

Interactions

As for the sedating antihistamines in general, p. 614.3.

Pharmacokinetics

Peak plasma concentrations of doxylamine succinate occur 2 to 3 hours after oral doses. An elimination half-life of about 10 hours has been reported.

References.

1. Friedman H, *et al.* Clearance of the antihistamine doxylamine: reduced in elderly men but not in elderly women. *Clin Pharmacokinet* 1989; **16**: 312-16.

Preparations

Proprietary Preparations (details are given in Volume B)

Single-ingredient Preparations. *Austral.:* Dozile; Restaviv; *Canad.:* Unison-2; *Chile:* Calmex; Dorminocitl; Noczap; *Zar. cop. Fr.:* Donormyl; Lidene; Noctyl; *Ger.:* Gitalun; Hoggar Night; Mereprine; SchlafTabs; Sedaplus; Valocordin-Doxylamine; *Hong Kong:* Sominar; *Israel:* Sleep Aid; Tonight; *NZ:* Dozile; *Philipp.:* Unison; *Port.:* Dormidina; *Rus.:* Donormyl (Донормил); *S.Afr.:* Restwel; Somnil; *Spain:* Dormidina; Dormirel; *Switz.:* Sanalepsi N; *Thai.:* Hoggar N; Sominar; *Turk.:* Unison; *Ukr.:* Donormyl (Донормил); Somnil (Сонмил); *USA:* Aldex AN; Doxytex; Unison SleepTabs.

Multi-ingredient Preparations. *Arg.:* Epidac; *Austral.:* Analgesic/Calmative; Chemists Own Dolased Day/Night Pain Relief; Codagesic; Codalgol Plus; Dimetapp Cold & Flu Night Relief; Dimetapp Cough, Cold & Flu; Dolased Analgesic-Calmative; Fiorinal; Maxydol; Mersyndol; Panadeine Plus; Panalgescic; Tensodeine; *Austria:* Wick Erkaltungs-Saft fur die Nacht; Wick Erkaltungssirup fur die Nacht; Wick Hustensaft; *Belg.:* Pholco-Mereprine; *Braz.:* EMS Expectorante; Hytos Plus; Revenil Dospan; Revenil Expectorante; Revenil; Silencium; Xpe Expectorante; *Canad.:* Buckley's Nighttime Cold and Sinus; Cold & Flu Nighttime; Cold Flu Relief; Cold/Flu Medicine; Dalmaco; Diclectin; Medicament Sinus pour La Nuit; Mersyndol with Codeine; Night Relief Cold & Flu; Nighttime Cold & Flu Relief; Nighttime Cold & Flu; Nighttime; Nitetime Cold Medicine; ratio-Calmaydone; Regular Strength Sinus Medication; Sinus Medication Night; Sinus Medication; Tylenol Cold and Flu Nighttime; Tylenol Sinus (Nighttime Relief); Vicks Nyquil Cold & Flu; Vicks NyQuil Cough; Vicks NyQuil Sinus; Zicam Multi-Symptom Cold & Flu Nighttime; *Chile:* Pluriamin; *Fr.:* DolirhumePro; *Ger.:* Wick Medinait fur die Nacht; Wick Medinait mit Honig und Kamillenaroma; *India:* Bedoxin; Bookey Plus; Bookey; DBSIX; Dixip; Dolibird; Domi-6; Dopyx; Doria-F; Doris-F; Dosis-F; Doxilam; Doximon; Doxinate Plus; Doxinate; Doxyfem-B6; Doxyfol; Doxyla B6 Plus; Doxyla B6; Doxylic; DPF-OD; DPF; Dymip-P; E-Preg; Emestat; Env; Erywell; Evadox; Feel Good-HR; Feel Good; Floridox; Folifac; Foxydol; Freshita Plus; Freshita-DS; Fullday; Genis; Good Day; Gooday; Goodmorn Plus; Goodmorn; Ibeln; Indaxin-B6; Kan-Fresh; Kindvom; Lupinate; MFresh; Morsi; Morsik-R; Nausik; Nomit; Nons; Nona; Norvom; Nosic; Novoter; NVDP; Onat; Optidox; Oxidox; Rest-Aid; Vominat; *Indon.:* Dexmolex; Siladex; *Irl.:* Syndol; *Ital.:* Vicks Medinait; *NZ:* Mersyndol; Pharmacist's Own Pain Relief Plus; *Pol.:* Tabin Impakt; *Port.:* Nausefe; *S. Afr.:* Abflex; Accurate; Adco-Dol; Asic; B-Dol; Betapyn; Cepacol Cough; Codoxol; Doxsyn; Lenapain; Nethaprin Dospan; Nethaprin Expectorant; Nomopain; Paxidal; Pynstop; Sedapain; Sedinol; Syndol; Tensopyn; Vicks Medinait; *Spain:* Cariban; Medinait; *Switz.:* Vicks Medinait; *Turk.:* Vicks Medinait; *UK:* Painex; Propain Plus; Syndol; Vicks Medinait; *USA:* Alka-Seltzer Plus Day & Night Cold; Alka-Seltzer Plus Day & Night Cold; Alka-Seltzer Plus Night Cold; Alka-Seltzer Plus Night-Time Cold; Alka-Seltzer Plus Severe Sinus Congestion Allergy & Cough; All-Nite Cold Formula; Diclegis; Genite; Lortuss DM; Lortuss DM; Lortuss LQ; Night Time Cold/Flu Relief; Nite Time Cold Formula; NyQuil Hot Therapy; NyQuil Night-time Cold/Flu; Nyctcold Medicine; Vicks NyQuil LiquiCaps; Vicks NyQuil Multi-Symptom Cold Flu Relief; Vicks NyQuil Sinex; *Venez.:* Mercindol.

