

- Marchetti G, *et al.* Use of N-acetylcysteine in the management of coronary artery diseases. *Cardiologia* 1999; **44**: 633–7.
- Sochman J. N-acetylcysteine in acute cardiology: 10 years later: what do we know and what would we like to know? *J Am Coll Cardiol* 2002; **39**: 1422–8.

**Nitrate tolerance.** Acetylcysteine appears to be able to potentiate the peripheral and coronary effects of glyceryl trinitrate.<sup>1</sup> While some studies<sup>2–5</sup> have suggested that acetylcysteine can reverse tolerance to nitrates in patients with coronary heart disease or heart failure, others have failed to find any benefit,<sup>6</sup> although there may be a specific subgroup of responders.<sup>5</sup> The various attempts at overcoming nitrate tolerance are discussed on p.1297.

- Horowitz JD, *et al.* Combined use of nitroglycerin and N-acetylcysteine in the management of unstable angina pectoris. *Circulation* 1988; **77**: 787–94.
- Packer M, *et al.* Prevention and reversal of nitrate tolerance in patients with congestive heart failure. *N Engl J Med* 1987; **317**: 799–804.
- May DC, *et al.* In vivo induction and reversal of nitroglycerin tolerance in human coronary arteries. *N Engl J Med* 1987; **317**: 805–9.
- Boesgaard S, *et al.* Preventive administration of intravenous N-acetylcysteine and development of tolerance to isosorbide dinitrate in patients with angina pectoris. *Circulation* 1992; **85**: 143–9.
- Pizzulli L, *et al.* N-acetylcysteine attenuates nitroglycerin tolerance in patients with angina pectoris and normal left ventricular function. *Am J Cardiol* 1997; **79**: 28–33.
- Hogan JC, *et al.* Chronic administration of N-acetylcysteine fails to prevent nitrate tolerance in patients with stable angina pectoris. *Br J Clin Pharmacol* 1990; **30**: 573–7.

**Poisoning and toxicity.** Acetylcysteine has been studied for the potential treatment of many forms of toxicity,<sup>1</sup> but only treatment of acute paracetamol poisoning is widely accepted.

- Chyka PA, *et al.* Utility of acetylcysteine in treating poisonings and adverse drug reactions. *Drug Safety* 2000; **22**: 123–48.

**CARBON TETRACHLORIDE.** The treatment of carbon tetrachloride poisoning is discussed on p.2021. Reports suggest that prompt intravenous therapy with acetylcysteine may help to minimise hepatorenal damage in acute poisoning with carbon tetrachloride.<sup>1,2</sup> When added to supportive therapy the initial dosage regimen should be the same as that used for paracetamol poisoning but as carbon tetrachloride has a much longer half-life than paracetamol, the duration of treatment may need to be increased.<sup>3</sup>

- Ruprah M, *et al.* Acute carbon tetrachloride poisoning in 19 patients: implications for diagnosis and treatment. *Lancet* 1985; **i**: 1027–9.
- Mathieson PW, *et al.* Survival after massive ingestion of carbon tetrachloride treated by intravenous infusion of acetylcysteine. *Hum Toxicol* 1985; **4**: 627–31.
- Meredith TJ, *et al.* Diagnosis and treatment of acute poisoning with volatile substances. *Hum Toxicol* 1989; **8**: 277–86.

