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.

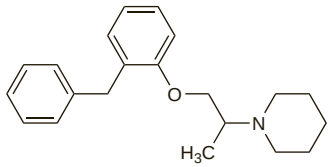
Multi-ingredient: numerous preparations are listed in Part 3.

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

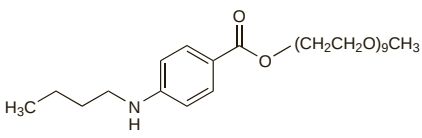
Proprietary Preparations (details are given in Part 3)
Ger.: Tussafug; ***Hong Kong:*** Cofrel; ***Jpn:*** Flaveric.

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.

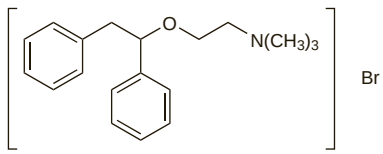
Proprietary Preparations (details are given in Part 3)
Mex.: Alzomed-F†; Beknol; Benzonal; Bronpax; Capsicof; D-Tato; Lemtosid; Nactol†; Novapsyl; Parven†; Pebegal; Pharben; Supracof; Tesalon; Tesopen; Texoven; Tusical; Tusitato; Tuzzil; Velpro; ***USA:*** Tessalon.

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

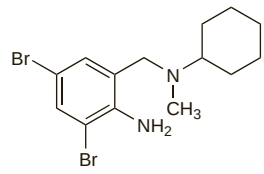
Proprietary Preparations (details are given in Part 3)
Austria: Lysbex.

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.

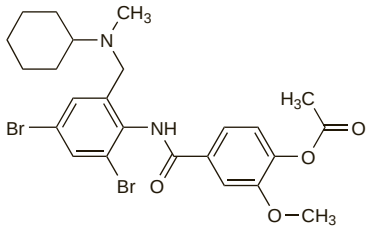
Brovanexine Hydrochloride *(rINNM)*

Brovanexine, Chlorhydrate de; Brovanexini Hydrochloridum; Hidrocloruro de brovanexina. 4-(Acetyloxy)-*N*-[2,4-dibromo-6-[(cyclohexylmethylamino)methyl]phenyl]-3-methoxybenzamide monohydrochloride.

Брованексина Гидрохлорид

$C_{24}H_{29}Br_2ClN_2O_4$ = 604.8.

CAS — 54340-61-3 (brovanexine); 54340-60-2 (brovanexine hydrochloride).



(brovanexine)

Profile

Brovanexine is a derivative of bromhexine (above) and is given orally as the hydrochloride, usually as an adjunct to antibacterials in preparations for the treatment of respiratory-tract infections.

Preparations

Proprietary Preparations (details are given in Part 3)
Braz.: Bronquimucil; ***Port.:*** Bronquimucil†; Pulmo-San†; ***Spain:*** Broncimucil.

Multi-ingredient: ***Arg.:*** Trifamox Bronquial; ***Spain:*** Bronquimucil†; Eupen Bronquial.

Butamirate Citrate *(BANM, USAN, rINNM)*

Abbott-36581; Butamirát-citrát; Butamirate, Citrate de; Butamirati Citras; Butamyrate Citrate; Citrato de butamirato; HH-197. 2-(2-Diethylaminoethoxy)ethyl 2-phenylbutyrate dihydrogen citrate.

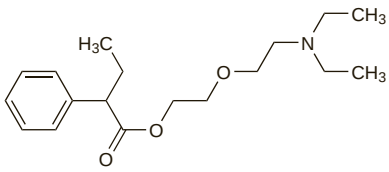
Бутамирата Цитрат

$C_{18}H_{29}NO_3.C_6H_8O_7$ = 499.6.

CAS — 18109-80-3 (butamirate); 18109-81-4 (butamirate citrate).

ATC — R05DB13.

ATC Vet — QR05DB13.