Pharmacopoeial Preparations

USP 36: Acetaminophen, Dextromethorphan Hydrobromide, Doxylamine Succinate, and Pseudoephedrine Hydrochloride Oral Solution; Doxylamine Succinate Syrup; Doxylamine Succinate Tablets.

Ebastine (BAN, USAN, rINN)

Ebastini; Ebastin; Ebastina; Ebastinas; Ébastine; Ebastinum; LAS-W-090; W-090; Эбастин.

4'-tert-Butyl-4-[4-(diphenylmethoxy)piperidino]butyrophene.

C₂₂H₂₉NO₂=469.7

CAS — 90729-43-4.

ATC — R06AX22.

ATC Vet — QR06AX22.

UNII — TQD7Q784P1.

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

Ph. Eur. 8: (Ebastine). A white or almost white crystalline powder. M.p. about 86 degrees. Practically insoluble in water; very soluble in dichloromethane; sparingly soluble in methyl alcohol. Protect from light.

All cross-references refer to entries in Volume A

Profile

Ebastine, a piperidine derivative, is a non-sedating antihistamine (p. 610.1) with a long duration of action. It does not have significant sedative or antimuscarinic actions.

Ebastine is given for the symptomatic relief of allergic conditions including rhinitis (p. 612.1) and in pruritic skin disorders (p. 612.1). The usual oral dose is 10 to 20 mg daily. It is also used with a decongestant such as pseudoephedrine hydrochloride.

References.

1. Luria X. Comparative clinical studies with ebastine: efficacy and tolerability. *Drug Safety* 1999; **21** (suppl 1): 63-7.
2. Hurst M, Spencer CM. Ebastine: an update of its use in allergic disorders. *Drugs* 2000; **59**: 981-1006.
3. Lasseter KC, *et al.* Pharmacokinetics and safety of ebastine in patients with impaired hepatic function compared with healthy volunteers: a phase I open-label study. *Clin Pharmacokinet* 2004; **43**: 121-9.
4. Noveck RJ, *et al.* Pharmacokinetics and safety of ebastine in healthy subjects and patients with renal impairment. *Clin Pharmacokinet* 2007; **46**: 525-34.
5. Sastre J. Ebastine in allergic rhinitis and chronic idiopathic urticaria. *Allergy* 2008; **63** (suppl 89): 1-20.

