Bepotastine (rINN)

Bepotastina; Bépotastine; Bepotastinum; Betotastine. (+)-4-{[(S)p-Chloro-α-2-pyridylbenzyl]oxy}- I-piperidinebutyric acid. Бепотастин

 $C_{21}H_{25}CIN_2O_3 = 388.9.$ - 125602-71-3; 190786-43-7.

Bepotastine Besilate (rINNM)

Bépotastine, Bésilate de; Bepotastini Besilas; Besilato de bepotastina; Betotastine Besilate; TAU-284.

Бепотастина Безилат

 $C_{21}H_{25}CIN_2O_3$, $C_6H_6O_3S = 547.1$. CAS - 190786-44-8.

Bepotastine is an antihistamine (p.561) used as the besilate in the treatment of allergic rhinitis. It is also used for the symptomatic relief of urticaria and pruritic skin disorders. The usual oral dose is 10 mg of bepotastine besilate twice daily.

Preparations

Proprietary Preparations (details are given in Part 3) **Jpn:** Talion.

Bisulepin

4-[3-(Dimethylamino)propylidene]-4,9-dihydrothienol[2,3b]benzo[e]thiepin.

 $C_{17}H_{19}NS_2 = 301.5$. CAS — 5802-61-9 (bisulepin); 1154-12-7 (bisulepin hydrochloride).

Profile

Bisulepin is given orally as an antihistamine; the hydrochloride salt is used similarly.

Preparations

Proprietary Preparations (details are given in Part 3) **Cz.:** Dithiaden; **Hung.:** Dithiaden†.

Bromazine Hydrochloride (BANM, rINNM)

Bromazine, Chlorhydrate de; Bromazini Hydrochloridum; Bromodiphenhydramine Hydrochloride: Hidrocloruro de bromazina. 2-(4-Bromobenzhydryloxy)-NN-dimethylethylamine hydrochloride.

Бромазина Гидрохлорид

 $C_{17}H_{20}BrNO,HCI = 370.7$

– 118-23-0 (bromazine); 1808-12-4 (bromazine hydrochloride). ATC — R06AA01

ATC Vet — QR06AA01.

Pharmacopoeias. In US.

USP 31 (Bromodiphenhydramine Hydrochloride). A white to pale buff-coloured, crystalline powder having no more than a

faint odour. Soluble 1 in less than 1 of water, 1 in 2 of alcohol and of chloroform, 1 in 3500 of ether, and 1 in 31 of isopropyl alcohol; insoluble in petroleum spirit. Store in airtight containers

Bromazine hydrochloride, a monoethanolamine derivative, is a sedating antihistamine (p.561) with antimuscarinic and marked sedative actions. It is used in combination preparations for the symptomatic treatment of coughs and the common cold (p.564) in an oral dose of 12.5 to 25 mg every 4 to 6 hours. The recommended maximum dose in such preparations is 150 mg daily. Children over 6 years of age may be given 6.25 to 12.5 mg every 6 hours

Preparations

USP 31: Bromodiphenhydramine Hydrochloride and Codeine Phosphate Oral Solution; Bromodiphenhydramine Hydrochloride Elixii

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: USA: Ambenyl Cough Syrup; Amgenal Cough; Bro-

Brompheniramine Maleate

Bromfeniramin Maleat; Bromfeniraminmaleat; Brómfeniraminmaleát; Bromfeniramin-maleinát; Bromfeniramino maleatas; Bromifeniramiinimaleaatti; Bromphéniramine, maléate de; Brompheniramini maleas; Maleato de bromfeniramina; Parabromdylamine Maleate. (±)-3-(4-Bromophenyl)-NN-dimethyl-3-(2-pyridyl)propylamine hydrogen maleate.

Бромфенирамина Малеат

 $C_{16}H_{19}BrN_2, C_4H_4O_4 = 435.3.$

CAS — 86-22-6 (brompheniramine); 980-71-2 (brompheniramine maleate).

ATC - RO6ABOI.

ATC Vet — QR06AB01.

