

Metizoline Hydrochloride (BANM, USAN, rINN) ⊗

EX-10-781; Hidrocloruro de metizolina; Métizoline, Chlorhydrate de; Metizolini Hydrochloridum; Metizoline Hydrochloride; RMI-10482A. 2-(2-Methylbenzo[b]thienylmethyl)-2-imidazoline hydrochloride.

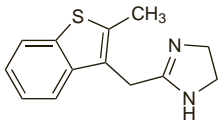
Метизолина Гидрохлорид

$C_{13}H_{14}N_2S \cdot HCl = 266.8$.

CAS — 17692-22-7 (metizoline); 5090-37-9 (metizoline hydrochloride).

ATC — R01AA10.

ATC Vet — QR01AA10.



(metizoline)

NOTE. The name benzoline has been used as a synonym for metizoline. Care should be taken to distinguish it from benzolin (4-chloro-2,3-dihydro-2-oxo-1,3-benzothiazol-3-ylacetic acid, $C_8H_6ClNO_3S = 243.7$), which is a herbicide. Also do not confuse with benzoline (see Tolazoline, p.1415), which is a vasodilator.

Profile

Metizoline hydrochloride is a sympathomimetic with effects similar to those of naphazoline (p.1565) that has been used for its vasoconstrictor activity in the treatment of nasal congestion.

Morclofone (rINN)

Dimeclofenone; Morclofona; Morclofonum; Morclophon. 4'-Chloro-3,5-dimethoxy-4-(2-morpholinoethoxy)benzophenone.

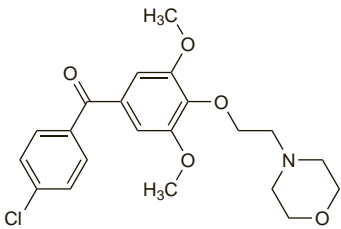
Морклофон

$C_{21}H_{24}ClNO_5 = 405.9$.

CAS — 31848-01-8 (morclofone); 31848-02-9 (morclofone hydrochloride).

ATC — R05DB25.

ATC Vet — QR05DB25.

**Profile**

Morclofone is a centrally acting cough suppressant used for non-productive cough (p.1547); it is given orally in usual doses of 150 mg four or five times daily. It has also been given as the hydrochloride.

Preparations

Proprietary Preparations (details are given in Part 3)

Ital.: Plausitin; **Switz.:** Nitux.

Naphazoline (BAN, rINN) ⊗

Nafatsoliini; Nafazolin; Nafazolina; Naphazolinum. 2-(1-Naphthylmethyl)-2-imidazoline.

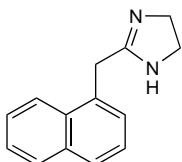
Нафазолин

$C_{14}H_{14}N_2 = 210.3$.

CAS — 835-310-4.

ATC — R01AA08; R01AB02; S01GA01.

ATC Vet — QR01AA08; QR01AB02; QSO1GA01.

**Naphazoline Hydrochloride** (BANM, rINN) ⊗

Hidrocloruro de nafazolina; Nafatsoliinihydrokloridi; Nafazolin Hidroklorid; Nafazolin-hidroklorid; Nafazolin-hydrochlorid; Nafazolinhydroklorid; Nafazolin hydrochloridas; Naphazoline, chlorhydrate de; Naphazolini hydrochloridum.

Нафазолина Гидрохлорид

$C_{14}H_{14}N_2 \cdot HCl = 246.7$.

CAS — 550-99-2.

ATC — R01AA08; R01AB02; S01GA01.

ATC Vet — QR01AA08; QR01AB02; QSO1GA01.

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

Ph. Eur. 6.2 (Naphazoline Hydrochloride). A white or almost white, crystalline powder. Freely soluble in water; soluble in alcohol. Protect from light.

USP 31 (Naphazoline Hydrochloride). A white, odourless, crystalline powder. Freely soluble in water and in alcohol; very slightly soluble in chloroform; practically insoluble in ether. pH of a 1% solution in water is between 5.0 and 6.6. Store in airtight containers. Protect from light.

