

Bergamot Oil

Bergamot Essence; Bergamota, aceite esencial de; Oleum Bergamottae.

Pharmacopoeias. In *Fr.* and *It.*

Profile

Bergamot oil is a greenish or brownish-yellow volatile oil with a characteristic fragrant odour and a bitter aromatic taste, obtained by expression from the fresh peel of fruit of *Citrus bergamia* (Rutaceae). Constituents include linalyl acetate and 5-methoxypsoralen (p.1607) and photosensitivity reactions have occurred following the topical use of preparations containing bergamot oil.

Bergamot oil is used in perfumery and as a flavour in Earl Grey tea. It has been included in some preparations for upper respiratory-tract disorders and hyperhidrosis. It is also used in aromatherapy.

◇ Muscle cramps have been reported¹ in a patient who drank up to 4 litres of 'Earl Grey' tea daily.

1. Finsterer J. Earl Grey tea intoxication. *Lancet* 2002; **359**: 1484.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: *Fr.*: Ephydrol; *Ital.*: Bergacid; **Philipp.**: Kamillosan M; **Switz.**: Perskindol Classic.

Bethahistine (*BAN*, *rINN*)

Bethahistini; Bethahistin; Bethahistina; Bétahistine; Bethahistinum. *N*-Methyl-2-(2-pyridyl)ethylamine.

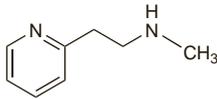
Бетагистин

$C_8H_{12}N_2 = 136.2$.

CAS — 5638-76-6.

ATC — *N07CA01*.

ATC Vet — *QN07CA01*.

**Bethahistine Hydrochloride** (*USAN*, *rINN*)

Bethahistini dihidrokloridi; Bethahistin Dihidroklorür; Bethahistin-dihydrochlorid; Bethahistindihydrochlorid; Bétahistine, Chlorhydrate de; Bétahistine, dichlorhydrate de; Bethahistine Dihydrochloride (*BANM*); Bethahistini dihydrochloridum; Bethahistini Hydrochloridum; Bethahistino dihydrochloridas; Hidrocloruro de bethahistina; PT-9. *N*-Methyl-2-(2-pyridyl)ethylamine dihydrochloride.

Бетагистина Гидрохлорид

$C_8H_{12}N_2 \cdot 2HCl = 209.1$.

CAS — 5579-84-0.

ATC — *N07CA01*.

ATC Vet — *QN07CA01*.

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

Ph. Eur. 6.2 (Bethahistine Dihydrochloride). A white to slightly yellow, very hygroscopic, powder. Very soluble in water; soluble in alcohol; practically insoluble in isopropyl alcohol. A 10% solution in water has a pH of 2.0 to 3.0. Store in airtight containers.

USP 31 (Bethahistine Hydrochloride). A white to almost yellow, very hygroscopic, crystalline powder. Very soluble in water; freely soluble in alcohol; practically insoluble in isopropyl alcohol. pH of a 10% solution in water is between 2.0 and 3.0.

Bethahistine Mesilate (*BANM*, *rINN*)

Bethahistini mesilaatti; Bethahistin-dimesilát; Bétahistine, mésilate de; Bethahistine Mesylate; Bethahistini Dimesilas; Bethahistini mesilas; Bethahistinmesilat; Bethahistino mesilasas; Bethahistin-mezilát; Mesilato de bethahistina. *N*-Methyl-2-(2-pyridyl)ethylamine bismethanesulphonate.

Бетагистин Мезилат

$C_8H_{12}N_2 \cdot (CH_4O_3S)_2 = 328.4$.

CAS — 54856-23-4.

ATC — *N07CA01*.

ATC Vet — *QN07CA01*.

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

Ph. Eur. 6.2 (Bethahistine Mesilate). A white or almost white, crystalline, very hygroscopic powder. Very soluble in water; freely soluble in alcohol; very slightly soluble in isopropyl alcohol. A 10% solution in water has a pH of 2.0 to 3.0. Store in airtight containers.

Adverse Effects

Gastrointestinal disturbances, headache, skin rashes, and pruritus have been reported.

Precautions

Bethahistine should not be given to patients with phaeochromocytoma. It should be given with care to patients with asthma, peptic ulcer disease, or a history of peptic ulcer disease.

Porphyria. Bethahistine hydrochloride is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *in-vitro* systems.

Uses and Administration

Bethahistine is an analogue of histamine and is claimed to improve the microcirculation of the labyrinth resulting in reduced endolymphatic pressure. It is used to reduce the symptoms of vertigo (p.565), tinnitus (p.1866), and hearing loss associated with Ménière's disease (p.564).

Bethahistine is given orally as the hydrochloride or mesilate. The usual initial dose (of the hydrochloride) is 16 mg three times daily taken preferably with meals; maintenance doses are generally in the range of 24 to 48 mg daily. Bethahistine mesilate is used in similar doses.