**PARACETAMOL.** Acetylcysteine is usually the antidote of choice for paracetamol overdose (see p.108). The intravenous route is favoured in the UK, despite possible anaphylactic reaction, mainly because of concerns over the effects of vomiting and activated charcoal on oral absorption.<sup>1</sup> In the USA the oral route has conventionally been used, despite the unpleasant odour and taste of acetylcysteine solutions, with no evident reduction in effect by charcoal.<sup>2</sup> The intravenous route is now also licensed in the USA. Oral and intravenous formulations appear to be equally effective.<sup>3</sup> A disadvantage of the oral route is therapeutic failure in those patients who develop nausea and vomiting, which occurs in most patients with severe poisoning; delays in absorption may also be of concern especially when the end of the critical 8-hour interval is approaching. However, with oral doses, the whole absorbed dose passes through the liver, producing high local concentrations at the site of toxicity.<sup>4</sup> Some consider the intravenous route to be more reliable, and to require fewer doses and a shorter duration of treatment.<sup>5</sup> The major disadvantage of intravenous use is possible anaphylactic reaction. Although these reactions are considered uncommon in patients with paracetamol poisoning, rare fatalities have been reported, and patients with asthma appear to be at particular risk (see also above).<sup>4</sup> Some infuse the first dose of acetylcysteine over 60 minutes instead of the recommended 15 minutes<sup>5</sup> in order to reduce the incidence and severity of reactions. However, a multicentre, randomised study found no reduction in adverse outcomes with a 60-minute infusion compared to the standard infusion period of 15 minutes.<sup>6</sup> It has been suggested that intravenous acetylcysteine may be preferred in those patients with severe poisoning, who present late, who have nausea and vomiting, or who have problems with absorption. Oral use might be preferred in those who present early with uncomplicated mild to moderate poisoning, or who have asthma.<sup>4,7</sup> Whichever route is given, the interval is considered the single most important factor for the prevention of severe hepatic damage.<sup>3,4</sup>

- Vale JA, Proudfoot AT. Paracetamol (acetaminophen) poisoning. *Lancet* 1995; **346**: 547–52.
- Bowden CA, Krenzok EP. Clinical applications of commonly used contemporary antidotes: a US perspective. *Drug Safety* 1997; **16**: 9–47.

- Brok J, *et al.* Interventions for paracetamol (acetaminophen) overdose. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2006 (accessed 13/10/06).
- Prescott L. Oral or intravenous N-acetylcysteine for acetaminophen poisoning? *Ann Emerg Med* 2005; **45**: 409–13.
- Anonymous. Acetylcysteine (Acetadote) for acetaminophen overdose. *Med Lett Drugs Ther* 2005; **47**: 70–1.
- Kerr F, *et al.* The Australasian Clinical Toxicology Investigators Collaboration randomized trial of different loading infusion rates of N-acetylcysteine. *Ann Emerg Med* 2005; **45**: 402–8.
- Kanter MZ. Comparison of oral and i.v. acetylcysteine in the treatment of acetaminophen poisoning. *Am J Health-Syst Pharm* 2006; **63**: 1821–7.

**Respiratory disorders.** Acetylcysteine has been used as a mucolytic in a variety of respiratory disorders associated with productive cough (p.1547). Although there is controversy over the benefits of mucolytics in treating chronic bronchitis or chronic obstructive pulmonary disease (COPD), there is some evidence that they may reduce exacerbations (see p.1112). However, a double-blind multicentre study in patients with COPD failed to find evidence that acetylcysteine 600 mg daily by mouth reduced exacerbations;<sup>1</sup> like most other interventions in this condition, it could also not be shown to reduce the rate of decline in lung function.

For the use of aerosolised heparin and acetylcysteine to treat inhalation injury see Burns, above. It has been suggested that intravenous acetylcysteine might also be of use in acute respiratory distress syndrome (ARDS—p.1498),<sup>2</sup> possibly due to its action as a free radical scavenger,<sup>2,3</sup> but controlled studies in established ARDS failed to show benefit.<sup>4,5</sup>

Acetylcysteine has been investigated in idiopathic pulmonary fibrosis (see Diffuse Parenchymal Lung Disease, above). See also above for the use of acetylcysteine in the management of cystic fibrosis.