Naphazoline Nitrate (BANM, rINN) ⊗

Nafatsoliiniitraatti; Nafazolin Nitrat; Nafazolinnitrat; Nafazolin-nitrat; Nafazolino nitratas; Nafazolin azotan; Naphazoline, nitrate de; Naphazolini nitratis; Naphazolinium Nitricum; Naphthizinum; Nitrate de nafazolina.

Нафазолина Нитрат

$C_{14}H_{14}N_2 \cdot HNO_3 = 273.3$.

CAS — 5144-52-5.

ATC — R01AA08; R01AB02; S01GA01.

ATC Vet — QR01AA08; QR01AB02; QSO1GA01.

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

Ph. Eur. 6.2 (Naphazoline Nitrate). A white or almost white, crystalline powder. Sparingly soluble in water; soluble in alcohol. A 1% solution in water has a pH of 5.0 to 6.5. Protect from light.

Adverse Effects, Treatment, and Precautions

As for Sympathomimetics, p.1407; naphazoline has mainly alpha-agonist effects. After local use, transient irritation may occur. Rebound congestion may occur after frequent or prolonged use. Systemic effects, including nausea, headache, and dizziness have occurred after topical use. Overdosage or accidental dosage by mouth may cause CNS depression with marked reduction of body temperature and bradycardia, sweating, drowsiness, and coma, particularly in children; it should be used with great caution, if at all, in infants and young children. Use of naphazoline in the eye may liberate pigment granules from the iris, especially when given in high doses to elderly patients. Hypertension may be followed by rebound hypotension. Treatment of adverse effects is symptomatic.

Effects on the eyes. For mention of conjunctivitis induced by ophthalmic decongestant preparations containing naphazoline, see under Phenylephrine, p.1568.

Intraoperative use. A report¹ of 2 cases of toxicity associated with intraoperative use of a naphazoline-soaked sponge to control excessive bleeding after adenoidectomy. Both patients experienced hypertension and reflex bradycardia, which evolved in one case into marked hypotension. There was evidence of CNS depression with a reduced respiration rate and prolonged recovery from anaesthesia.

1. Wenzel S, et al. Course and therapy of intoxication with imidazoline derivate naphazoline. *Int J Pediatr Otorhinolaryngol* 2004; **68**: 979–83.

Interactions

Since naphazoline is absorbed through the nasal mucosa interactions may follow topical application. The *BNF* considers that all sympathomimetic nasal decongestants may cause a hypertensive crisis if used during treatment with an MAOI. For the interactions of sympathomimetics in general, see p.1407.

Pharmacokinetics

Systemic absorption has been reported after topical use of solutions of naphazoline. It is not given systemically, but it is readily absorbed from the gastrointestinal tract. Naphazoline instilled into the eye causes conjunctival vasoconstriction within 10 minutes and effects can last for up to 6 hours.

Uses and Administration

Naphazoline is a sympathomimetic (p.1408) with marked alpha-adrenergic activity. It is a vasoconstrictor with a rapid and prolonged action in reducing swelling and congestion when applied to mucous membranes.

Naphazoline and its salts are used for the symptomatic relief of nasal congestion (p.1548). Solutions containing 0.05 to 0.1% of the hydrochloride or the nitrate may be applied topically as nasal drops or a spray usually up to once every 6 hours. Children aged 7 years and over have used a preparation containing 0.05%.

Solutions containing up to 0.1% of naphazoline hydrochloride have been instilled into the eye as a conjunctival decongestant (see Conjunctivitis, p.564).

Naphazoline has been used as a vasoconstrictor with local anaesthetics.

Naphazoline acetate has also been used in nasal preparations.

Preparations

USP 31: Naphazoline Hydrochloride and Pheniramine Maleate Ophthalmic Solution; Naphazoline Hydrochloride Nasal Solution; Naphazoline Hydrochloride Ophthalmic Solution.