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

Ph. Eur. 6.2 (Brompheniramine Maleate). A white or almost white, crystalline powder. Soluble in water; freely soluble in alcohol, in dichloromethane, and in methyl alcohol. A 1% solution in water has a pH of 4.0 to 5.0. Protect from light.

USP 31 (Brompheniramine Maleate). A white, odourless, crystalline powder. Soluble 1 in 5 of water, 1 in 15 of alcohol and of chloroform; slightly soluble in ether and in benzene. pH of a 1% solution in water is between 4.0 and 5.0. Store in airtight containers. Protect from light.

Incompatibility. Brompheniramine maleate has been reported to be incompatible with some amidotrizoate, adipiodone, and io-

Dexbrompheniramine Maleate (BANM, rINNM)

Dexbromphéniramine, Maléate de; Dexbrompheniramini Maleas; Maleato de dexbromfeniramina.

Дексбромфенирамина Малеат

CAS - 2391-03-9. ATC — RO6ABO6

ATC Vet - QR06AB06

Pharmacopoeias. In US.

USP 31 (Dexbrompheniramine Maleate). A white, odourless, crystalline powder. It exists in two polymorphic forms, one melting between 106° and 107°, and the other between 112° and 113°; a mixture of the two forms may melt between 105° and 113°. Soluble 1 in 1.2 of water, 1 in 2.5 of alcohol, 1 in 2 of chloroform, and 1 in 3000 of ether. pH of a 1% solution in water is about 5. Store in airtight containers. Protect from light.

Adverse Effects and Precautions

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

Breast feeding. The American Academy of Pediatrics¹ states that, although usually compatible with breast feeding, preparations used by breast-feeding mothers which contain dexbrompheniramine maleate with pseudoephedrine have resulted in crying, irritability, and poor sleep patterns in the infant.

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)

Effects on the blood. A report¹ that agranulocytosis in a 34year-old alcoholic man was possibly associated with brompheniramine therapy.

Hardin AS, Padilla F. Agranulocytosis during therapy with a brompheniramine-medication. J Arkansas Med Soc 1978; 75:

Extrapyramidal disorders. Facial dyskinesias have been reported1,2 after use of antihistamines including brompheniramine or dexbrompheniramine maleate.

- 1. Thach BT, et al. Oral facial dyskinesia associated with prolonged use of antihistaminic decongestants. N Engl J Med 1975; 293: 486–7 (brompheniramine maleate, chlorpheniramine maleate, and phenindamine tartrate).
- Barone DA, Raniolo J. Facial dyskinesia from overdose of an antihistamine. N Engl J Med 1980; 303: 107 (dexbrompheniramine maleate)

Withdrawal. Withdrawal symptoms have been reported¹ after stopping long-term therapy with brompheniramine maleate. A patient had been taking 48 mg almost every day for 20 years and developed tremor, nausea, depression, and apyrexial sweating within 48 hours of stopping treatment; symptoms resolved over the following weeks.

1. Kavanagh GM, et al. Withdrawal symptoms after discontinuation of long-acting brompheniramine maleate. Br J Dermatol 1994; 131: 913–14.

Interactions

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

Pharmacokinetics

Brompheniramine maleate appears to be well absorbed from the gastrointestinal tract after oral doses. Peak plasma concentrations are achieved within about 5 hours. An elimination half-life of about 25 hours has been reported. Unchanged drug and metabolites are excreted primarily in the urine.

♦ References.

- 1. Simons FER, et al. The pharmacokinetics and antihistaminic effects of brompheniramine. J Allergy Clin Immunol 1982; **70**: 458–64.
- Paton DM, Webster DR. Clinical pharmacokinetics of H -receptor antagonists (the antihistamines). Clin Pharmacokinet 1985;

Uses and Administration

Brompheniramine maleate, an alkylamine derivative, is a sedating antihistamine with antimuscarinic and moderate sedative actions.

