60 to 120 mg of the hydrochloride in 2 divided doses. Ambroxol has also been given by inhalation, injection, or rectally.

Adverse effects. ***HYPERSENSITIVITY.*** A report[1] of contact allergy to ambroxol, but not bromhexine.

1. Mancuso G, Berdondini RM. Contact allergy to ambroxol. *Contact Dermatitis* 1989; **20:** 154.

Pharmacokinetics. References to pharmacokinetic studies of ambroxol.

1. Hammer R, *et al*. Speziesvergleich in Pharmakokinetik und Metabolismus von NA 872 Cl Ambroxol bei Ratte, Kaninchen, Hund und Mensch. *Arzneimittelforschung* 1978; **28:** 899–903.
2. Jauch R, *et al*. Ambroxol, Untersuchungen zum Stoffwechsel beim Menschen und zum quantitativen Nachweis in biologischen Proben. *Arzneimittelforschung* 1978; **28:** 904–11.
3. Vergin H, *et al*. Untersuchungen zur Pharmakokinetik und Bioäquivalenz unterscheidlicher Darreichungsformen von Ambroxol. *Arzneimittelforschung* 1985; **35:** 1591–5.

Respiratory disorders. Mixed results[1-3] were obtained when ambroxol was used in chronic bronchitis or chronic obstructive pulmonary disease (COPD—p.1112); in a randomised study, it was no better than placebo in preventing acute exacerbations of COPD; however, in a subset of patients with more severe disease, ambroxol therapy reduced the number of exacerbations.[4] It was ineffective[5] when given to mothers for the prophylaxis of neonatal respiratory distress syndrome (p.1508), although it may be of modest benefit in the early treatment of established disease in infants.[6,7]

Inhalation of ambroxol aerosol has also produced beneficial effects in a patient with alveolar proteinosis who refused alveolar lavage.[8]

For the use of mucolytics in productive cough see p.1547.

1. Olivieri D, *et al*. Ambroxol for the prevention of chronic exacerbations: long-term multicenter trial: protective effect of ambroxol against winter semester exacerbations: a double-blind study versus placebo. *Respiration* 1987; **51** (suppl 1): 42–51.
2. Guyatt GH, *et al*. A controlled trial of ambroxol in chronic bronchitis. *Chest* 1987; **92:** 618–20.
3. Alcozer G, *et al*. Prevention of chronic bronchitis exacerbations with ambroxol (Mucosolvan Retard): an open, long-term, multicenter study in 5,635 patients. *Respiration* 1989; **55** (suppl 1): 84–96.
4. Malerba M, *et al*. Effect of twelve-months therapy with oral ambroxol in preventing exacerbations in patients with COPD: double-blind, randomized, multicenter, placebo-controlled study (the AMETHIST Trial). *Pulm Pharmacol Ther* 2004; **17:** 27–34.
5. Dani C, *et al*. Antenatal ambroxol treatment does not prevent the respiratory distress syndrome in premature infants. *Eur J Pediatr* 1997; **156:** 392–3.
6. Wauer RR, *et al*. Randomized double blind trial of Ambroxol for the treatment of respiratory distress syndrome. *Eur J Pediatr* 1992; **151:** 357–63.
7. Schmalisch G, *et al*. Changes in pulmonary function in preterm infants recovering from RDS following early treatment with ambroxol: results of a randomized trial. *Pediatr Pulmonol* 1999; **27:** 104–12.
8. Diaz JP, *et al*. Response to surfactant activator (ambroxol) in alveolar proteinosis. *Lancet* 1984; **i:** 1023.

Uricosuric action. A study[1] was carried out in 48 young male healthy subjects to examine the uricosuric effect of ambroxol. The minimum effective dose for lowering plasma-uric acid concentrations was found to be between 250 and 500 mg daily given in 2 divided doses. Although these doses are much higher than those used to treat bronchopulmonary disease, doses as high as l g daily were well tolerated.

