Benzatropine Mesilate *(BANM, rINNM)*

Benzatropine, Mésilate de; Benzatropine Methanesulfonate; Benzatropini Mesilas; Benztropine Mesylate; Mesilato de benzatropina. (1*R*,3*r*,5*S*)-3-Benzhydryloxytropane methanesulphonate.

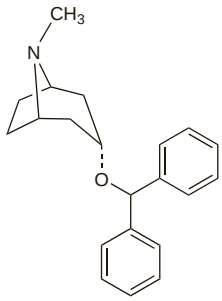
Бензатропина Мезилат

$C_{21}H_{25}NO,CH_4O_3S$ = 403.5.

CAS — 86-13-5 (benzatropine); 132-17-2 (benzatropine mesilate).

ATC — N04AC01.

ATC Vet — QN04AC01.



(benzatropine)

Pharmacopoeias. In *Br.* and *US*.

BP 2008 (Benzatropine Mesilate). A white, odourless or almost odourless, crystalline powder. Very soluble in water; freely soluble in alcohol; practically insoluble in ether.

USP 31 (Benztropine Mesylate). A white, slightly hygroscopic, crystalline powder. Very soluble in water; freely soluble in alcohol; very slightly soluble in ether. Store in airtight containers.

Adverse Effects, Treatment, and Precautions

As for Atropine Sulfate, p.1219. Drowsiness may be severe in some patients and patients so affected should not drive or operate machinery. Mental disturbances and excitement may occur with large doses or in susceptible patients.

Abuse. For mention of abuse of benzatropine see under Trihexyphenidyl Hydrochloride, p.820.

Effects on the heart. Paradoxical sinus bradycardia in a patient with depression and psychotic symptoms was attributed to benzatropine since it persisted despite modification to other treatment and resolved only when benzatropine was withdrawn.[1]

1. Voinov H, *et al.* Sinus bradycardia related to the use of benztropine mesylate. *Am J Psychiatry* 1992; **149:** 711.

Interactions

As for antimuscarinics in general (see Atropine Sulfate, p.1220).

Antidepressants. A report[1] of 5 patients who developed delirium while taking an antipsychotic, an *SSRI*, and benzatropine suggested that there might be an interaction between SSRIs and benzatropine.

1. Roth A, *et al.* Delirium associated with the combination of a neuroleptic, an SSRI, and benztropine. *J Clin Psychiatry* 1994; **55:** 492–5.

Antipsychotics. Fatal heat stroke after exposure to an ambient temperature of over 29° has been reported[1,2] in patients receiving benzatropine with antipsychotics. Paralytic ileus, sometimes fatal, has also been seen in patients taking benzatropine with antipsychotics.[3]

1. Stadnyk AN, Glezos JD. Drug-induced heat stroke. *Can Med Assoc J* 1983; **128:** 957–9.
2. Tyndel F, Labonté R. Drug-facilitated heat stroke. *Can Med Assoc J* 1983; **129:** 680.
3. Wade LC, Ellenor GL. Combination mesoridazine- and benztropine mesylate-induced paralytic ileus: two case reports. *Drug Intell Clin Pharm* 1980; **14:** 17–22.

Uses and Administration

Benzatropine mesilate is a tertiary amine antimuscarinic with actions and uses similar to those of trihexyphenidyl (p.820); it also has antihistaminic properties.

Benzatropine is used for the symptomatic treatment of parkinsonism (p.791), including the alleviation of the extrapyramidal syndrome induced by drugs such as phenothiazines, but, like other antimuscarinics, is of no value against tardive dyskinesias. It has been used in the treatment of dystonias (see under Uses and Administration of Levodopa, p.809).

Benzatropine mesilate is given orally or, if necessary, by intramuscular or intravenous injection.

In idiopathic **parkinsonism** benzatropine mesilate is usually given orally in an initial daily dose of 0.5 to 1 mg at bedtime. Its actions are cumulative, and may not be manifest for several days after beginning therapy. Patients with post-encephalitic parkinsonism often tolerate an initial daily dose of 2 mg. The dose may be gradually increased by 500 micrograms every 5 to 6 days to a maximum of 6 mg daily until the optimum dose is reached. Maintenance therapy may be given as a single daily dose at bedtime or in divided doses 2 to 4 times daily.