Proprietary Preparations (details are given in Part 3)

Arg.: Actifedrin Nasal; Bactio Rhin; Bano Ocular Agrand; Dazolin; Disel; Gotabiotin D; Gotinal; Let-Nasak; Mirasan; Mirus-S; Nafazolex; Nasalax; Privina; Rhinal; **Austral.:** Albalon; Clear Eyes; Naphcon; Optazine; **Austria:** Aconex; Coldan; Isoflax; Mertan; Privin; Rhinon; Rhinoperd; **Belg.:** Albalon; Deltarhinol-Mono; Naphcon; Neusonin; Priciasol; Vasocedine; **Braz.:** Clarivitt; Clarof; Multisor; Nariaf; Nariax; Nazicol; Neosoro; Privina; Rino Resfenol; Rinos-A; **Canada:** Ak-Con; Albalon; Allergy Drops; Clear Eyes; Dioptron; Naphcon Forte; Red Away; Vasocort; **Chile:** Albasol; Clarimir; Red Off; Vi-Clear; **Cz.:** Proclint; Sanorin; **Ger.:** Idril N sine; Pniol Nasenspray; Privin; Proclun; Rhinex mit Naphazolin; Tele-Stullin; **Gr.:** Coldan; Naphcon; **Hong Kong:** Albalon; All Clear; **Hung.:** Naphcon; Proclun; **India:** Clearine; Ocustress; **Indon.:** Optrine; **Israel:** Naphasal; Naphcon Forte; **Ital.:** Colliro Alfa; Desamin Same; Imidazy; Indiniana Due; Nafazolina; Pupilla; Rinazina; **Mex.:** Afazol; Alphadinal; Celunaf; Fazolil; Gotinal; Nazil; **Neth.:** Albalon; **NZ:** Albalon; Clear Eyes; Naphcon; **Philipp.:** Cosooth; **Pol.:** Rhinazin; **Rus.:** Naphthyzin (Нафтизин); Sanorin (Санорин); **S.Afr.:** Murine Clear Eyes; Salfy Bleu; **Spain:** Alfa; Euboral; Miraclor; Vasoconstrictor Clear; **Swed.:** Rimidof; **Switz.:** Albalon; Mirinhat; **Thai.:** Albalon; Naphcon; **Turk.:** Deltarhinol; Enflucide; **UK:** Murine; **USA:** Ak-Con; Albalon; All Clear; Allerest; Allergy Drops; Clear Eyes; Clear Eyes Plus Redness Relief; Comfort Eye Drops; Dagest; Nafazair; Napha Forte; Naphcon; Privine; Vasocort; **Venez.:** Clarasol; Clearize; Fanasaf; Fazolil; Fazonil; Gotinal; Nafin; Naphcon; Nas; Niazol; Ninazo.