1. Oosterhuis B, *et al*. Dose-dependent uricosuric effect of ambroxol. *Eur J Clin Pharmacol* 1993; **44:** 237–41.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Ambril; Apracur Expectorante; Cortos; Graneodin Expectorante†; Mucosolvon; Tabcin Expectorante†; Tavinex Expectorante; Tavinex Expectotabs; Tosambrex; ***Austria:*** Ambrobene; Ambrohexal; Ambrolan; Ambrolos†; Ambronorm; Bisolangin†; Bisolaryn; Broxol; Mucoangin; Mucosolvan; Sekretovit; ***Belg.:*** Mucoangin; Surbronc; ***Braz.:*** Ambrizol†; Ambrol†; Ambroten; Ambrox†; Anabron; Broncoflux; Bronxol; Expectuss; Fluibron; Fluidin; Fluxol†; Mucibron; Mucoclean†; Mucolin; Mucosolvan; Mucoxolan; Neossolvan; Probec†; Pulmosolvan†; Surfactil†; ***Chile:*** Bronchopront†; Broncot; Fluibron; Fluomit; Milbron†; Mintamox; Mucosolvan; Muxol; Tocalm; ***Cz.:*** Ambex; Ambrobene; Ambrosan; Ambrospray; Bronchopront†; Dignobroxol†; Dr Rentschler Hustenloser; Fervex†; Flavamed; Halixol; Mucosin; Mucosolvan; Neo-Bronchol; Solvolan; ***Denm.:*** Mucoangin; ***Fr.:*** Lysopadol; Muxol; Surbronc; ***Ger.:*** Ambril; Ambro; Ambro-Puren†; Ambrobeta; Ambrodoc; Ambrohexal; Ambroinfant†; Ambrolos†; Ambropp†; Bronchopront; Bronchowern; duramucal†; Expit; frenopect; Frubizin akut; Larylin Husten-Loser Pastillen; Larylin Husten-Loser Saft†; Lindoxyl; Muco-Aspecton†; Mucoangin; Mucobroxol†; Mucophlogat†; Mucosolvan; Neo-Bronchol†; Padiamuc; Pulmotin Hustenloser; Sigabroxol†; stas-Hustenloser†; tuss†; ***Gr.:*** Abrobion; Abrolen; Afrodor; Amboral; Ambrobion†; Ambromyc; Anavix; Aprinol; Auroxidol; Bunafon; Celibron; Dolcevin; Ebertuss; Effercet; Erosil; Fluibrox; Grenovix; Hivotex; Kriolen; Lextarol; Mavixan; Mucolin; Mucosolvan; Mucovix; Nibren; Olbenorm; Provixen-N; Puntol; Respirol; Saribal; Stefolant; Strubelin; Tevonil; Tosse; Tussefar; Zyrantol; ***Hong Kong:*** Amxol; Bronchopront; Marbroxol; Max; Medovent†; Mucosolvan; Qualisolvon; ***Hung.:*** Ambrobene; Ambrohexal; Bronchopront†; Halixol; Mucoangin; Solvolan; ***India:*** Acocontin; Acolyt; Ambrodil; Inhalex; ***Indon.:*** Ambril; Brommer; Bronchopront; Broncozol; Broxal; Epexol; Extropect; Gunapect; Interpec; Lapimuc; Molapect; Mucera; Mucolica; Mucopect; Mucos; Mucoxol; Nufanibrox; Silopect; Sohopect; Transbroncho; Transmuco; ***Ital.:*** Ambrotus; Amobronc; Atus; Broxol; Fluibron; Fluixol; Lintos; Lisopulm†; Muciclar; Mucoaricodil; Mucobron; Mucosolvan; Secretil; Surfactal; Tauxolo; Viscomucil; ***Jpn:*** Mucosal; Mucosolvan; ***Malaysia:*** Amxol; Axol; Mucosolvan; Shinoxol; Strepsils Chesty Cough; ***Mex.:*** Ambrofur; Amocol; Axol; Balsibron; Bionoxol; Boxolam; Brogal; Bronolban; Brosolan; Broxaquim; Broxofar; Broxoffler; Broxol; Broxolim; Cloxan; Ebromin; Euroxol; Exabrol†; Expeflen; Fantrodol†; Ital-Ultra; Loexom; Loxibrin; Mucibron; Mucoangin; Mucosolvan; Mucovibrol; Mucovibrol T†; Mucoxol; Musalten; Musvan; Muxol†; Oxolvan; Prospec; Protitus; Randex; Rimoxol†; Sekretovit; Septacin; Seraxol-S; Softixol†; Solpat; Tobrin; Tradexol†; Trimexine; Tunitol-BX; Tusibron; Ulax-F; Viaxol; Weisal; ***Neth.:*** Mucoangin; ***Philipp.:*** Ambrolex; Atrivex; Brocof; Bromace; Bromacef; Broxan; Broxifil; Broxil-M; Broxitrol; Broxolvan; Exolpen; Expel; Medibron; Mepebrox; Mucosolin; Mucosolvan; Mucovis; Phlemasol; Pontef; Pulmobrol; Venteze; Voxoll; Zobrixol; ***Pol.:*** Aflegan; Ambro; Ambrohexal; Ambroksol; Ambrosan; Ambrosol; Deflegmin; Flavamed; Mucoangin; Mucosolvan; Mukobron; Tussal Expectorans; ***Port.:*** Benflux; Bromax; Bronchopront†; Broncoliber; Bronxol; Drenoxol; Fluidox; Fluidrenol; Hipotosse; Mucodrenol; Mucosolvan; Mucotosse; ***Rus.:*** Ambrobene (Амбробене); Ambrohexal (Амброгексал); Ambrosan (Амбросан); Ambrosol (Амбросол); Bronchowern (Бронховерн); Halixol (Халиксол); Lasolvan (Лазолван); Medovent (Медовент); Suprima-Kof (Суприма-Коф); ***Singapore:*** Amxol; Axol; Bronchopront†; Max; Mucosolvan; Shinoxol; ***Spain:*** Ambrolitic; Dinobroxol; Motosol; Mucibron; Mucosan; Naxpa; ***Swed.:*** Mucoangin; ***Switz.:*** Fluibron†; Mucabrox; Mucoangin; Mucosolvon; ***Thai.:*** Ambrol†; Ambrolytic†; Ambrox†; Ambroxan; Ampromed; Amtuss; Amxol; Bronchopront†; Broncol; Broxol; Broxsa†; Max; Medovent; Misovan; Movent†; Mucodic; Mucolan; Mucolid; Mucomed; Mucopec; Mucosolvan; Mucoxine-F; Mucozan; Musocan; Nucobrox; Polibroxol; Simusol; Strepsils Chesty Cough; Streptuss-AX; ***Turk.:*** Ambreks; Fluibron; Mukoral; Pulmor; Sekrol; Tusilin; ***UAE:*** Mucum; ***Venez.:*** Ambril; Ambromuco; Ambrox; Benflux; Brocantol; Bronchopront; Litusix; Misulvan; Mucoangin; Mucorama; Mucosolvan; Muxen; Xolvax.

