Profile
Chlorphenoxamine, a congener of diphenhydramine (p.577), has antimuscarinic and antihistaminic properties. It has been used in nausea, vomiting, and vertigo, and was formerly used in the symptomatic treatment of parkinsonism. Chlorphenoxamine has also been used in hypersensitivity reactions.

Preparations
Proprietary Preparations (details are given in Part 3)
Ger.: Systral; ***Hong Kong:*** Systral†; ***Indon.:*** Systral; ***Philipp.:*** Systral; ***Port.:*** Systral; ***Thai.:*** Systral; ***Turk.:*** Sistral; Systral.

Multi-ingredient: ***Austria:*** Spirbon; ***Ger.:*** Systral C†; ***S.Afr.:*** Analgen-SA†.

Cinnarizine *(BAN, USAN, rINN)*

Cinarizin; Cinarizina; Cinarizinas; Cinnarizin; Cinnarizinum; Cynaryzyna; 516-MD; R-516; R-1575; Sinarizin; Sinnaritsiini. 1-Benzhydryl-4-cinnamylpiperazine; (*E*)-1-(Diphenylmethyl)-4-(3-phenylprop-2-enyl)piperazine.

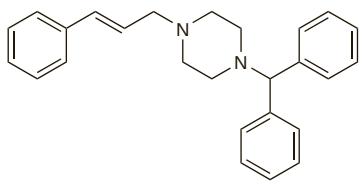
Циннаризин

$C_{26}H_{28}N_2$ = 368.5.

CAS — 298-57-7.

ATC — N07CA02.

ATC Vet — QN07CA02.



Pharmacopoeias. In *Chin.* and *Eur.* (see p.vii).
Ph. Eur. 6.2 (Cinnarizine). A white or almost white powder. Practically insoluble in water; slightly soluble in alcohol and in methyl alcohol; soluble in acetone; freely soluble in dichloromethane. Protect from light.

Adverse Effects and Precautions
As for the sedating antihistamines in general, p.561.

There have been rare reports of extrapyramidal symptoms after taking cinnarizine, sometimes associated with depressive feelings.

High doses of cinnarizine should be used with caution in patients with hypotension because of the possibility of decreasing blood pressure further.

Extrapyramidal disorders. For reference to extrapyramidal disorders associated with the use of cinnarizine, see Flunarizine, p.580.

Hypersensitivity. Immunologically-defined lichen planus pemphigoides has been reported[1] in a 72-year-old woman taking cinnarizine. Lesions began to clear when treatment was stopped but challenge with cinnarizine provoked severe itching and reactivation of pigmented lesions. Another case[2] has also been described.

1. Miyagawa S, *et al.* Lichen planus pemphigoides-like lesions induced by cinnarizine. *Br J Dermatol* 1985; **112:** 607–13.
2. Ramallal M, *et al.* Lichenoid eruption associated with cinnarizine use. *Pharm World Sci* 2002; **24:** 215–16.

Porphyria. Cinnarizine is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *animals*.

Tinnitus. The Spanish System of Pharmacovigilance had received reports[1] of tinnitus associated with calcium-channel blockers; some of the reports, including the one relating to cinnarizine, were in patients also receiving other ototoxic drugs. WHO was said to have additional reports of tinnitus associated with calcium-channel blockers including cinnarizine.

1. Narváez M, *et al.* Tinnitus with calcium-channel blockers. *Lancet* 1994; **343:** 1229–30.

Weight gain. There has been a report[1] of weight gain in 4 patients who had taken cinnarizine for 1 to 2 years; in all cases the weight gain was associated with increased appetite.

1. Navarro-Badenes J, *et al.* Weight-gain associated with cinnarizine. *Ann Pharmacother* 1992; **26:** 928–30.

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

Pharmacokinetics
Cinnarizine is absorbed from the gastrointestinal tract, peak plasma concentrations occurring 2 to 4 hours after oral doses. It undergoes metabolism and has a half-life of 3 to 6 hours. Cinnarizine is excreted in the faeces mainly as unchanged drug, and in the urine predominantly as metabolites.

Uses and Administration
Cinnarizine is a piperazine derivative with antihistamine, sedative, and calcium-channel blocking activity. It is used for the symptomatic treatment of nausea and vertigo caused by Ménière's disease and other vestibular disorders (see Vertigo, p.565) and for the prevention and treatment of motion sickness (p.564). It is also used in the management of various peripheral and cerebral vascular disorders.

In the UK, the usual oral dose for vertigo and vestibular disorders is 30 mg three times daily. For motion sickness a dose of 30 mg is taken 2 hours before the start of the journey and 15 mg every 8 hours during the journey if necessary. Children aged 5 to 12 years are given half the adult dose for both indications. In other European countries, a dose of 75 mg once or twice daily has been given for vertigo and vestibular disorders. Doses of 75 mg have also been given 1 to 3 times daily for cerebrovascular disorders and 2 or 3 times daily for peripheral vascular disorders.