In the management of **drug-induced extrapyramidal symptoms** doses of 1 to 4 mg once or twice daily have been given orally or parenterally. Therapy may be withdrawn after 1 to 2 weeks to assess whether it is still necessary.

In an emergency, benzatropine mesilate may be injected intramuscularly or intravenously in a dose of 1 to 2 mg; intramuscular injection is reported to produce an effect as quickly as intravenous dosage so the latter is rarely necessary.

For management of **dystonias in children**, the *BNFC* suggests that in an emergency, single doses of 20 to 100 micrograms/kg (maximum of 2 mg) may be given by intravenous or intramuscular injection to children aged 3 to 12 years, and 1 to 2 mg to those aged 12 to 18 years.

Benzatropine has also been given as the hydrochloride.

Preparations

BP 2008: Benzatropine Injection; Benzatropine Tablets;
USP 31: Benztropine Mesylate Injection; Benztropine Mesylate Tablets.

Proprietary Preparations (details are given in Part 3)
Austral.: Benztrop; Cogentin; ***Austria:*** Cogentin; ***Canad.:*** Cogentin†; ***Cz.:*** Apo-Benztropine; ***Denm.:*** Cogentin†; ***Hong Kong:*** Cogentin; ***Irl.:*** Cogentin†; ***Norw.:*** Cogentin†; ***NZ:*** Benztrop; Cogentin; ***Port.:*** Cogentin†; ***Thai.:*** Cogentin; ***UK:*** Cogentin; ***USA:*** Cogentin.

Biperiden *(BAN, rINN)*

Biperideeni; Bipéridène; Biperideno; Biperidenum. 1-(Bicyclo-[2.2.1]hept-5-en-2-yl)-1-phenyl-3-piperidinopropan-1-ol.

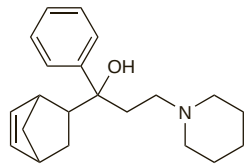
Бипериден

$C_{21}H_{29}NO$ = 311.5.

CAS — 514-65-8.

ATC — N04AA02.

ATC Vet — QN04AA02.



Pharmacopoeias. In *Int.* and *US*.

USP 31 (Biperiden). A white, practically odourless, crystalline powder. Practically insoluble in water; sparingly soluble in alcohol; freely soluble in chloroform. Protect from light.

Biperiden Hydrochloride *(BANM, rINNM)*

Biperideenihydrokloridi; Biperiden Hidroklorür; Bipéridène, chlorhydrate de; Biperidén-hidroklorid; Biperiden-hydrochlorid; Biperidenhydroklorid; Biperideni hydrochloridum; Biperideno hidrochloridas; Hidrocloruro de biperideno.

Бипериден Гидрохлорид

$C_{21}H_{29}NO,HCl$ = 347.9.

CAS — 1235-82-1.

ATC — N04AA02.

ATC Vet — QN04AA02.

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

Ph. Eur. 6.2 (Biperiden Hydrochloride). A white or almost white, crystalline powder. Slightly soluble in water and in alcohol; very slightly soluble in dichloromethane. A 0.2% solution in water has a pH of 5.0 to 6.5. Store in airtight containers. Protect from light.

USP 31 (Biperiden Hydrochloride). A white, practically odourless, crystalline powder. Slightly soluble in water, in alcohol, in chloroform, and in ether; sparingly soluble in methyl alcohol. Protect from light.

Biperiden Lactate *(BANM, rINNM)*

Biperiden Laktat; Bipéridène, Lactate de; Biperideni Lactas; Lactato de biperideno.

Бипериден Лактат

$C_{21}H_{29}NO,C_3H_6O_3$ = 401.5.

CAS — 7085-45-2.

ATC — N04AA02.

ATC Vet — QN04AA02.

Pharmacopoeias. *US* includes Biperiden Lactate Injection.

Adverse Effects, Treatment, and Precautions

As for Atropine Sulfate, p.1219.

Parenteral use may be followed by slight transient hypotension.

Abuse. Abuse of biperiden has been reported in psychiatric patients.[1]

1. Pullen GP, *et al.* Anticholinergic drug abuse: a common problem? *BMJ* 1984; **289**: 612–13.

Interactions

As for antimuscarinics in general (see Atropine Sulfate, p.1220).