Multi-ingredient: ***Arg.:*** Amoxi Respiratorio†; Amoxidal Respiratorio; Amoxidal Respiratorio Duo; Amoxigrand Bronquial; Amoxipenil Bronquial; Amoxitenk Respiratorio†; Aseptobron Respiratorio; Bronco Biotaer†; Bronquisedan; Bronquisedan Mucolitico; Cefacar Mucolitico†; Cefacilina Bronquial; Gentiabron†; Letondal; Muco Cortos†; Muco Dosodos; Muco Dosodos Biotic; Mucoprednibron; Mucosolvon Compositum; No-Tos Biotic; Nobactam Bronquial; Oxibron NF; Oximar Respiratorio; Pulmonix Plus; Toraxan; Trexirol NF†; Trifamox Bronquial Duo; ***Austria:*** Mucospas; ***Braz.:*** Penetro†; ***Chile:*** Ambrotos; ***Cz.:*** Doxycyclin Al Comp; ***Ger.:*** Ambrodoxy; Ambroxol AL comp; Ambroxol comp; Amdox-Puren†; Azudoxat comp†; Broncho-Euphyllin; Doxam; Doximucol; Doxy Comp; Doxy Lindoxyl; Doxy Plus; Doxy-Wolff Mucolyt†; Doxysolvat†; Jenabroxol comp†; Sigamuc†; Spasmo-Mucosolvan; Terelit†; ***India:*** Ambrodil Plus; Ambrodil-S; Amcof; Amcold; Asthalin AX; Axalin-AX; Axalin†; Kofarest; Mucaryl-AX†; Novamox AX; Roxeptin-ME; Suprivent-A; ***Mex.:*** Acimox-Ex; Aeroflux; Alerfin Ex; Alexing; Ambodil-C; Aminoefedrison; Balsibron-C; Biovicam Ex; Bisincof; Bolbamox†; Brogal Compositum; Brogal-T; Brogamax; Brominol-C; Bronar; Bronolban-M; Broquixol; Brosolan C; Broxofar Compuesto; Broxol Air; Broxol Plus; Broxolim-AM†; Broxolim-C; Brumax; Cefabroxil; Cibronal; Cobadex; Coricidin Expec; Dexol; Dexoltryn; Dofaxil; Doralan-Ax; Ebromin P; Epicol NF†; Faribrox; Ferlex; Flamebin; Fludexol-CL; Fluvicil; Fluxibit; Fluxol; Fultac; Gimabrol; Histiacil NF; Laritol Ex; Linfarden; Loexom FC; Loexom FS; Loxorol; Mucoflux; Mucosolvan Compositum; Mucovibrol Amoxi; Mucovibrol C; Musaldox; Neumyn-AS; Pentibroxil; Plexus; Ravotaf; Removil; Rezplen; Rombox; Salamflux; Sekretovit Amoxi; Sekretovit Ex; Sensibit XP; Septacin Amoxi; Septacin Ex; Seraxol; Serbol; Sermoxol; Sibilex; Solcibrol; Tadinar-C; Tavexyl; TheraFlu Tenalif; Torva; Toxol; Ulax-C; Vanmoxol; ***Port.:*** Clembroxol; Lactucol; Mucospas; Ventoliber; ***Rus.:*** Coldact Broncho (Колдакт Бронхо)†; Rinicold-Broncho (Риниколд Бронхо); ***Venez.:*** Aeroflux; Ambroclar; Ambromuco Compositum; Arbixil; Clenbuxol; Litusix Compositum; Mucolin; Mucosolvan Compositum.