- Decramer M, *et al.* Effects of N-acetylcysteine on outcomes in chronic obstructive pulmonary disease (Bronchitis Randomized on NAC Cost-Utility Study, BRONCUS): a randomised placebo-controlled trial. *Lancet* 2005; **365**: 1552–60.
- Bernard GR. Potential of N-acetylcysteine as treatment for the adult respiratory distress syndrome. *Eur Respir J* 1990; **3** (suppl 11): 496S–498S.
- Skolnick A. Inflammation-mediator blockers may be weapons against sepsis syndrome. *JAMA* 1990; **263**: 930–1.
- Jepsen S, *et al.* Antioxidant treatment with N-acetylcysteine during adult respiratory distress syndrome: a prospective, randomized, placebo-controlled study. *Crit Care Med* 1992; **20**: 918–23.
- Domenighetti G, *et al.* Treatment with N-acetylcysteine during acute respiratory distress syndrome: a randomized, double-blind, placebo-controlled clinical study. *J Crit Care* 1997; **12**: 177–82.

**Scleroderma.** Acetylcysteine has also been reported to be of benefit in Raynaud's syndrome resulting from scleroderma (see p.1817).

## Preparations

**BP 2008:** Acetylcysteine Injection;

**USP 31:** Acetylcysteine and Isoproterenol Hydrochloride Inhalation Solution; Acetylcysteine Solution.

**Proprietary Preparations** (details are given in Part 3)

**Arg.:** AC Lan; **ACC:** Acemuc; Fluimucil; Lubrisect; **Austral.:** Mucomyst; Parvex; **Austria:** ACC; Aeromuc; Aerosolv; Bronchohexal; Bronchoplus; Cimelin; Cimexyl; Fluimucil; Husten ACC; Hustenloser; Mucobene; Mucomyst; NAC; Pulmovent; Siccoral; **Belg.:** Docacetyl; Lysodrop; Lysomucil; Lysox; Mucomyst; Pectomucil; **Braz.:** Bromuc; Flucistex; Fluimucil; Fluimucil Solucao Nasal NAC; **Canada:** Mucomyst; Parvex; **Chile:** Mucolitico; **Cz.:** ACC; Broncholyzin; Fluimucil; L-Cimexyl; Mucobene; NAC; Solmucol; **Denn.:** Alcurt; Granon; Mucosyl; Mucomyst; **Fin.:** Mucomyst; Mucoporett; **Fr.:** Bronclac; Codotussyl Expectorant; Exomuc; Fluimucil; Genac Humex Expectorant; Muculator; Mucomyst; Mucomystendo; Mucospire; Solmucol; Tixair; **Ger.:** ACC; Acemuc; Acetabs; Acetyl; Atset; Azubronch-in; Bromuc; Durabronchalt; Fluimucil; Muciteran; Muco Sanigen; Mucocetyl; Mucret; Myxofat; NAC; Phamuc; Pulmicret; Sirant; **Gr.:** Chri-cetyl; Elicort; Flumil Antidot; Flustaren; Kantrenol; Mucomyst; Neocof; Ovotil; Parvex; Saloril; Spacyl; Trebon; Vaden; Vlenolys; **Hong Kong:** Exomuc; Fluimucil; Hidonac; Muculator; Mutasol; Parvex; Solmucol; **Hung.:** Ac-Pulmin; ACC; Fluimucil; NAC; Solmucol; Solv-Ac T; Sputopur; **India:** Mucomix; **Indon.:** Hidonac; **Irl.:** Parvex; **Israel:** Mucomyst; Reolin; Siran; **Ital.:** Altersol; Brunac; Fluimucil; Hidonac; Mucisol; Mucofat; Mucofrin; Mucosan; Solmucol; Tirocular; Ultraflu; **Malaysia:** Acypront; Fluimucil; Hidonac; Muculator; Parvex; **Mex.:** ACC; **Neth.:** Bisolbrus; Fluimucil; Mucomyst; Solmucol; **Norw.:** Bronkyl; Mucomyst; **NZ:** Parvex; **Philipp.:** Fluimucil; Hidonac; Solmucol; **Pol.:** ACC; Fluimucil; Syntemucol; Tussicom; **Port.:** Fluimucil; Flumil; Muculator; Pulmosal; Tirocular; **Rus.:** ACC (ALLIL); Exomuc (Экзомюк); Fluimucil (Флуимуцил); Muconex (Муконекс); **S.Afr.:** ACC; Parvex; Solmucol; **Singapore:** Fluimucil; Mucosa; Solmucol; Spatam; **Spain:** Fluimucil; Flumil; Flumil Antidot; Flumonac; Frenacil; Locomucil; Mucosal; Mucolix; Solmucol; **Swed.:** Mucomyst; Viskoferm; **Switz.:** ACC; Acemuc; Acetabs; Bisolapid; Demolibral; Dynamucil; Ecomuc; Fluimucil; L-Cimexyl; Muco-Mepha; Mucoluid; Mucostop; NeoCitran Expectorant; Robitussin Expectorant; Secresol; Solmucol; **Thai.:** Acetin; Flemex-ACC; Flucil; Fluimucil; Hidonac; Mucil; Mucocil; Mucotic; Mucosa; Mysoven; NAC; Simucin; **Turk.:** Asist; Brunac; Mentopin; Muconex; NAC; Oxxa; **UK:** Parvex; **USA:** Acetadote; Mucomyst; Mucosil.