Brompheniramine is a racemic mixture; dexbrompheniramine, the dextrorotatory isomer, has about twice the activity of brompheniramine by weight. Brompheniramine maleate and dexbrompheniramine maleate are used for the symptomatic relief of allergic conditions, mainly rhinitis (p.565) and conjunctivitis (p.564). They are common ingredients of compound preparations for the symptomatic treatment of coughs and the common cold (p.564). However, such preparations should be used with caution in children, and generally avoided in those under 2 years of age (see p.562). Brompheniramine tannate has been used similarly.

Brompheniramine maleate is given in usual oral doses of 4 to 8 mg three or four times daily. Children up to 3 years of age are given 0.4 to 1 mg/kg over 24 hours in four divided doses. Children aged 3 to 6 years are given 1 to 2 mg three or four times daily and those aged 6 to 12 years 2 to 4 mg three or four times daily.

Brompheniramine maleate has also been given by subcutaneous, intramuscular, or slow intravenous injection; the dose is usually 10 mg every 8 to 12 hours as necessary and the total parenteral dose should not exceed 40 mg in 24 hours.

Dexbrompheniramine maleate is normally given as an ingredient of decongestant preparations containing pseudoephedrine. The dose of dexbrompheniramine maleate by mouth in these combinations is 2 mg up to four times daily. Children over 6 years can be given 1 mg up to four times daily.

Modified-release oral preparations of brompheniramine maleate or dexbrompheniramine maleate are available in some countries; dosage is specific to a particular formulation.

Preparations

BP 2008: Brompheniramine Tablets;

USP 31: Brompheniramine Maleate Elixir; Brompheniramine Maleate Injection; Brompheniramine Maleate Tablets; Dexbrompheniramine Maleate Tablets; Dexbrompheniramine Maleate and Pseudoephedrine Sulfate Oral Solution.

Proprietary Preparations (details are given in Part 3)

Fr.: Dimegan, Malaysia: Bomex; Singapore: Bomex†; Thai.: Babycold; Bomine; Dimetane; UK: Dimotane†; USA: Bidhist; Dimetane†; J-Tan; Lodrane 12; Lodrane 24; Oraminic II; P-Tex.

drane 12; Lodrane 24; Oraminic II; P-Tex.