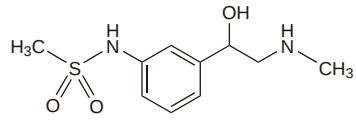
Amidefrine Mesilate *(BANM, rINN)* ⊗

5190; Amidéfrine, Mésilate d'; Amidefrini Mesilas; Amidephrine Mesylate *(USAN)*; Mesilato de amidefrina; MJ-5190. 3-(1-Hydroxy-2-methylaminoethyl)methanesulphonanilide methanesulphonate.

Амидефрина Мезилат

$C_{10}H_{16}N_2O_3S,CH_4O_3S$ = 340.4.

CAS — 3354-67-4 (amidefrine); 1421-68-7 (amidefrine mesilate).



(amidefrine)

Profile
Amidefrine mesilate is a sympathomimetic with alpha-adrenergic activity similar to that of phenylephrine (p.1568). It is used for its vasoconstrictor properties in the local treatment of nasal congestion.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Fentrinol.

Ammonium Acetate

Amonio, acetato de; Amonowy octan.

Ацетат Аммония; Уксуснокислый Аммоний

$CH_3CO_2NH_4$ = 77.08.

CAS — 631-61-8 (ammonium acetate); 8013-61-4 (ammonium acetate solution).

Pharmacopoeias. *Br.* includes Strong Ammonium Acetate Solution.

Ammonium Bicarbonate *(BAN)*

Ammonii hydrogenocarbonas; Ammonium, bicarbonate d'; Ammónium-hidrogén-karbonát; Ammoniumvätekarbonat; Ammoniumvetykarbonaatti; Amonio, bicarbonato de; Amonio-vandenilio karbonatas; E503; Hydrogenuhličitan amonný. Ammonium hydrogen carbonate.

Бикарбонат Аммония; Гидрокарбонат Аммония; Двууглекислый Аммоний

NH_4HCO_3 = 79.06.

CAS — 1066-33-7.

Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Ammonium Hydrogen Carbonate; Ammonium Bicarbonate BP 2008). A fine, white or almost white, slightly hygroscopic, crystalline powder or white or almost white crystals. It volatilises rapidly at 60°; volatilisation takes place slowly at ambient temperatures if slightly moist. It is in a state of equilibrium with ammonium carbamate. Freely soluble in water; practically insoluble in alcohol. Store in airtight containers.
The BP 2008 directs that when Ammonium Carbonate is prescribed or demanded Ammonium Bicarbonate shall be dispensed or supplied.

Ammonium Carbonate

Amonio, carbonato de; Amonowy węglan; Carbonato de Amonio; E503.

Карбонат Аммония; Углекислый Аммоний

CAS — 8000-73-5.