Porphyria. The Drug Database for Acute Porphyria, compiled by the Norwegian Porphyria Centre (NAPoS) and the Porphyria Centre Sweden, classifies ebastine as probably porphyrinogenic; it should be prescribed only for compelling reasons and precautions should be considered in all patients.¹

1. The Drug Database for Acute Porphyria. Available at: <http://www.drugs-porphyria.org> (accessed 07/10/11)

Preparations

Proprietary Preparations (details are given in Volume B)

Single-ingredient Preparations. *Austria:* Ebastel; *Belg.:* Estivan; *Braz.:* Ebastel; *China:* Kestine (开思亭); Si Jin (思金); Su Di (苏迪); *Denm.:* Durfin; *Kestine (Fin.:* Kestine; Kestox; *Fr.:* Kestin; Kestinylo; *Ger.:* Ebastel; *Gr.:* Kestine; *Hong Kong:* Kestine; *India:* Ebast; Erostin; *Irl.:* Kestine; *Ital.:* Clever; Kestine; *Jpn.:* Ebastel; *Mex.:* Evastel; Pinaval-T; *Neth.:* Kestine; Netan; *Norw.:* Kestine; *Philipp.:* Aleva; *Port.:* Ebastion; Estivan; Kestine; Ribastex; *Rus.:* Kestine (Кестин); *S.Afr.:* Kestine; *Singapore:* Kestine; *Spain:* Alastina; Bactil; Ebastel; *Swed.:* Kestine; *Turk.:* Kestine; *Venez.:* Ebastel.

Multi-ingredient Preparations. *Braz.:* Ebastel D; *India:* EBA-P; Ebast-DC; Erostin-DC; *Mex.:* Evastel-D; *Philipp.:* Co-Aleva; *Spain:* Rino Ebastel; Rinobactil.

Embramine Hydrochloride (BANM, rNNM)

Embramina, hidrocloruro de; Embramine, Chlorhydrate d'; Embramini Hydrochloridum; Embraminium Chloratum; Hidrocloruro de embramina; Mebrophenhydramine Hydrochloride; Mebrophenhydraminium Chloratum; Эмбрамина Гидрохлорид.

2-(4-Bromo- α -methylbenzhydryloxy)-NM-dimethylethylamine hydrochloride.

C₁₆H₂₂BrNO₂HCl=384.7

CAS — 3565-72-8 (embramine); 13977-28-1 (embramine hydrochloride); 21661-63-2 (embramine teoclate).

UNII — 7BJ3V657VC.

Profile

Embramine hydrochloride, a monoethanolamine derivative, is a sedating antihistamine (p. 610.1). Embramine hydrochloride and embramine teoclate have been given orally for their antihistamine and antiemetic properties.

Preparations

Proprietary Preparations (details are given in Volume B)

Single-ingredient Preparations. *Cz.:* Medtrin; *India:* Mebryl.

Emedastine Fumarate (BANM, rNNM)

AL-3432A; Emedastinidifumaraatti; Emedastin difumarat; Emedastin Fumarat; Emedastina, fumarato de; Emedastindifumarat; Emedastine Difumarate (USAN); Émedastine, difumarate d'; Émedastine, Fumarate d'; Emedastini Difumaras; Emedastini Fumaras; Emedastyny difumaran; Fumarato de emedastina; KB-2413; KG-2413; LY-188695; Эмедастина Фумарат.

1-(2-Ethoxyethyl)-2-(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)benzimidazole fumarate (1:2).

C₁₇H₂₆N₄O₂·2C₄H₄O₄=534.6

CAS — 87233-61-2 (emedastine); 87233-62-3 (emedastine fumarate).

ATC — S01GX06.

ATC Vet — QS01GX06.

UNII — 4ZMB894QOSM.

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

Ph. Eur. 8: (Emedastine Difumarate). A white or yellowish powder. It exhibits polymorphism. Soluble in water; sparingly soluble in dehydrated alcohol; very slightly soluble in acetone. A 0.2% solution in water has a pH of 3.0 to 4.5. Protect from light.