**Multi-ingredient:** **Arg.:** Acemuc Biotic; Fluimucil Biotic; **Braz.:** Rinofluimucil; **Fr.:** Rinofluimucil; **Ger.:** Rinofluimucil-S; **Hong Kong:** Rinofluimucil; **Hung.:** Rinofluimucil; **Indon.:** Dorbigot; Fluimucil; Sistenol; **Irl.:** Ilube; **Ital.:** Migel; Rinofluimucil; **Port.:** Rinofluimucil; **Rus.:** Rinofluimucil (Ринофлуимуцил); **Spain:** Flumil Antibiotic; Rinofluimil; **Switz.:** Rinofluimucil; Mucalcaine; Solmucalm; **Thai.:** Fluimucil Antibiotic; Rinofluimucil; **UK:** Ilube.

## Acetyldihydrocodeine Hydrochloride

Acetildihidrocodeina, hidrocloruro de. 4,5-Epoxy-3-methoxy-9a-methylmorphinan-6-yl acetate hydrochloride.

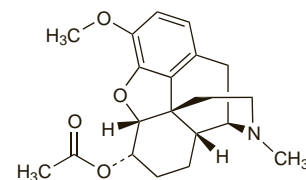
Ацетилдигидрокодеина Гидрохлорид

$C_{20}H_{25}NO_4 \cdot HCl = 379.9$ .

CAS — 3861-72-1 (acetyldihydrocodeine).

ATC — R05DA12.

ATC Vet — QR05DA12.



## Profile

Acetyldihydrocodeine hydrochloride is an opioid derivative related to dihydrocodeine (p.48). It is used as a centrally acting cough suppressant for non-productive cough (p.1547) and has been given in a usual oral daily dose of 20 to 50 mg; no more than 20 mg should be taken as a single dose.

## Preparations

**Proprietary Preparations** (details are given in Part 3)

**Belg.:** Acetylcodone.

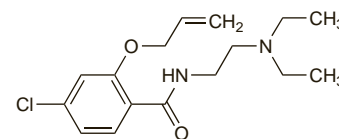
## Alloclamide Hydrochloride (rINN)

Alloclamide, Chlorhydrate d'; Alloclamid Hydrochloridum; CE-264; Hidrocloruro de aloclamida. 2-Allyloxy-4-chloro-N-(2-diethylaminoethyl)benzamide hydrochloride.

Аллокламида Гидрохлорид

$C_{16}H_{23}ClN_2O_2 \cdot HCl = 347.3$ .

CAS — 5486-77-1 (alloclamide); 5107-01-7 (alloclamide hydrochloride).



## Profile

Alloclamide hydrochloride is a cough suppressant.

## Ambroxol Hydrochloride (BAN, rINN)

Ambroksolihidrokloridi; Ambroksolio hidrochloridas; Ambroxol, chlorhydrate d'; Ambroxol hydrochlorid; Ambroxol-hidroklorid; Ambroxolhidrokloridi; Ambroxoli hidrochloridum; Hidrocloruro de ambroxol; NA-872 (ambroxol). trans-4-(2-Amino-3,5-dibromobenzylamino)cyclohexanol hydrochloride.