Pharmacopoeias. In *Fr.* Also in *USNF*.
USNF 26 (Ammonium Carbonate). A white powder, or hard, white or translucent masses having a strong odour of ammonia, without empyreuma. It consists of ammonium bicarbonate and ammonium carbamate, in varying proportions. It yields 30 to 34% of NH_3. On exposure to air it loses ammonia and carbon dioxide, becoming opaque, and is finally converted into friable porous lumps or a white powder of ammonium bicarbonate. Soluble 1 in 4 of water. It is decomposed by hot water. Its solutions are alkaline to litmus. Store in airtight containers at a temperature not exceeding 30°. Protect from light.
NOTE. The **BP 2008** directs that Ammonium Bicarbonate shall be dispensed or supplied when Ammonium Carbonate is prescribed or demanded.

Ammonium Chloride

510; Ammonii chloridum; Ammonium Chloratum; Ammonium, chlorure d'; Ammoniumklorid; Ammónium-klorid; Ammoniumkloridi; Amonio chloridas; Amonio, cloruro de; Amonowy chlorek; Chlorid amonný; Cloruro de Amonio; Muriate of Ammonia; Sal Ammoniac.

Хлорид Аммония; Хлористый Аммоний

NH_4Cl = 53.49.

CAS — 12125-02-9.
ATC — B05XA04; G04BA01.
ATC Vet — QB05XA04; QG04BA01.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *US*, and *Viet.*
Ph. Eur. 6.2 (Ammonium Chloride). A white or almost white, crystalline powder or colourless crystals. Freely soluble in water.
USP 31 (Ammonium Chloride). Colourless crystals or white, fine or course, crystalline powder. Is somewhat hygroscopic. Freely soluble in water and in glycerol, and even more so in boiling water; sparingly soluble in alcohol. pH of a 5% solution in water is between 4.6 and 6.0. Store in airtight containers.

Adverse Effects and Treatment
Ammonium salts are irritant to the gastric mucosa and may produce nausea and vomiting particularly in large doses. Large doses of ammonium chloride may cause a profound acidosis and hypokalaemia which should be treated symptomatically. Intravenous ammonium chloride can cause pain and irritation at the site of injection, which may be decreased by slowing the rate of infusion.

Excessive doses of ammonium salts, particularly if given by rapid intravenous injection, may give rise to hepatic encephalopathy due to the inability of the liver to convert the increased load of ammonium ions to urea.

Precautions
Ammonium salts are contra-indicated in patients with hepatic or renal impairment.

Pharmacokinetics
Ammonium chloride is absorbed from the gastrointestinal tract. The ammonium ion is converted into urea in the liver; the anion thus liberated into the blood and extracellular fluid causes a metabolic acidosis and decreases the pH of the urine; this is followed by transient diuresis.

Uses and Administration
Ammonium chloride is used as an expectorant in productive cough (p.1547). Other ammonium salts that have been used similarly include the acetate, bicarbonate, camphorate, carbonate, citrate (p.2256), and glycyrrhizate (p.2316).

Giving ammonium chloride produces a transient diuresis and acidosis. It may be used in the treatment of severe metabolic alkalosis (p.1667). Each g of ammonium chloride represents 18.69 mmol of chloride. It is usually given as a 1 to 2% solution by slow intravenous infusion, in a dosage depending on the severity of the alkalosis. A concentrated solution of ammonium chloride may be diluted by sodium chloride injection.

Ammonium chloride may also be used to maintain the urine at an acid pH in the treatment of some urinary-tract disorders. It is usually given orally, often as enteric-coated tablets, in a dose of 1 to 2 g every four to six hours. Higher doses were sometimes used in forced acid diuresis procedures to aid the excretion of basic drugs, such as amfetamines, in severe cases of overdosage (but see p.2153).

Ammonium chloride has been promoted for self administration as a diuretic, for example in premenstrual water retention; an oral dose of 650 mg three times daily for up to 6 days has been suggested, but such use is generally considered inappropriate.

Preparations

BP 2008: Ammonium Chloride Mixture; Aromatic Ammonia Solution; Aromatic Ammonia Spirit; Strong Ammonium Acetate Solution; White Liniment;
USP 31: Ammonium Chloride Delayed-release Tablets; Ammonium Chloride Injection; Aromatic Ammonia Spirit; Potassium Gluconate, Potassium Citrate, and Ammonium Chloride Oral Solution.

Proprietary Preparations (details are given in Part 3)
Austral.: Nyal Bronchitis; ***Fr.:*** Chlorammonic†; ***Ger.:*** Extin N; ***Switz.:*** Chloramon.