USP 36: (Emedastine Difumarate). A white to faintly yellow crystalline powder. Soluble in water. pH of a 0.2% solution in water is between 3.0 and 4.5. Store in airtight containers. Protect from light.

Uses and Administration

Emedastine is an antihistamine. It is instilled twice daily as the fumarate as eye drops containing the equivalent of 0.05% of emedastine for the symptomatic relief of allergic conjunctivitis (p. 611.1). It is also given orally in usual doses of 2 to 4 mg of the fumarate daily in two divided doses for allergic rhinitis (p. 612.1), urticaria (p. 612.3), and pruritic skin disorders (p. 612.1).

Adverse Effects and Precautions

As for the antihistamines in general, p. 613.1 and p. 613.3, respectively.

Ocular corneal infiltrates, local irritation, photophobia, rhinitis, and headaches have been reported after use of emedastine eye drops. Treatment should be stopped if corneal infiltrates develop.

Porphyria. The Drug Database for Acute Porphyria, compiled by the Norwegian Porphyria Centre (NAPoS) and the Porphyria Centre Sweden, classifies emedastine as not porphyrinogenic; it may be used as a drug of first choice and no precautions are needed.¹

1. The Drug Database for Acute Porphyria. Available at: <http://www.drugs-porphyria.org> (accessed 07/10/11)

Pharmacokinetics

Emedastine is absorbed from the gastrointestinal tract and peak plasma concentrations occur about 3 hours after an oral dose. Small amounts of emedastine are absorbed after application to the eye. It is mainly metabolised in the liver to two primary metabolites 5- and 6-hydroxyemedastine which are excreted in the urine along with a small amount of unchanged drug. The elimination half-life is reported to be 7 hours after an oral dose and 10 hours after topical use.

Preparations

Proprietary Preparations (details are given in Volume B)

Single-ingredient Preparations. *Austria:* Emadine; *Belg.:* Emadine; *Braz.:* Emadine; *Canad.:* Emadine; *China:* Emadine (埃美丁); *Cz.:* Emadine; *Denm.:* Emadine; *Fin.:* Emadine; *Fr.:* Emadine; *Ger.:* Emadine; *Gr.:* Emadine; *Hong Kong:* Emadine; *Hung.:* Emadine; *Irl.:* Emadine; *Israel:* Emadine; *Ital.:* Emadine; *Jpn.:* Daren; Remicut; *Malaysia:* Emadine; *Neth.:* Emadine; *Norw.:* Emadine; *Pol.:* Emadine; *Port.:* Emadine; *S.Afr.:* Emadine; *Spain:* Emadine; *Swed.:* Emadine; *Switz.:* Emadine; *Thai.:* Emadine; *Turk.:* Emadine; *UK:* Emadine; *USA:* Emadine.

Pharmacopoeial Preparations

USP 36: Emedastine Ophthalmic Solution.

Epinastine Hydrochloride (BANM, rINN)

Epinastina, hidrocloruro de; Epinastine, chlorhydrate d'; Epinastine, Chlorhydrate d'; Epinastinhydrochlorid; Epinastini hydrochloridum; Hidrocloruro de epinastina; WAL-801-CI; Эпинастина Гидрохлорид.

3-Amino-9,13b-dihydro-1H-dibenz[c,f]imidazo[1,5-a]azepine hydrochloride.

C₁₆H₁₅N₃·HCl=285.8

CAS — 80012-43-7 (epinastine).

ATC — R06AX24; S01GX10.

ATC Vet — QR06AX24; QS01GX10.

UNII — GFM41555XL.

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

Ph. Eur. 8: (Epinastine Hydrochloride). A white or almost white, hygroscopic, crystalline powder. Freely soluble in water and in methyl alcohol; slightly soluble in acetonitrile; sparingly soluble in dichloromethane. Store in airtight containers.

Profile

Epinastine hydrochloride is an antihistamine (p. 610.1) reported to have no significant sedative activity. It has been given orally in the management of allergic rhinitis and pruritic skin disorders. It is also used twice daily as eye