◊ References.

1. Shupak A, *et al.* Cinnarizine in the prophylaxis of seasickness: laboratory vestibular evaluation and sea study. *Clin Pharmacol Ther* 1994; **55:** 670–80.

Preparations
Proprietary Preparations (details are given in Part 3)
Arg.: Dismaren; Fabracin; Folcodal; Iroplex†; Natropas; Stugeron; ***Austria:*** Cinnabene; Pericephal; Stutgeron; ***Belg.:*** Stugeron; ***Braz.:*** Antigeron; Cinaran; Cinarivert†; Cinarix†; Cinazin†; Cinazon; Civertim; Cronogeron; Fluxon; Laberitin†; Labigeron; Nerizina†; Stugerina†; Stugeron; Vertigeron; Verzum; Vessel†; ***Chile:*** Cinergil; Siridone; Stugeron; ***Cz.:*** Cinedil†; Cinnabene; Stugeron; ***Denm.:*** Sepan; ***Gr.:*** Derozin; Stugeron; ***Hong Kong:*** Celenid†; Medozine; Stugeron; ***Hung.:*** Stugeron; ***India:*** Avidazine; Cintigo; Diziron; Stugeron; Vertiron; ***Indon.:*** Merron; Nariz; Penfas; Stugeron; Vertizine; ***Irl.:*** Stugeron; ***Israel:*** Stunarone; ***Ital.:*** Cinazyn; Stugeron; Toliman; ***Malaysia:*** Celenid†; Cereron†; Cinna; Cinnaron; Stugeron; Uphageron; ***Mex.:*** Bulasan; Cisaken; Dilateron-F; Dilper-INA; Karilex; Oblant; Stugeron; Venoxil; Winpar; ***Philipp.:*** Dizzinon; Niziran; Stugeron; Vertisin; ***Port.:*** Cinon; Stugeron; ***Rus.:*** Phezam (Фезам); Stugeron (Структум); ***S.Afr.:*** Purazine; Stugeron; ***Singapore:*** Celenid; Cinna; Cinnar; Cinnaron; Stugeron†; Urizine†; ***Spain:*** Stugeron; ***Switz.:*** Cerepar; Cinnageron; Cinnamed†; Stugeron; ***Thai.:*** C-Pela†; Celenid; Cenai; Cerebroad; Ceremin; Cinerine; Cinna; Cinnar; Cinnaza; Cinrizine; CN-25†; Linazine; Manoron; Med-Circuron†; Medozine; Siarizine; Silicin; Sorebral; Stugeron; Stugin; Stuno; Urizine; Vernarin; ***Turk.:*** Sefal; ***UK:*** Arlevert; Cinaziere†; Stugeron; ***Venez.:*** Cinaren; Cinarin; Sinver; Stugeron; Vericin.

Multi-ingredient: ***Arg.:*** Cadencial Plus; Cinacris; Difusil; Ribex; Vasodual†; ***Austria:*** Cinnarplus; ***Belg.:*** Touristil; ***Braz.:*** Coldrin; Exit; Forgrip†; Sureptil; ***Cz.:*** Arlevert; ***Fin.:*** Rinomar; ***Ger.:*** Arlevert; ***Hong Kong:*** C-Sik†; ***Hung.:*** Arlevert; ***India:*** Vertigil; ***Neth.:*** Primatour; ***Rus.:*** Omaron (Омарон); Piracezine (Пирацезин); ***Spain:*** Clinadil; Clinadil Compositum; Diclamina; ***Swed.:*** Rinomar.

Clemastine Fumarate
(BANM, USAN, rINNM)

Clémastine, fumarate de; Clemastini fumaras; Fumarato de clemastina; HS-592 (clemastine); Klemastiinifumaraatti; Klemastin fumarát; Klemastin Hidrojen Fumarat; Klemastinfumarat; Klemastino fumaratas; Klemastyny fumaran; Klemasztin-fumarát; Meclastine Fumarate; Mecloprodine Fumarate. (+)-(2*R*)-2-{2-[(*R*)-4-Chloro-α-methylbenzhydryloxy]ethyl}-1-methylpyrrolidine hydrogen fumarate.

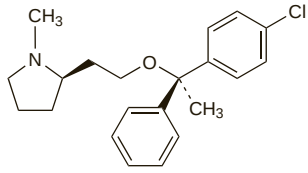
Клемастина Фумарат

$C_{21}H_{26}ClNO,C_4H_4O_4$ = 460.0.