Pharmacokinetics

Biperiden is readily absorbed from the gastrointestinal tract, but bioavailability is only about 30% suggesting that it undergoes extensive first-pass metabolism. Biperiden has an elimination half-life of about 20 hours.

◊ References.

1. Hollmann M, *et al.* Biperiden effects and plasma levels in volunteers. *Eur J Clin Pharmacol* 1984; **27:** 619–21.
2. Grimaldi R, *et al.* Pharmacokinetic and pharmacodynamic studies following the intravenous and oral administration of the antiparkinsonian drug biperiden to normal subjects. *Eur J Clin Pharmacol* 1986; **29:** 735–7.

Uses and Administration

Biperiden is a tertiary amine antimuscarinic with actions and uses similar to those of trihexyphenidyl (p.820) but with more potent antinicotinic properties.

Biperiden is used in the symptomatic treatment of parkinsonism (p.791), including the alleviation of the extrapyramidal syndrome induced by drugs such as phenothiazines, but, like other antimuscarinics, is of no value against tardive dyskinesias.

Biperiden is given orally as the hydrochloride and by injection as the lactate; doses are expressed in terms of the relevant salt. The initial oral dose for **Parkinson's disease** is 2 mg of the hydrochloride three or four times daily increased according to response to a maximum of 16 mg daily. The dose for **drug-induced extrapyramidal symptoms** is 2 mg of the hydrochloride orally one to three times daily; alternatively, 2 mg of biperiden lactate may be given by intramuscular or slow intravenous injection and repeated every 30 minutes if needed up to a maximum of 4 doses in 24 hours.

Preparations

USP 31: Biperiden Hydrochloride Tablets; Biperiden Lactate Injection.

Proprietary Preparations (details are given in Part 3)
Arg.: Akineton; Berofin; Darcipireno; Sinekin; ***Austral.:*** Akineton; ***Austria:*** Akineton; ***Belg.:*** Akineton; ***Braz.:*** Akineton; Cinetol; Parkinsol; ***Canad.:*** Akineton; ***Chile:*** Akineton; ***Cz.:*** Akineton; ***Denm.:*** Akineton; ***Fin.:*** Akineton; Ipsatol; ***Fr.:*** Akineton; ***Ger.:*** Akineton; Norakin N†; ***Gr.:*** Akineton; ***Hung.:*** Akineton; ***India:*** Dyskinon†; ***Irl.:*** Akineton; ***Israel:*** Dekinet; ***Ital.:*** Akineton; ***Mex.:*** Akineton; Bikipen; Kinex; ***Neth.:*** Akineton; ***Norw.:*** Akineton†; ***Philipp.:*** Akineton; ***Pol.:*** Akineton; ***Port.:*** Akineton; ***Rus.:*** Akineton (Акинетон)†; ***S.Afr.:*** Akineton; ***Spain:*** Akineton; ***Swed.:*** Akineton†; ***Switz.:*** Akineton; ***Turk.:*** Akineton; ***USA:*** Akineton; ***Venez.:*** Akineton.

Bornaprine Hydrochloride *(BANM, rINNM)*

Bornaprin Hidroklorür; Bornaprine, Chlorhydrate de; Bornaprini Hydrochloridum; Hidrocloruro de bornaprina. 3-Diethylaminopropyl 2-phenylbicyclo[2.2.1]heptane-2-carboxylate hydrochloride.

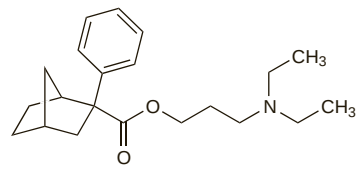
Борнаприна Гидрохлорид

$C_{21}H_{31}NO_2,HCl$ = 365.9.

CAS — 20448-86-6 (bornaprine); 26908-91-8 (bornaprine hydrochloride).

ATC — N04AA11.

ATC Vet — QN04AA11.



(bornaprine)

Profile

Bornaprine hydrochloride is a quaternary ammonium antimuscarinic with actions and uses similar to those of trihexyphenidyl (p.820). It is used in the symptomatic treatment of **parkinsonism** (p.791), including the alleviation of the extrapyramidal syndrome induced by drugs such as phenothiazines, but, like other antimuscarinics, is of no value against tardive dyskinesias; it is