Multi-ingredient: Arg.: Factus; Austral.: Dimetapp; Dimetapp DM; Braz.: Bilalerge; Deconges Plus; Decongex Plus Expectorante†; Dimetapp; Winter AP; Canad.: Dimetane Expectorant C; Dimetape Cold; Dimetapp DM Cough & Cold; Dimetape Doral Infant Cold & Fever Drops; Dimetapp Oral Infant Drops; Dimetapp-C; Drixoral; Drixoral Day/Night; Chile: Disofrin†; Cz.: Disophrof; Fin.: Disofrol†; Fr.: Dimetape Expectorant Enfant†; Martigene†; Gr.: Dimetapp New†; Hong Kong: Brom-PP; Brom-Ramine Compound; Bromhexine Compound; Bromphenex; DF Multi-Symptom; Dimaxin†; Dimeta-2; Dimetapp; Nevr; Hong College; Chile; Dimetapp; Drixoral; Eascold; ENT†; Eurotapp; Univist; Vidatapp; Vidatapp Forte; Hung; Disophrol†; Indon.: Alco Plus; Alco Plus DMP; Drixoral; Irl.: Dimotane Co; Malaysia: Drixoral†; Rinafort; Mex.: Afrinex; Cripofer; Dimetapp; Mz: Dimetapp; Drixoral†; Rinafort; Mex.: Afrinex; Cripofer; Dimetapp; Micc; Singapore: Dimetapp; Pot.: Constipal; Ilvico N; S.Afr.: Dimetapp; Ilvico; Singapore: Dimetapp; Drixoral†; Rinafort; Spalin: Disofrol; Ilvico, Swed.: Disofpore: Directapp; Drixoral†; Rinafort; Spain: Disofrol; Ilvico; Swed.: Disofrol; Spain: Disofrol; Rupton†; Thali: Asiatapp; Bepeno; Bepeno-G; Bluco; Bromavon; Bromesep Elixir; Bromesep Expectorant; Bromped; Bromtussia DC†; Brontus; Centapp; Daminate; Directapp; Meditapp; Medit Ominist, Turk: Dispiritor, W. Dirindarie CV, Dirindarie Expection and, promotane Plust; USA: 12 Hour Antihistamine Nasal Decongestant; 12 Hour Cold; Accuhist: Accuhist DM Pediatric; Accuhist PDX; Alacol DM; Allent; Anaplex DM; Anaplex HD; Andehist DM; Andehist PDX; Bromdien DM; Bromarest DX; Bromatan-DM; Bromarest DX; Bromatan-DM; Bromhist-DN; Bromhist-DM; Bromhist-DN; Bromhist-DN; Bromhist-DM; Bromhist-DN; Bromhist-DM; Bromhist-D Pro, C-Iari D, Carbolek Dri, Collet Dri, Comitex Aute Head Cold, CPB WC; Cytuss-HC NR; Dallergy DM; DEKA; Dexaphen-SA; Dimetape Decongestant; Dimetapp: Dimetapp Cold & Fever; Dimetapp DM; Dimetapp Nighttime Flu; Disobrom; Disophrol; Dristan Allergy; Dristan Dimetapp Nighttime Flu; Disobrom; Disophrol; Dristan Allergy; Dristan Cold Maximum Strength Multi-symptom Formula; Drixomed; Drixoral; Drixoral Cold & Allergy; Drixoral Cold & Flu; Drixoral Plus; Drocon-CS; Endáfed; Histacol DM; Histussin HC; lofed; Lodrane; Lodrane 12D; Lodrane D; Lortuss DM; M-END WC; Maximum Strength Dristan Cold; Myphetane DX; Nalex AC; Neo DM; P-Hist DM; PBM Allergy; Pediahist DM; Q-Tapp DM; Respahist; Resperal-DM; Rondamine-DM; Rondec; Seradex-LA; Sildec-DM; Sinadrin Plus; Touro A & H; Touro Allergy, Tusdec-DM; Tusnel-HC; Tussall; ULTRAbrom; VaZol-D; Vazotab; Vazotan; Vazotuss HC; Zotex-PE; Venez.: Dimetapp; Ilvico; Metorfedrin.

Buclizine Hydrochloride (BANM, USAN, rINNM)

Buclizine, Chlorhydrate de; Buclizini Hydrochloridum; Buklizin Hidroklorür: Hidrocloruro de buclizina: NSC-25141: UCB-4445. $(RS) \ I-(4-tert-Butylbenzyl)-4-(4-chlorobenzhydryl) piperazine \ di$ hydrochloride.

Буклизина Гидрохлорид $C_{28}H_{33}CIN_{2},2HCI = 505.9.$ CAS — 82-95-1 (huclizing

- 82-95-1 (buclizine); 129-74-8 (buclizine hydrochloride).

ATC — R06AE01. ATC Vet — QR06AE01.

C(CH₃)₃ (buclizine)

Pharmacopoeias. In Br.

BP 2008 (Buclizine Hydrochloride). A white or slightly yellowish, crystalline powder. Practically insoluble in water; very slightly soluble in alcohol; sparingly soluble in chloroform and in propylene glycol.

Adverse Effects and Precautions

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

Interactions

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

Uses and Administration

Buclizine hydrochloride, a piperazine derivative, is a sedating antihistamine with antimuscarinic and moderate sedative actions. It is used mainly for its antiemetic action, particularly in the prevention of motion sickness (p.564) and with analgesics in the treatment of migraine (p.616). In some countries it is given in the management of allergic conditions and in pruritic skin disorders (p.565). Buclizine has also been used in the treatment of vertigo (p.565) associated with disorders of the vestibular system, although its value in these conditions remains to be established.

To prevent motion sickness, buclizine hydrochloride is given at least 30 minutes before travelling in an oral dose of 25 or 50 mg, which may be repeated, if necessary, after 4 to 6 hours. The usual dose to alleviate nausea is 25 or 50 mg daily up to 100 mg daily in divided doses; in severe cases up to 150 mg daily has been given.