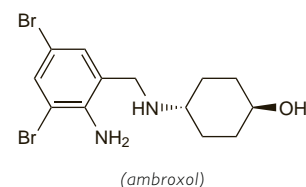
Амброксоль Гидрохлорид

$C_{13}H_{18}Br_2N_2O \cdot HCl = 414.6$ .

CAS — 18683-91-5 (ambroxol); 15942-05-9 (ambroxol hydrochloride); 23828-92-4 (ambroxol hydrochloride).

ATC — R05CB06.

ATC Vet — QR05CB06.



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

**Ph. Eur. 6.2** (Ambroxol Hydrochloride). A white or yellowish crystalline powder. Sparingly soluble in water; practically insoluble in dichloromethane; soluble in methyl alcohol. A 1% solution in water has a pH of 4.5 to 6.0. Protect from light.

## Profile

Ambroxol is a metabolite of bromhexine (p.1552) and is used similarly as a mucolytic. It is given in a usual oral daily dose of

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<sup>1</sup> 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 unterschiedlicher Darreichungsformen von Ambroxol. *Arzneimittelforschung* 1985; **35**: 1591-5.

**Respiratory disorders.** Mixed results<sup>1-3</sup> 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.<sup>4</sup> It was ineffective<sup>5</sup> 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.<sup>6,7</sup>

Inhalation of ambroxol aerosol has also produced beneficial effects in a patient with alveolar proteinosis who refused alveolar lavage.<sup>8</sup>

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<sup>1</sup> 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 1 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.:** Ambrit; Apracur Expectorante; Cortos; Graneodin Expectorante; Mucosolvan; Tabin Expectorante; Tavinex Expectorante; Tavinex Expectotabs; Tosambrex. **Austria:** Ambrobene; Ambrohexal; Ambrolan; Ambrolol; Ambronorm; Bisolangin; Bisolary; Broxol; Mucoangin; Mucosolvan; Sekretovit. **Belg.:** Mucoangin; Surbronc. **Braz.:** Ambrozil; Ambrol; Ambroten; Ambrox; Anabron; Broncoflux; Bronxol; Expectuss; Fluibron; Fluidin; Fluxol; Mucibron; Mucodeant; Mucolin; Mucosolvan; Mucosolan; Neossolvan; Probec; Pulmosolvan; Surfactil. **Chile:** Bronchopront; Broncot; Fluibron; Fluomit; Milbron; Mintamox; Mucosolvan; Muxol; Tocalm; **Cz.:** Ambex; Ambrobene; Ambrosan; Ambrospray; Bronchopront; Dignobroxol; Dr Rentschler Hustenlöser; Fervec; Flavamed; Halixol; Mucosin; Mucosolan; Neo-Bronchol; Solvolan; **Denm.:** Mucoangin; **Fr.:** Lysopadol; Muxol; Surbronc. **Ger.:** Ambrit; Ambro; Ambro-Puren; Ambrobeta; Ambrodec; Ambrohexal; Ambroinflat; Ambrolol; Ambropp; Bronchopront; Bronchowerm; duramucal; Expit; frenopect; Frubizin akut; Larylin Husten-Löser Pastillen; Larylin Husten-Löser Saft; Linoxyl; Muco-Aspecton; Mucoangin; Mucobroxol; Mucophlogat; Mucosolvan; Neo-Bronchol; Padimuc; Pulmotin Hustenlöser; Sigabroxol; stas-Hustenlöser; tuss; **Gr.:** Ambrobion; Abrolen; Afrodor; Amboral; Ambrobion; Ambromy; Anavix; Aprinol; Auroxol; Bunafon; Celibron; Dolcevin; Ebertuss; Effercet; Erosil; Fluibrox; Grenovix; Hivotex; Kriolen; Lextarol; Mavixan; Mucolin; Mucosolvan; Mucovic; Nibren; Olbenorm; Proxiven-N; Puntol; Respirol; Saribal; Stefalant; Strubelin; Tevoril; Tosse; Tussefar; Zyrantol. **Hong Kong:** Amxol; Bronchopront; Marbroxol; Max; Medovent; Mucosolvan; Quali-solvan; **Hung.:** Ambrobene; Ambrohexal; Bronchopront; Halixol; Mucoangin; Solvolan; **India:** Accotintin; Acolyt; Ambrodi; Inhalax; **Indon.:** Ambrit; Brommer; Bronchopront; Broncozol; Broxal; Epexol; Extopect; Gunapect; Interpec; Lapimuc; Molapect; Mucera; Mucolica; Mucopect; Mucos; Mucolol; Nufanibrox; Silopect; Sohopen; Transbroncho; Transmucol; **Ital.:** Ambrotus; Ambrobron; Atus; Broxol; Fluibron; Fluxol; Lintos; Lisopulm; Mucilar; Mucosolvan; Mucobron; Mucosolvan; Secretil; Surfactil; Tauxol; Viscomucil; **Jpn.:** Mucosal; Mucosolvan; **Malaysia:** Amxol; Axol; Mucosolvan; Shinoxol; Strepsils Chesty Cough; **Mex.:** Ambrofr; Amocel; Axol; Balsibron; Bionoxol; Boxolan; Brogal; Bronolban; Brosolan; Broxaquim; Broxofar; Broxoffler; Broxol; Broxilim; Cloxan; Ebromin; Euroxol;