CAS — 15686-51-8 (clemastine); 14976-57-9 (clemastine fumarate).

ATC — D04AA14; R06AA04.

ATC Vet — QD04AA14; QR06AA04.



(clemastine)

Pharmacopoeias. In *Chin., Eur.* (see p.vii), *Jpn*, and *US*.
Ph. Eur. 6.2 (Clemastine Fumarate). A white or almost white, crystalline powder. Very slightly soluble in water; sparingly soluble in alcohol (70%); slightly soluble in alcohol (50%) and in methyl alcohol. A 10% suspension in water has a pH of 3.2 to 4.2.
USP 31 (Clemastine Fumarate). A colourless to faintly yellow, odourless, crystalline powder. Very slightly soluble in water; very slightly soluble in chloroform; slightly soluble in methyl alcohol. pH of a 10% suspension in water is between 3.2 to 4.2. Store in airtight containers at a temperature not exceeding 25°. Protect from light.

Adverse Effects and Precautions
As for the sedating antihistamines in general, p.561.

Breast feeding. The American Academy of Pediatrics[1] considers that clemastine should be given with caution to breast-feeding mothers, since it has been associated with adverse effects in the infant. Drowsiness, irritability, a high-pitched cry, neck stiffness, and refusal to feed in a 10-week-old breast-fed baby occurred 12 hours after her mother started treatment with clemastine.[2] Clemastine was detected in the mother's breast milk. The baby recovered and was feeding normally on the day after the drug was stopped.

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. Kok THHG, *et al.* Drowsiness due to clemastine transmitted in breast milk. *Lancet* 1982; **i:** 914–15.

Porphyria. Clemastine has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

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

Pharmacokinetics
Clemastine fumarate is rapidly and almost completely absorbed from the gastrointestinal tract; peak plasma concentrations are achieved in 2 to 4 hours. Unchanged drug and metabolites are excreted principally in the urine. An elimination half-life of about 21 hours has been reported. Clemastine is distributed into breast milk.

◊ References.

1. Schran HF, *et al.* The pharmacokinetics and bioavailability of clemastine and phenylpropanolamine in single-component and combination formulations. *J Clin Pharmacol* 1996; **36:** 911–22.

Uses and Administration
Clemastine fumarate, a monoethanolamine derivative, is a sedating antihistamine with antimuscarinic and moderate sedative properties. It has been reported to have a duration of action of about 10 to 12 hours. It is used for the symptomatic relief of allergic conditions including urticaria and angioedema (p.565), rhinitis (p.565) and conjunctivitis (p.564), and in pruritic skin disorders (p.565).

Clemastine is given as the fumarate although doses are expressed in terms of the base. Clemastine fumarate 1.34 mg is equivalent to about 1 mg of clemastine base. The usual oral dose is 1 mg twice daily. Up to 6 mg daily has been given, particularly for urticaria and angioedema. Children aged 1 to 3 years may be given 250 to 500 micrograms twice daily; those aged 3 to 6 years, 500 micrograms twice daily; and those aged 6 to 12 years, 0.5 to 1 mg twice daily.

Clemastine fumarate may be given by intramuscular or slow intravenous injection in a total daily dose equivalent to 4 mg of clemastine for acute allergic reactions; for prophylaxis 2 mg is given by intravenous injection. The dose for children is 25 micrograms/kg daily in two divided doses by intramuscular injection.

Clemastine fumarate has also been used topically, although as with other antihistamines, there is a risk of sensitisation.

Preparations
BP 2008: Clemastine Oral Solution; Clemastine Tablets;
USP 31: Clemastine Fumarate Tablets.

Proprietary Preparations (details are given in Part 3)
Austria: Tavegyl; ***Braz.:*** Agasten; ***Canad.:*** Tavist; ***Cz.:*** Tavegyl; ***Denm.:*** Tavegyl; ***Ger.:*** Tavegil; ***India:*** Clamist; ***Indon.:*** Tavegyl; ***Ital.:*** Tavegil†; ***Mex.:*** Tavist; ***Neth.:*** Tavegil; ***Philipp.:*** Marsthine; Tavegyl; Tavist; ***Port.:*** Tavegyl; Tavist; ***Rus.:*** Tavegyl (Тавегил); ***S.Afr.:*** Tavegyl; ***Spain:*** Tavegil; ***Swed.:*** Tavegyl; ***Switz.:*** Tavegyl; ***Turk.:*** Tavegyl; ***UK:*** Tavegil; ***USA:*** Contac 12 Hour Allergy; Dayhist-1; Tavist Allergy.

Multi-ingredient: ***Braz.:*** Emistin; ***Ger.:*** Corto-Tavegil†; ***Mex.:*** Tavist-D†; ***Spain:*** Dexa Tavegil.