In the treatment of migraine, buclizine hydrochloride is given in usual doses of 12.5 mg at the start of an attack or when one is known to be imminent; children aged 10 to 14 years may be given 6.25 mg and older children the usual adult dose.

In pruritic skin disorders the usual dose of buclizine hydrochloride is 25 to 50 mg daily.

Preparations

Proprietary Preparations (details are given in Part 3)
Belg.: Longifene; Braz.: Buclina; Postafen; Fr.: Aphilan; Hong Kong:
Longifene†: India: Longifene; Malaysia: Buchzine†; Longifene;
Longimin†: Port.: Buclina; Postafeno†; S.Afr.: Longifene; Singapore:
Longifene†; Panzimine†; Turk.: Longifene; USA: Bucladin-S Softab.

Longiener; Fanziminer; Turk: Longiener, OSA: Buciadin-S Softab. Multi-ingredient: Brazz: Apetibe; Apeti; Buciamin; Budlien-Vit; Buclimax; Budiplex; Carnabol; Complevit; Klizin; Nutri-Ped; Nutrimaiz SM; Pepsivit; Pondusvitam; Profol; Propan; Yitiaer; Gez: Migraleve; Hugigaleve; Pragelave; Philipp: Appebon; Appebon with Iron; Appetason; Biotermin AS; Ferlette; Medifortan-AS; Pediafortan-AS; Propan; Propan with Iron; Regeron-E Plus; Port: Migraleve; S.Afrz: Vomifene; Spain: Migraleve; Switz.: Migraleve; UK: Migraleve; Venez.: Dexapostafen.

Carbinoxamine Maleate (BANM, rINNM)

Carbinoxamine, Maléate de; Carbinoxamini Maleas; Karbinoksamin Maleat; Maleato de carbinoxamina. 2-[4-Chloro-α-(2-pyridyl)benzyloxy]-NN-dimethylethylamine hydrogen maleate.

Карбиноксамина Малеат

C₁₆H₁₉CIN₂O,C₄H₄O₄ = 406.9. CAS — 486-16-8 (carbinoxamine); 3505-38-2 (carbinoxamine maleate).

– R06AA08

ATC Vet — QR06AA08.

Pharmacopoeias. In US.

USP 31 (Carbinoxamine Maleate). A white, odourless, crystalline powder. Soluble 1 in less than 1 of water, 1 in 1.5 of alcohol and of chloroform, and 1 in 8300 of ether. pH of a 1% solution in water is between 4.6 and 5.1. Store in airtight containers, Protect

Adverse Effects and Precautions

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

Interactions

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

Uses and Administration

Carbinoxamine maleate, a monoethanolamine derivative, is a sedating antihistamine with antimuscarinic, significant sedative, and serotonin antagonist effects. Carbinoxamine maleate is used for the relief of allergic conditions such as rhinitis (p.565), and is a common ingredient of compound preparations for symptomatic treatment of coughs and the common cold (p.564).

Dose recommendations for carbinoxamine maleate may vary between preparations. Licensed US product information suggests a usual oral dose of carbinoxamine maleate in adults of 4 to 8 mg given 3 or 4 times daily. Children of 2 to 3 years of age may be given a dose of 2 mg three or four times daily, children aged 3 to 6 years given 2 to 4 mg three or four times daily, and those above 6 years given 4 to 6 mg three or four times daily. Lower doses, sometimes less than half these licensed in the US, may be used in other countries. Carbinoxamine polistirex has also been given

Preparations

USP 31: Carbinoxamine Maleate Tablets; Pseudoephedrine Hydrochloride, Carbinoxamine Maleate, and Dextromethorphan Hydrobromide

Proprietary Preparations (details are given in Part 3) Arg.: Omega 100; Mon.: Allergefon; Thai.: Histin; Sinumine†; USA: Carboxine†; Histex CT; Histex I/E; Histex PD; Palgic; Pediatex.