Multi-ingredient. Arg.: Alercortil; Alvo Nasal; Antibiocort; Bactio Rhin Prednisolona; Bideon; Biotaer Nasal; Dexafurazon; Dexalergin; Disel Hydrocortisona; Drynasin; Factione; Fadanasal; Gramicortil; Hyalcom; Mira Klonal; Mirus; Nasjof; Nasomicina; Neo-Currino; Neodexa Plus; Neoefodil; Neosona; Nexadron Compusto; Nexadron Plus; Panoptic; Provacsin Nasal; Refenax Colirio; Refenax Gostas Nasales; Rinoflax AG M; Rinogel; Suavithiol; Vistacoloran; **Austral.:** Albalon-A; Antistine-Privine; In A Wink; Naphcon-A; Oprex; Visine Allergy with Antihistamine; **Austria:** Coldistan; Coldophthal; Histophthal; Luuf-Nasenspray; Ophtaguttal; Rhinodrin; Rhinon; Rhinoperd comp; **Belg.:** Diphenhydramine Constrictor; Minhavez; Naphcon-A; Neofenox; Sofraline; Sofrasolone; Zincfrin Antihistaminicum; **Braz.:** Alergortox Nasal; Clari; Colirio Legrand; Colirio Moura Brasil; Colirio Teuto; Conidrin; Fluo-Vaso; Hemodott; Hidrocin; Inhdnina; Lerin; Maxibel; Mentodrin; Nardirin; Nanflux; Naso-Josp; Nazobel; Nazobio; Neo Quimica Colirio; Nitriolen; Novo Rino; Rhinosept; Rinisone; Rinosite; Sinustrat Vasoconstrictor; Somne Adulto; Stilux; Visazul; Visiplex; Visolon; Visual; Zincoloc; **Canada:** Albalon-A; Clear Eyes Allergy; Collyre Bleu; Dioptron A; Naphcon-A; Onrectal; Opcon-A; Vasocon-A; Visine Advance Allergy; Zincfrin-A; **Chile:** Albasol A; Clamrin F; Dessolets; Miral; Mirus; Naphcon-A; Naphtears; Nico Drops; Novo-Tears; Oculosan; Oftalirio; Red Off Aqua; Red Off Plus; **Cz.:** Sanorin-Analergin; **Denm.:** Albalon; Antistina-Privine; Sesal; **Fin.:** Antistin-Privin; Zincfrin-A; **Fr.:** Collyre Bleu; Derinox; **Ger.:** Antistin-Privin; Diabenyf-Rhinex; duraultra; Konjunktival Thilof; Oculosan N; Rhinoguttae Dexamethasoni cum Naphazolinol; Rhinosovilt; Siozwo; Stipog; **Gr.:** Neo-Priphen; Oculosan; Septobore; Zabysept; **Hong Kong:** Clear Blue; Frazoline; Konjunktival; Naphcon-A; Nazin; Oculosan; Opcon-A; **Hung.:** Coldistan; **India:** Andre; Andre-I-Kul; Betnesol-N Nasal; Eforclin; Fenox; Ocuress; Ocuress-AH; Ocuress-Z; Proto-Boric; **Indon.:** Flamerig; Indofrin-A; Isotic Azora; Naphcon-A; Oculosan; Zincopto; **Israel:** Alnase; Antistin-Privin; Nodryl; Optry; Phenylphrine-Azol; Proaf; **Ital.:** Alfalfor; Antisettico Astringente Sedativo; Antistin-Privina; Colirio Alfa Antistaminico; Conzina; Deltarhinol; Fotofil; Genalfa; Idronemilcil; Imidazy Antistaminico; Indaco; Istamina; Nafcon A; Oftalmil; Pupilla Antistaminico; Rinocidina; Rinofomentil; Zinc-Imizol; **Malaysia:** Alergofal; Napha A; Naphcon-A; Oculosan; **Mex.:** Afazol Z; Bioflin; Biotarson O; Eyrasil; Istasol; Midazol Ofteno; Mirus; Naphcel; Naphtears; Oftalirio; Opcon-A; Soltictror con Lagrflim; Solutina; Sulvi; Zincfrin-A; **NZ:** Albalon-A; Betnesol Aqueous; Clear Eyes ACR; Dagest 2; Naphcon-A; Oprex Red-Eye Relief; Visine Allergy; **Philipp.:** Decocon A; Moisturizing All Clear; Naphcon-A; Oculosan; Optaphen; **Pol.:** Betadrin; Cincol; Dermophenazol; Mibalin; Oculosan; Oftophenazol; Rhinophenazol; Sulfaninol; **Port.:** Alergitalmina; Colircusi Anestésico; Naso-Privelina; **Rus.:** Betadrin (Бетадрин); Polynadim (Полинадим); Sanorin (Санорин); Sanorin-Analergin (Санорин-аналергин); **S.Afr.:** Albalon-A; Antistin-Privin; Covomycin; Covosan; ENT; Nasdro; Oculosan; Universal Nasal Drops; Zincfrin-A; **Singapore:** Antistin-Privin; Flucur; Naphcon-A; **Spain:** Alergofal; Centlux; Cloram Zinc; Coliriocilina Adren Astr; Epistaxol; Kanafosal; Kanafosal Predni; Oftalmol Ocular; Ojoseb; Rinovel; Zolina; **Swed.:** Antasten-Privin; **Switz.:** Antistin-Privin; Collyre Alpha; Collyre Bleu Laiter; Gouttes nasales N; Oculosan; Spray nasal comp pour adultes; **Thai.:** Levoptin; Naphcon-A; Oculosan; **Turk.:** Alergofal; Sulfarhin; **UK:** Eye Dew; Oprex Red Eyes; **USA:** 4-Way Fast Acting; Antazoline-V; Clear Eyes Seasonal Relief; Maximum Strength Allergy Drops; Nafazair A; Naphazoline Plus; Naphcon-A;