Reviews

1. Lacour M, Sterkers O. Histamine and bethahistine in the treatment of vertigo: elucidation of mechanisms of action. *CNS Drugs* 2001; **15**: 853-70.

2. James AL, Burton MJ. Bethahistine for Ménière's disease or syndrome. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2001 (accessed 30/05/06).

Preparations

BP 2008: Bethahistine Dihydrochloride Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Microser; Ronistina; Travelimin; **Austral.:** Serc; **Austria:** Betaser; **Belg.:** Bethahistop; Betaser; Docbetahi; **Braz.:** Betaser; Labirin; **Canad.:** Serc; **Chile:** Microser; **Cz.:** Avertin; Betaser; Microser; Polvertic; Zenostig; **Denm.:** Betaser; **Fin.:** Betaser; **Fr.:** Betaser; Evolis; Extovyt; Lectil; **Serc.:** **Ger.:** Aequamen; Betavert; Meloplat; Vasomotal; **Gr.:** Antivom; Betaser; Katabexin; Ribrain; Riva; **Hong Kong:** Beta-Synto; Betaser; Bymerien; Menier; **Hung.:** Betagen; Betaser; Elven; **India:** Bethahist; Vertin; **Indon.:** Betaser; Merislon; Vertigo; Noverly; Vastigo; Vercur; Versilon; Vertex; **Irl.:** By-Vertin; Serc; Vertigon; **Israel:** Agiser; Betisline; **Ital.:** Microser; Sincrover; Vertiser; **Jpn:** Merislon; **Malaysia:** Alfinor; Betaser; Merislon; **Mex.:** Serc; **Neth.:** Betaser; **NZ:** Serc; Vergo; **Philipp.:** Merislon; Serc; Vertilate; **Pol.:** Betaser; Histimerk; Microser; **Port.:** Betaser; Merislon; **Rus.:** Betaser (Бетасерп); Vestibo (Вестибо); **S.Afr.:** Serc; **Singapore:** Betaser; Merislon; **Spain:** Fidium; **Switz.:** Betaser; **Thai.:** Behistin; Bethahist-B; Merislon; Merlin; Serc; **Turk.:** Betaser; Vasoser; **UK:** Serc; **Venez.:** Microser; Serc.

Betaine

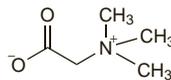
Betaína; Glycine Betaine; Glycocol Betaine; Lycine; Trimethylglycine. (Carboxymethyl)trimethylammonium hydroxide inner salt.

$C_5H_{11}NO_2 = 117.1$.

CAS — 107-43-7.

ATC — *A16AA06*.

ATC Vet — *QA16AA06*.

**Betaine Hydrochloride**

Betaïni dihidrokloridi; Betaína, hidrocloruro de; Betain dihidroklorid; Betaini Hydrochloridum; Trimethylglycine Hydrochloride. (Carboxymethyl)trimethylammonium hydroxide inner salt hydrochloride.

$C_5H_{11}NO_2 \cdot HCl = 153.6$.

CAS — 590-46-5.

ATC — *A09AB02*.

ATC Vet — *QA09AB02*.

Pharmacopoeias. In *US*.

USP 31 (Betaine Hydrochloride). A white crystalline powder. Soluble in water and in alcohol; practically insoluble in chloroform and in ether. A 25% solution in water has a pH of 0.8 to 1.2.

Profile

Betaine is used as a methyl donor to remethylate homocysteine to methionine in the treatment of patients with homocystinuria (see Amino Acid Metabolic Disorders, p.1922). It is given orally in a usual dose of 3 g twice daily. Doses are adjusted according to plasma-homocysteine concentrations; up to 20 g daily has been required in some patients. In children under 3 years old, an initial dose of 100 mg/kg daily given in 2 divided doses may be used.

Severe cerebral oedema and hypermethioninaemia have been reported in a few patients, and it is recommended that plasma-methionine concentrations should be monitored at the start of betaine treatment and periodically thereafter. Patients being treated for cystathionine beta-synthase deficiency may pose particular problems because betaine may further raise their already elevated methionine concentrations increasing the risk of cerebral oedema.

Betaine has also been used as a variety of salts in preparations for liver and gastrointestinal disorders. The hydrochloride has been given as a source of hydrochloric acid in the treatment of hypochlorhydria.

Adverse effects. References.

1. Devlin AM, *et al.* Cerebral edema associated with betaine treatment in classical homocystinuria. *J Pediatr* 2004; **144**: 545-8.

Homocystinuria. References.

- Smolin LA, *et al.* The use of betaine for the treatment of homocystinuria. *J Pediatr* 1981; **99**: 467-72.
- Wilcken DEL, *et al.* Homocystinuria—the effects of betaine in the treatment of patients non responsive to pyridoxine. *N Engl J Med* 1983; **309**: 448-53.
- Holme E, *et al.* Betaine for treatment of homocystinuria caused by methylenetetrahydrofolate reductase deficiency. *Arch Dis Child* 1989; **64**: 1061-4.
- Anonymous. Betaine for homocystinuria. *Med Lett Drugs Ther* 1997; **39**: 12.