Multi-ingredient: Arg.: Aseptobron C; Cobenzil Compuesto†; 100 Expectorante†; Rondec Compositum†; Rondec†; Torfan H†; Austria: Rhinopront; Belg.: Rhinopront; Braz.: Afebrin†; Gegrip†; lodeto de Potassio Composto†; Naldecon; Naldecon Pediatrico; Nasalıv, Neolefini; Neolefini Baby, Resprin; Chile: Matinor; Rhinopront; Rinofimi; Cz.: Rhinopront; Rhinotussal†; Ger.: Rhinopront; Rhinopront; Rhinopront; Rhinopront; Rhinopront; Rhinopront; Rhinopront; India: Clistin; Indon.: Kenantist; Israel: Rhinopront; Maysia: Became; Rhinopront; Mex.: Lentostamir; Prindex; Singopore: Became; Rhinopront; Mex.: Lentostamir; Prindex; Singopore: Became; Rhinopront; Spain: Rinomax; Rinoprotard†; Switz.: Rhinopront; Rhinotussal; UAE: Fluzal†; USA: Andehist DM†; Andehist; Andex; Carbodex; Carbodex;

Cetirizine Hydrochloride

(BANM, USAN, rINNM)

Cetirizin-dihidroklorid; Cetirizin-dihydrochlorid; Cetirizindihydroklorid; Cétirizine, Chlorhydrate de; Cétirizine, dichlorhydrate de; Cetirizini dihydrochloridum; Cetirizini Hydrochloridum; Cetirizino dihidrochloridas; Cetyryzyny dichlorowodorek; Hidro-cloruro de cetirizina; P-071; Setiritsiinidihydrokloridi; Setirizin Hidroklorür; UCB-P071. The dihydrochloride of 2-[4-(4-chlorobenzhydryl)piperazin-I-yl]ethoxyacetic acid.

Цетиризина Гидрохлорид

 $C_{21}H_{25}CIN_2O_3,2HCI = 461.8.$

CAS — 83881-51-0 (cetirizine); 83881-52-1 (cetirizine hydrochloride).

ATC - RO6AE07

ATC Vet - QR06AE07.

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

Ph. Eur. 6.2 (Cetirizine Dihydrochloride; Cetirizine Hydrochloride BP 2008). A white or almost white powder. Freely soluble in water; practically insoluble in acetone and in dichloromethane. A 5% solution in water has a pH of 1.2 to 1.8. Protect from light.

Adverse Effects and Precautions

As for the non-sedating antihistamines in general, p.561. Reduced dosage is recommended for patients with hepatic or renal impairment (see under Uses and Administration, below).

Arrhythmias. The ECG effects of cetirizine were studied1 in normal subjects; doses of up to six times the usual recommended dose did not prolong the QT interval. Additionally, the FDA2 in the USA and representatives of the manufacturers³ in Belgium did not find any association between cetirizine and the development of ventricular arrhythmias. However, there has been a subsequent report4 of torsade de pointes after overdosage with cetirizine in a hypokalaemic patient undergoing haemodialysis for chronic renal failure. See also p.562.

- Sale ME, et al. The electrocardiographic effects of cetirizine in normal subjects. Clin Pharmacol Ther 1994; 56: 295–301.
- 2. Himmel MH, et al. Dangers of non-sedating antihistamines. Lancet 1997; 350: 69.
- 3. Coulie P, et al. Non-sedating antihistamines and cardiac arrhythmias. Lancet 1998: 351: 451
- Renard S, et al. Torsades de pointes induites par surdosage en cétirizine. Arch Mal Coeur Vaiss 2005; 98: 157–61.

Effects on the liver. Life-threatening hepatitis developed in a 23-year-old man who had been taking cetirizine long-term for atopic dermatitis.1 He recovered after treatment with prednisolo-

There has been a report of recurrent acute hepatitis associated with the short-term use of cetirizine for seasonal allergic rhinitis in a 26-year-old man.2

- Watanabe M, et al. Severe hepatitis in a patient taking cetirizine. Ann Intern Med 2001; 135: 142–3.
- Pompili M, et al. Recurrent acute hepatitis associated with use of cetirizine. Ann Pharmacother 2004; 38: 1844–7.