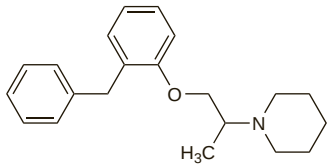
Multi-ingredient: numerous preparations are listed in Part 3.

Benproperine *(rINN)*

ASA-158/5 (benproperine phosphate); Benproperiini; Benproperin; Benproperina; Benpropérine; Benproperinum. 1-[2-(2-Benzylphenoxy)-1-methylethyl]piperidine.

Бенпроперин

$C_{21}H_{27}NO$ = 309.4.
CAS — 2156-27-6.
ATC — R05DB02.
ATC Vet — QR05DB02.



Pharmacopoeias. *Chin.* includes the phosphate.

Profile

Benproperine is used as a cough suppressant in non-productive cough (p.1547). It is reported to have a peripheral and central action and has been given in usual oral doses of 25 to 50 mg two to four times daily as the phosphate. Benproperine embonate has been used similarly.

Preparations

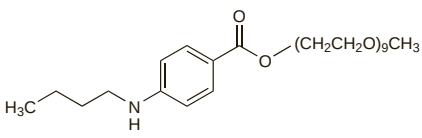
Proprietary Preparations (details are given in Part 3)
Ger.: Tussafug; ***Hong Kong:*** Cofrel; ***Jpn:*** Flaveric.

Benzonatate *(BAN, rINN)*

Bensonatat; Bentsonataatti; Benzonatato; Benzonatatum; Benzononatine; KM-65. 3,6,9,12,15,18,21,24,27-Nonaoxaoctacosyl 4-butylaminobenzoate.

Бензонатат

$C_{13}H_{18}NO_2(OCH_2CH_2)_nOCH_3$, where *n* has an average value of 8.
CAS — 104-31-4 (where n = 8).
ATC — R05DB01.
ATC Vet — QR05DB01.



Pharmacopoeias. In *US.*
USP 31 (Benzonatate). A clear, pale yellow, viscous liquid having a faint characteristic odour. Soluble 1 in less than 1 of water, of alcohol, of chloroform, and of ether; freely soluble in benzene. Store in airtight containers. Protect from light.

Adverse Effects

Headache, dizziness, gastrointestinal disturbances, nasal congestion, hypersensitivity, pruritus, and skin rash have been reported. There may be drowsiness. Benzonatate has local anaesthetic properties and can produce numbness of the mouth, tongue, and pharynx. CNS stimulation and convulsions, followed by CNS depression, may occur in overdosage.

Uses and Administration

Benzonatate is a cough suppressant used in non-productive cough (p.1547); it is stated to act peripherally. It is related to tetracaine (p.1871) and has a local anaesthetic action on mucosa. It is given to adults and children over the age of 10 years in an oral dose of 100 mg three times daily; up to 600 mg daily in divided doses may be given if necessary. Benzonatate is reported to act within about 20 minutes and its effects are reported to last for 3 to 8 hours.

Preparations

USP 31: Benzonatate Capsules.

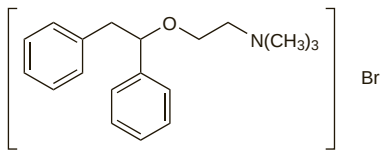
Proprietary Preparations (details are given in Part 3)
Mex.: Alzomed-F†; Beknol; Benzonal; Bronpax; Capsicof; D-Tato; Lemtosid; Nactol†; Novapsyl; Parven†; Pebegal; Pharben; Supracof; Tesalon; Tesopen; Texoven; Tusical; Tusitato; Tuzzil; Velpro; ***USA:*** Tessalon.

Bibenzonium Bromide *(BAN, rINN)*

Bibenzonii Bromidum; Bibenzonium, Bromure de; Bromuro de bibenzonio; Diphenetholine Bromide; ES-132. [2-(1,2-Diphenylethoxy)ethyl]trimethylammonium bromide.

Бибензония Бромид

$C_{19}H_{26}BrNO$ = 364.3.
CAS — 59866-76-1 (bibenzonium); 15585-70-3 (bibenzonium bromide).
ATC — R05DB12.
ATC Vet — QR05DB12.



Profile

Bibenzonium bromide is a cough suppressant used in non-productive cough (p.1547) which is stated to have a central action. It has been given in a usual oral dose of 30 to 60 mg two or three times daily.