Liver disorders. Betaine has also been investigated for the treatment of nonalcoholic steatohepatitis.

References.

- Miglio F, *et al.* Efficacy and safety of oral betaine glucuronate in non-alcoholic steatohepatitis: a double-blind, randomized, parallel-group, placebo-controlled prospective clinical study. *Arzneimittelforschung* 2000; **50**: 722-7.
- Abdelmalek MF, *et al.* Betaine, a promising new agent for patients with nonalcoholic steatohepatitis: results of a pilot study. *Am J Gastroenterol* 2001; **96**: 2711-7.

Pharmacokinetics. References.

- Schwahn BC, *et al.* Pharmacokinetics of oral betaine in healthy subjects and patients with homocystinuria. *Br J Clin Pharmacol* 2003; **55**: 6-13.

Preparations

Proprietary Preparations (details are given in Part 3)

Austral.: Cystadane; **Canad.:** Cystadane; **Cz.:** Cystadane; **Israel:** Cystadan; **Ital.:** Somaty; **Port.:** Cystadane; **USA:** Cystadane.

Multi-ingredient: **Arg.:** Eucos-L; **Austral.:** Betaine Digestive Aid; Bioglan Digestive Zyme; Digestaid; **Austria:** CO Granulat; Oroacid; **Belg.:** Digestomen; **Braz.:** Aminotox; Anekron; Betaliver; Biohexa; Colachof; Enteroflon; Epodler; Heparactron; Hepalin; Hepatobef; Hepatox; Hormo Hepatico; Metiocolin Composto; Necro B-6; Xantion Complex; **Cz.:** Citrarginin; CO Granulat; **Fr.:** Citrarginine; Gastrobul; Hepagrum; Nivabel; Ornitate; **Ger.:** CO Granulat; Flacar; Unexym MD S; **Gr.:** Kloref; **Hong Kong:** Jetejar; **Hung.:** Betacidi; Gastrobul; **Indon.:** Naturica DMF; **Israel:** Betazim; **Ital.:** Citroepatina; Epabetina; Jetejar; **Malaysia:** Jetejar; **Neth.:** Gastro; **Philipp.:** Jetejar; **S.Afr.:** Kloref; **Singapore:** Jetejar; **Switz.:** Pepsi-Chlor; **UK:** Enzyme Digest; Enzyme Plus; Kloref.

Bethanechol Chloride (*BAN*)

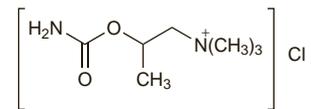
Betanechol, cloruro de; Betanekolikloridi; Betanekolklorid; Bethanecholi Chloridum; Carbamylmethylcholine Chloride. (2-Carbamoyloxypropyl)trimethylammonium chloride.

$C_7H_{17}ClN_2O_2 = 196.7$.

CAS — 674-38-4 (bethanechol); 590-63-6 (bethanechol chloride).

ATC — *N07AB02*.

ATC Vet — *QN07AB02*.



Pharmacopoeias. In *Jpn* and *US*.

USP 31 (Bethanechol Chloride). Colourless or white crystals, or white crystalline powder, usually having a slight, amine-like odour. It is hygroscopic and exhibits polymorphism. Freely soluble in water and in alcohol; insoluble in chloroform and in ether. pH of a 1% solution in water is between 5.5 and 6.5. Store in airtight containers.

Stability. References to the stability of oral liquid preparations of bethanechol chloride prepared extemporaneously from tablets.

- Schlatter JL, Saulnier J-L. Bethanechol chloride oral solutions: stability and use in infants. *Ann Pharmacother* 1997; **31**: 294-6.
- Allen LV, Erickson MA. Stability of bethanechol chloride, pyrazinamide, quinidine sulfate, rifampin, and tetracycline hydrochloride in extemporaneously compounded oral liquids. *Am J Health-Syst Pharm* 1998; **55**: 1804-9.

Sterilisation. The US manufacturers state that solutions of bethanechol chloride may be autoclaved at 120° for 20 minutes without discoloration or loss of potency.

Adverse Effects and Treatment

As described for choline esters under Acetylcholine Chloride, p.1877.

Precautions

As described for choline esters under Acetylcholine Chloride, p.1877.

Bethanechol should not be given by the intravenous or intramuscular routes as very severe muscarinic adverse effects are liable to occur, calling for emergency use of atropine.

Autonomic neuropathy. Patients with autonomic neuropathy might be more susceptible to the adverse effects of bethanechol and they should be started on low-dosage regimens and observed closely for signs of toxicity.¹

- Caraco Y, *et al.* Bethanechol-induced cholinergic toxicity in diabetic neuropathy. *DICP Ann Pharmacother* 1990; **24**: 327-8.

Interactions

As for Neostigmine, p.632.

The symbol † denotes a preparation no longer actively marketed