Exabrol; Expeffen; Fantrodol; Ital-Ultra; Loexom; Loxibron; Mucibron; Mucoangin; Mucosolvan; Mucovibrol; Mucovibrol T; Mucosol; Musalten; Musvan; Muxol; Oxolvan; Prospect; Protitus; Randex; Rimoxol; Sekretovit; Septacin; Seraxol-S; Softxol; Solpat; Tobrin; Tradexol; Trimexin; Tunitol-BX; Tusibron; Ula-X; Vialox; Weisal; **Neth.:** Mucoangin; **Philipp.:** Ambrolol; Atrivex; Brocol; Bromace; Bromacef; Broxan; Broxifol; Broxil-M; Broxitol; Broxolvan; Ebrocol; Expel; Medibron; Mepebrol; Mucosol; Mucosolvan; Mucovic; Phlemasol; Pontef; Pulmobrol; Venteez; Vioxol; Zobroxol; **Pol.:** Allegan; Amox; Ambrohexal; Ambroksol; Ambrosan; Ambrosol; Deflegmin; Flavamed; Mucoangin; Mucosolvan; Mucobron; Tussal Expectorans; **Port.:** Benflux; Bromax; Bronchopront; Broncolber; Bronxol; Drenoxol; Fluidox; Fluidrenol; Hipotosse; Mucodrenol; Mucosolvan; Mucotosse; **Rus.:** Ambrobene (Амбробене); Ambrohexal (Амброгексал); Ambrosan (Амбросан); Ambrosol (Амбросол); Bronchowerm (Бронхверм); Halixol (Халиксол); Lasolvan (Лазолван); Medovent (Медовент); Suprima-Kof (Суприма-Коф); **Singapore:** Amxol; Axol; Bronchopront; Max; Mucosolvan; Mucosolvan; **Spain:** Ambrolit; Dinobroxol; Motosol; Mucibron; Mucosin; Naxpa; **Swed.:** Mucoangin; **Switz.:** Fluibron; Mucabrox; Mucoangin; Mucosolvan; **Thai.:** Ambrol; Ambrolit; Ambrolit; Ambrox; Ambroxan; Ampromed; Amtuss; Amxol; Bronchopront; Broncol; Broxol; Broxsa; Max; Medovent; Misovan; Movent; Mucodil; Mucolan; Mucolil; Mucomed; Mucopex; Mucosolvan; Mucosine-F; Mucosin; Muscan; Mucobrox; Polibroxol; Simusol; Strepsils Chesty Cough; Streptussol-C; **Turk.:** Ambreks; Fluibron; Mukoral; Pulmor; Sekrol; Tuslin; **UAE:** Mucum; **Venez.:** Ambrit; Ambromucol; Ambrox; Benflux; Brocantol; Bronchopront; Lituxil; Misulvan; Mucoangin; Mucoramat; Mucosolvan; Muxen; Xolvan.