Preparations

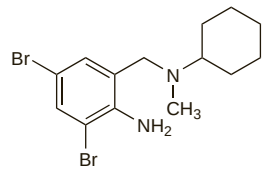
Proprietary Preparations (details are given in Part 3)
Austria: Lysbex.

Bromhexine *(BAN, rINN)*

Bromexina; Bromhexin; Bromhexina; Bromhexinum; Bromiheksiini; Butamirat. 2-Amino-3,5-dibromobenzyl(cyclohexyl)methylamine.

Бромгексин

$C_{14}H_{20}Br_2N_2$ = 376.1.
CAS — 3572-43-8.
ATC — R05CB02.
ATC Vet — QR05CB02.



Bromhexine Hydrochloride *(BANM, USAN, rINNM)*

Bromheksino hidrochloridas; Bromhexine, chlorhydrate de; Brómhexin-hidroklorid; Bromhexin-hydrochlorid; Bromhexinhydroklorid; Bromhexini hydrochloridum; Bromiheksiinihydrokloridi; Bromoheksyny chlorowodorek; Cloridrato de Bromexina; Hidrocloruro de bromhexina; NA-274.

Бромгексина Гидрохлорид

$C_{14}H_{20}Br_2N_2$,HCl = 412.6.
CAS — 611-75-6.
ATC — R05CB02.
ATC Vet — QR05CB02.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *Jpn.*
Ph. Eur. 6.2 (Bromhexine Hydrochloride). A white or almost white crystalline powder. It exhibits polymorphism. Very slightly soluble in water; slightly soluble in alcohol and in dichloromethane. Protect from light.

Adverse Effects

Gastrointestinal adverse effects may occur occasionally with bromhexine and a transient rise in serum aminotransferase values has been reported. Other reported adverse effects include headache, dizziness, sweating, and skin rashes. Inhalation of bromhexine has occasionally produced cough or bronchospasm in susceptible subjects.

Precautions

Since mucolytics may disrupt the gastric mucosal barrier bromhexine should be used with care in patients with a history of peptic ulcer disease. Care is also advisable in asthmatic patients. Clearance of bromhexine or its metabolites may be reduced in patients with severe hepatic or renal impairment.

Pharmacokinetics

Bromhexine hydrochloride is rapidly absorbed from the gastrointestinal tract; peak plasma concentrations occur after about 1 hour. Bromhexine undergoes extensive first-pass metabolism in the liver: its oral bioavailability is stated to be only about 20%. It is widely distributed to body tissues. About 85 to 90% of a dose is excreted in the urine mainly as metabolites. Ambroxol (p.1550) is a metabolite of bromhexine. Bromhexine is highly bound to plasma proteins. It has a terminal elimination half-life of 13 to 40 hours. Bromhexine crosses the blood-brain barrier and small amounts cross the placenta.

Uses and Administration

Bromhexine is a mucolytic used in the treatment of respiratory disorders associated with productive cough (p.1547). Bromhexine is usually given orally in a dose of 8 to 16 mg of the hydrochloride three times daily. It has also been given by deep intramuscular or slow intravenous injection or inhaled as an aerosol solution.

Bromhexine has also been used orally and topically in the treatment of dry eye syndromes associated with abnormal mucus production (see below).

Dry eye. Bromhexine has been used orally in the treatment of dry eye (p.2140) in Sjögren's syndrome but results have been conflicting; it appears to have no effect on tear secretion in healthy subjects.[1] It has also been tried topically.

1. Avisar R, *et al.* Oral bromhexine has no effect on tear secretion in healthy subjects. *Ann Pharmacother* 1996; **30:** 1498.

Respiratory-tract infection. ***USE WITH AN ANTIBACTERIAL.*** Bromhexine has been shown to enhance the penetration of erythromycin into bronchial secretions.[1] Although bromhexine is used as an adjuvant in the treatment of respiratory infections, few controlled studies appear to have been conducted to determine if any additional benefit is obtained. However, some studies have found improved responses with cefalexin[2] and amoxicillin.[3]