(butamirate)

Profile

Butamirate citrate is a cough suppressant used in non-productive cough (p.1547) and stated to have a central action. The usual oral dose is up to 30 mg daily in 3 or 4 divided doses; some countries permit up to 90 mg daily in divided doses. Modified-release tablets containing 50 mg have been given 2 or 3 times daily.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Dosodos; Talasa NF; Tossec; ***Belg.:*** Quintex†; Sinecod; ***Braz.:*** Besedan†; ***Cz.:*** Sinecod; Tussin; ***Gr.:*** Antis; Antitoss; Betavix; Boutavixal; Bronchofyl; Butacodin; Butagan; Butamir; Butrin; Buvastin; Chemisolv; Chributan; Codexine-R; Codimin; Cyne†; Devix; Doctamine; Drosten; Ellisek-S; Gertotus; Leogumil; Mebronol; Minatuss; Nontoss; Novamir; Oaxen; Pandigal; Pintal; Roctylan; Rondover; Safarol; Sinecod; Siroflex; Stilex; Velkacet; Verocod; Vilvom; Zeleven; Zestapron†; Zetapron; ***Hung.:*** NeoCitran Antitussive; Sinecod; ***Ital.:*** Butiran; Lenistar; Lexosedin; Sinecod Tosse Sedativo; ***Neth.:*** Sinecod; ***Philipp.:*** Sinecod; ***Pol.:*** Sinecod; Supremin; ***Port.:*** Sinecod; ***Rus.:*** Sinecod (Синекод); ***Switz.:*** DemoTussol; NeoCitran Antitussif; Sinecod; ***Thai.:*** Sinecod; ***Turk.:*** Kreval; Sinecod.

Multi-ingredient: ***Arg.:*** Muco Dosodos; ***Braz.:*** Novotussan†; ***Cz.:*** Stoptussin; ***Rus.:*** Stoptussin (Стоптуссин); ***Switz.:*** Hicoseen.

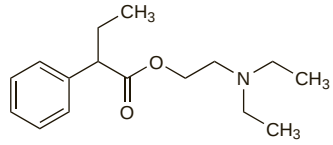
Butetamate Citrate *(BANM, rINNM)*

Butétamate, Citrate de; Butetamati Citras; Butethamate Citrate; Butethamate Dihydrogen Citrate; Citrato de butetamato. 2-Diethylaminoethyl 2-phenylbutyrate citrate.

Бутетамата Цитрат

$C_{16}H_{25}NO_2.C_6H_8O_7$ = 455.5.

CAS — 14007-64-8 (butetamate); 13900-12-4 (butetamate citrate).



(butetamate)

Profile

Butetamate citrate is reported to be an antispasmodic and bronchodilator and has been used alone or in combination preparations for the symptomatic treatment of coughs and other associated respiratory-tract disorders.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Heliphenicol.

Multi-ingredient: ***Arg.:*** Febrigrip; Fugafebril; Kiper; Mejoral Grip; Muco Cortos†; Mucoprednibron; Piritos; Pulmocler; Refenax Jarabe; Tavinex Antigripal; ***Austria:*** Coldadolin; Influbene; ***Switz.:*** Bronchotussine.

Calcium Iodide

Calcii Iodidum; Calciumjodid; Ioduro de calcio; Kalcio jodidas; Kalsiumjodidi.

Йодид Кальция

CaI_2 = 293.9.

CAS — 10102-68-8.

Pharmacopoeias. *Eur.* (see p.vii) includes the tetrahydrate for homoeopathic preparations.

Ph. Eur. 6.2 (Calcium Iodide Tetrahydrate for Homoeopathic Preparations; Calcii Iodidum Tetrahydricum ad Praeparationes Homoeopathicas). A white or almost white, very hygroscopic, powder. Very soluble to freely soluble in water and in alcohol. Store in airtight containers.

Profile

Calcium iodide has been used orally in expectorant mixtures. The limitations of iodides as expectorants are discussed under Cough, p.1547. The actions of the iodides are discussed under Iodine (p.2169).

Homoeopathy. Calcium iodide has been used in homoeopathic medicines under the following names: Calcium iodatum; Calcium jodatum; Calcarea iodata; Cal. iod.

Preparations

Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Arg.:*** Zantril†; ***Gr.:*** Vitreolent; ***USA:*** Calcidrine; Norisodrine with Calcium Iodide.

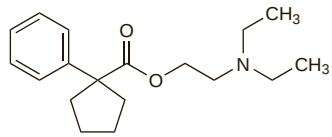
Caramiphen Edisilate *(BANM, rINNM)*

Caramiphen Edisylate; Caramiphène, Edisilate de; Caramipheni Edisilas; Edisilato de caramifeno. 2-Diethylaminoethyl 1-phenylcyclopentane-1-carboxylate ethane-1,2-disulphonate.

Карамифена Эдизилат

$C_{38}H_{60}N_2O_{10}S_2$ = 769.0.

CAS — 77-22-5 (caramiphen); 125-86-0 (caramiphen edisilate); 125-85-9 (caramiphen hydrochloride).



