile

Bamipine is a sedating antihistamine (p.561) with pronounced sedative effects.

Bamipine and its salts are used mainly for the symptomatic relief of allergic conditions such as urticaria (p.565) and in pruritic skin disorders. Bamipine hydrochloride has been given by mouth. Bamipine, bamipine lactate, and bamipine salicylate have all been applied topically.

Preparations

Proprietary Preparations (details are given in Part 3)

Austria: Soventol; ***Ger.:*** Soventol; ***Gr.:*** Soventol†; ***Neth.:*** Soventol; ***Pol.:*** Soventol.

Multi-ingredient: ***India:*** Multifungin H†; Multifungin†; Soventol†.