1. Bergogne-Berezin E, *et al.* Etude de l'influence d'un agent mucolytique (bromhexine) sur le passage de l'érythromycine dans les sécrétions bronchiques. *Therapie* 1979; **34:** 705–11.
2. Boraldi F, Palmieri B. Antibiotic and mucolytic therapy in elderly patients with different cases of bronchopulmonary diseases. *Curr Ther Res* 1983; **33:** 686–91.
3. Roa CC, Dantes RB. Clinical effectiveness of a combination of bromhexine and amoxicillin in lower respiratory tract infection: a randomized controlled trial. *Arzneimittelforschung* 1995; **45:** 267–72.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Amiorel; Aseptobron Expectorante; Balsasulf; Bisolvon; Brometos; Bromexidryl; Broncocalmine; Brondilax; Bronquisedan Elixir; Bronquisedan Paediatrico; Catarrosine; Expectosan Extra Forte; Funciobron B; Jarabe Medex; Lisi-Tos; Lorbi; Lorbi-Bis; Namir; Nastizol Expectorante; No-Tos Mucolitico; Pectoral Pagliano†; Pulmonix; Pulmosan; Qura Plus; Sandival; Toscalmin; Tostop; ***Austral.:*** Bisolvon Chesty; Duro-Tuss Mucolytic Cough Liquid; ***Austria:*** Bisolvon; ***Belg.:*** Bisolvon; Bromex; Bronchi-Mereprine; ***Braz.:*** Bisolvon; Clarus†; ***Chile:*** Bisolvon; Flumed; ***Cz.:*** Bisolvon†; Flegamina†; Mucohex; Paxirasol; ***Denm.:*** Bisolvon; Viscolyt†; ***Fin.:*** Bisolvon; Medipekt; Mucovin; ***Fr.:*** Bisolvon; ***Ger.:*** Aparsonin N†; Bisolvon; Hustentabs†; Omniapharm†; ***Gr.:*** Bisolvon; Bolisegna†; Bromiramin†; Bronchotussine; ***Hong Kong:*** Asthmaxine; Bisolvon; Bromoson; Bromxine; Duro-Tuss Mucolytic; Exolit; Vasican; ***Hung.:*** Paxirasol; ***India:*** Bromex; ***Indon.:*** Bisolvon; Bromika; Dexolut; Ethisolvan; Exovon; Farmavon; Hexon; Lexavon; Mucobron; Mucohexin; Mucosolvan; Poncosolvon; Solvinex; Thephidron; Yavon; ***Irl.:*** Bisolvon; ***Israel:*** Movex; Solvex; ***Ital.:*** Bisolvon; Broncokin†; ***Jpn:*** Bisolvon; ***Malaysia:*** Beacolytic; Bislan; Bisolvon†; Bromxine; Disol; Ekxine†; Hexolvon†; Vasican; ***Mex.:*** Bisolvon; Bromicof; Dibroxin†; Dizolvin†; Meroxan; Nastizol Ex; Normoflex; Tesacof; Toridran-N; ***Neth.:*** Bisolvon; Darolan Slijmoplossende; Famel Broomhexine†; Kruidvat Hoestelixer; Kruidvat Hoesttabletten; Streptuss vastzittende hoest†; Trekpleister Hoesttabletten†; ***Norw.:*** Bisolvon; ***NZ:*** Bisolvon; Duro-Tuss Mucolytic†; ***Philipp.:*** Bisolvon; Dur-Elix; Easepex; Fleminate; Mucolyptus; Xinebrom; ***Pol.:*** Flegamina; ***Port.:*** Bisolvon; Bromocal; Lisomucin; Tosseque; ***Rus.:*** Flegamin (Флегамин); ***S.Afr.:*** Bisolvon; Bronkese; ***Singapore:*** Bislan; Bisolvon; Bromxine; Broxine†; Duro-Tuss Mucolytic; Mucosol†; Vasican; ***Spain:*** Bisolvon; ***Swed.:*** Bisolvon; ***Switz.:*** Bisolvon; Hustosol†; Solvolin; ***Thai.:*** Asovon; Axistal; Behexine†; Bisoltab; Bisolvon; Bomexin; Bromex†; Bromoson; Bromso; Bromxin†; Bromxine; Bronclear; Disol; Dutross†; Exolit†; Ida; Manovon; Mihexine; Mucine†; Mucola†; Mucoxin; Ohexine; Romulin; Tromadil; ***Turk.:*** Bromek; Bromeksin; Viscol; ***UAE:*** Mucolyte; ***Venez.:*** Bedena; Bexilon; Bisectron; Bisolvon; Bromedrina; Brometix†; Bromexol; Bromox; Bronacim†; Drometox†; Inquixol; Kecnitril; Lisomucin; Mucobrol; Reosil; Teraflem; Tolmix†.

Multi-ingredient: numerous preparations are listed in Part 3.