(caramiphen)

Profile

Caramiphen is a centrally acting cough suppressant that has been used as the edisilate in combination preparations for coughs (p.1547). Caramiphen hydrochloride was originally used similarly to trihexyphenidyl (p.820) for its antimuscarinic actions.

Carbocisteine *(BAN, rINN)*

AHR-3053; Carbocisteína; Carbocistéine; Carbocisteinum; Carbocysteine *(USAN)*; Karbocistein; Karbocisteinas; Karbocisztein; Karbocystein; Karbocysteina; Karbosisteiini; Karbosistein; LJ-206. *S*-Carboxymethyl-L-cysteine.

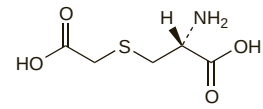
Карбоцистеин

$C_5H_9NO_4S$ = 179.2.

CAS — 2387-59-9; 638-23-3 (carbocisteine, L-form).

ATC — R05CB03.

ATC Vet — QR05CB03.



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

Ph. Eur. 6.2 (Carbocisteine). A white or almost white, crystalline powder. Practically insoluble in water and in alcohol; dissolves in dilute mineral acids and in dilute solutions of alkali hydroxides. A 1% suspension in water has a pH of 2.8 to 3.0. Protect from light.

Incompatibility. UK licensed product information states that mixing carbocisteine with pholcodine linctus causes precipitation of carbocisteine from solution but no information is given on whether this incompatibility is with the pholcodine or some component of the formulation used.

Carbocisteine Lysine *(BANM, rINNM)*

Carbocisteína lisina; Carbocistéine Lysine; Carbocisteinum Lysinum; Carbocysteine Lysine.

Карбоцистеина Лизин

CAS — 49673-81-6.

ATC — R05CB03.

ATC Vet — QR05CB03.

Carbocisteine Sodium *(BANM, rINNM)*

Carbocisteína sódica; Carbocistéine Sodique; Carbocysteine Sodium; Natrii Carbocisteinum.

Натрий Карбоцистеин

CAS — 49673-84-9 (carbocisteine sodium, L-form).

ATC — R05CB03.

ATC Vet — QR05CB03.

Adverse Effects and Precautions

Nausea and gastric discomfort, and gastrointestinal bleeding have occasionally occurred with carbocisteine. Skin rashes have also been reported.

Carbocisteine should be used with caution in patients with a history of peptic ulcer disease because of the risk that mucolytics may disrupt the gastric mucosal barrier.

Effects on endocrine function. Transient hypothyroidism associated with the use of carbocisteine developed in a patient with compromised thyroid function.[1]

1. Wiersinga WM. Antithyroid action of carbocisteine. *BMJ* 1986; **293:** 106.

Pharmacokinetics

Carbocisteine is rapidly and well absorbed from the gastrointestinal tract with peak plasma concentrations occurring about 2 hours after an oral dose. It appears to penetrate into lung tissue and respiratory mucus. Carbocisteine is excreted in the urine as unchanged drug and metabolites. Acetylation, decarboxylation, and sulfoxidation have been identified as the major metabolic pathways. Sulfoxidation may be governed by genetic polymorphism.

◊ References.

1. Karim EFIA, *et al.* An investigation of the metabolism of S-carboxymethyl-L-cysteine in man using a novel HPLC-ECD method. *Eur J Drug Metab Pharmacokinet* 1988; **13:** 253–6.
2. Brockmoller J, *et al.* Evaluation of proposed sulphoxidation pathways of carbocysteine in man by HPLC quantification. *Eur J Clin Pharmacol* 1991; **40:** 387–92.
3. Steventon GB. Diurnal variation in the metabolism of S-carboxymethyl-L-cysteine in humans. *Drug Metab Dispos* 1999; **27:** 1092–7.
4. Jovanovic D, *et al.* A comparative bioavailability study of a generic capsule formulation containing carbocysteine. *Pharmazie* 2006; **61:** 446–9.

Uses and Administration

Carbocisteine is used for its mucolytic activity in respiratory disorders associated with productive cough (p.1547). It is given orally in a dose of 750 mg three times daily, reduced by one-third when a response is obtained. Carbocisteine is also given orally as the sodium or lysine salts.

For children's doses, see Administration in Children, below.

Administration in children. Children from 2 to 5 years may be given oral carbocisteine 62.5 to 125 mg four times daily and those aged 5 to 12 years 250 mg three times daily.