**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; Cefaclina Bronquial; Gentibron; Letondal; Muco Cortos; Muco Dosados; Muco Dosados Biotic; Mucoprednibron; Mucosolvan Compositum; No-Tos Biotic; Nobactam Bronquial; Oxibron NF; Oximar Respiratorio; Pulmonix Plus; Toraxan; Trexilor NF; Trifamox Bronquial Duo; **Austria:** Mucospas; **Braz.:** Penetro; **Chile:** Ambrotos; **Cz.:** Doxycyclin Al comp; **Ger.:** Ambroxol; Ambroxol Al comp; Ambroxol comp; Amox-Curen; Azudoxat comp; Broncho-Euphyllin; Doxam; Doximucol; Doxy Comp; Doxy Lindoxyl; Doxy Plus; Doxy-Wolff Mucolyt; Doxysolvat; Jenabroxol comp; Sigamuc; Spasmo-Mucosolvan; Terilit; **India:** Ambrodi Plus; Ambrodi-S; Amcof; Amcold; Asthalin AX; Axalin-AX; Axalitin; Kofarest; Mucaryl-AX; Novamox AX; Roxelipin-ME; Surpivent-AX; **Mex.:** Acimox-AX; Aeroflux; Alerfin Ex; Alexing; Ambrodi-C; Aminofedrisin; Balsibron-C; Biovacin Ex; Biscin-ol; Bolbamox; Brogal Compositum; Brogal-T; Brogram; Brominol-C; Bronar; Bronolan-M; Broquixol; Brosolan C; Broxofar Compuesto; Broxol Air; Broxol Plus; Broxolim-AM; Broxolim-C; Brumax; Cefabronol; Clbronat; Cobadex; Coricidin Expec; Dexol; Dextoltrin; Dofaxil; Doralan-AX; Ebromin P; Epical NF; Fanbrox; Fleamex; Fludexol-CL; Fluvicil; Fluxibit; Fluxol; Futac; Gimabrol; Histical NF; Laritol Ex; Linfardex; Loexom FC; Loexom FS; Loxorol; Mucoflux; Mucosolvan Compositum; Mucovibrol Amoxi; Mucovibrol C; Musaldox; Neumyn-AS; Pentibroxil; Plexus; Ravotaf; Removil; Rezipen; Rombox; Salamlux; Sekretovit Amoxi; Sekretovit Ex; Sensibit XP; Septacin Amoxi; Septacin Ex; Seraxol; Serbol; Sermomox; Siblex; Solibrol; Tadinac-C; Taveksil; Theraflu Tenalif; Torva; Toxol; Ula-X; Vamoxol; **Port.:** Clembroxol; Lactucol; Mucospas; Ventolitol; **Rus.:** Col-dact Broncho (Колдакт Бронхо); Rinicold-Broncho (Риниколд Бронхо); **Venez.:** Aeroflux; Ambroclax; Ambromuco Compositum; Arbiel; Clenbuxol; Lituxil Compositum; Mucolin; Mucosolvan Compositum.

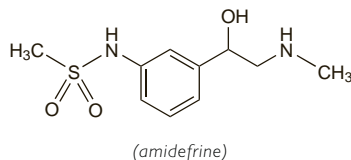
## Amidefrine Mesilate (BAN, INN) ⊗

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

АМИДЕФРИНА Мезилат

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

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



## 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'; Ammoniumhydrogen-karbonát; Ammoniumvätekarbonat; Ammoniumvetykarbonaatti; Amonio, bicarbonato de; Amonio-vandelilio karbonatas; E503; Hydrogenuhlíčan 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 chlorrek; 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 coarse, 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 glycyrhizate (p.2316).