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.

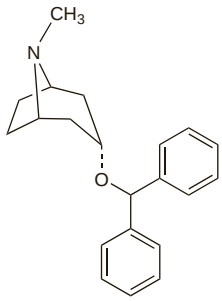
Бензатропина Мезилат

$C_{21}H_{25}NO,CH_4O_3S$ = 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to benzatropine since it persisted despite modification to other treatment and resolved only when benzatropine was withdrawn.[1]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.

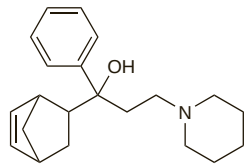
Бипериден

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

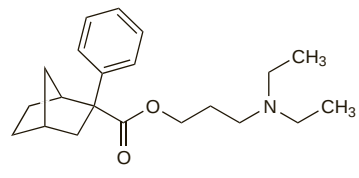
Борнаприна Гидрохлорид

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

claimed to be mainly effective against tremor. Bornaprine hydrochloride is given orally in initial doses of 2 mg daily gradually increased to 6 to 12 mg daily according to response. It is also used in the treatment of **hyperhidrosis** (p.1580) in a dose of 4 to 8 mg daily.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Sormodren; ***Ger.:*** Sormodren; ***Ital.:*** Sormodren; ***Turk.:*** Sormodren.

Bromocriptine Mesilate *(BANM, rINNM)*

Bromocriptine, mésilate de; Bromocriptine Mesylate *(USAN)*; Bromocriptine Methanesulphonate; Bromocriptini mesilas; Bromocryptine Mesylate; 2-Bromo-α-ergocryptine Mesylate; 2-Bromoergocryptine Monomethanesulfonate; Bromokriptiinimesilaatti; Bromokriptin Mesilat; Bromokriptinmesilat; Bromokriptin-mesylát; Brómokriptin-mezilát; Bromokriptino mesilatas; CB-154 (bromocriptine); Mesilato de bromocriptina. (5′*S*)-2-Bromo-12′-hydroxy-2′-(1-methylethyl)-5′-(2-methylpropyl)-ergotaman-3′,6′,18-trione methanesulphonate.

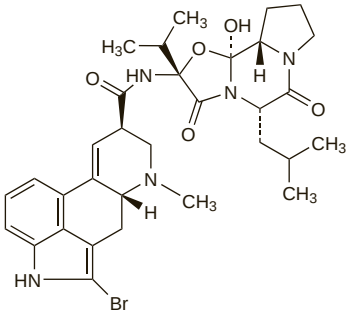
Бромокриптина Мезилат

$C_{32}H_{40}BrN_5O_5,CH_4O_3S$ = 750.7.

CAS — 25614-03-3 (bromocriptine); 22260-51-1 (bromocriptine mesilate).

ATC — G02CB01; N04BC01.

ATC Vet — QG02CB01; QN04BC01.



(bromocriptine)

Pharmacopoeias. In *Eur.* (see p.vii), *Jpn*, and *US*.
Ph. Eur. 6.2 (Bromocriptine Mesilate). A white or slightly coloured fine crystalline powder. Practically insoluble in water; soluble in alcohol; sparingly soluble in dichloromethane; freely soluble in methyl alcohol. A 1% solution in a mixture of 2 parts methyl alcohol to 8 of water has a pH of 3.1 to 3.8. Store in airtight containers at a temperature not exceeding −15°. Protect from light.
USP 31 (Bromocriptine Mesylate). A white or slightly coloured fine crystalline powder; odourless or having a weak characteristic odour. Store in airtight containers at a temperature not exceeding 8°. Protect from light.

Adverse Effects

Nausea is the most common adverse effect at the beginning of treatment with bromocriptine, but vomiting, dizziness, and orthostatic hypotension may also occur. Syncope has followed initial doses.

Adverse effects are generally dose-related and may therefore be more frequent with the higher doses that have been used in the treatment of parkinsonism and acromegaly. Reduction of the dosage, followed in a few days by a more gradual increase, may alleviate many adverse effects. Nausea may be reduced by taking bromocriptine with food; domperidone may also be given at least 1 hour before bromocriptine, for the first few days of therapy.

Bromocriptine and similar drugs are vasoconstrictors; Raynaud's syndrome or digital vasospasm, induced by cold, and leg cramps have been reported. Other cardiovascular effects have included erythromelalgia, prolonged severe hypotension, arrhythmias, and exacerbation of angina. Very rarely hypertension, myocardial infarction, seizures or stroke (both sometimes preceded by severe headache or visual disturbances), and psychiatric disorders have been reported in postpartum women given bromocriptine.

The use of ergot derivatives such as bromocriptine has been associated with retroperitoneal fibrosis, pleural thickening and effusions, and pericarditis and pericardial effusions.

Other adverse effects reported include headache, nasal congestion, drowsiness, dry mouth, constipation, diarrhoea, and altered liver-function tests. Dyskinesias and psychomotor excitation have occurred in patients suffering from parkinsonism. Gastrointestinal bleeding has been reported in acromegalic patients. Psychosis, with hallucinations, delusions, and confusion, occurs particularly when high doses are used to treat parkinsonism, but has also been reported with low doses. A neuroleptic malignant-like syndrome associated with abrupt withdrawal of bromocriptine has been reported very rarely.

Incidence of adverse effects. In 27 published studies of the treatment of Parkinson's disease, 217 of the 790 patients given bromocriptine had adverse effects.[1] Mental changes were noted in 90 patients, dyskinesia in 20, orthostatic hypotension in 40, and gastrointestinal effects in 40. The fewest adverse effects (9%) occurred with low-dose bromocriptine, more occurred with high-dose bromocriptine (27%) or with low-dose bromocriptine with levodopa (26%), and the most occurred with high-dose bromocriptine and levodopa (32%). However, those on high doses had more advanced disease and might have been more susceptible to mental changes and dyskinesias.

An analysis by the manufacturer of published reports on patients treated with bromocriptine for 1 to 10 years concluded that in general, adverse effects noted were no different from those associated with short-term treatment.[2]

1. Lieberman AN, Goldstein M. Bromocriptine in Parkinson disease. *Pharmacol Rev* 1985; **37:** 217–27.
2. Weil C. The safety of bromocriptine in long-term use: a review of the literature. *Curr Med Res Opin* 1986; **10:** 25–51.

Effects on the blood. Severe leucopenia and mild thrombocytopenia developed in a 23-year-old woman after treatment with bromocriptine 7.5 to 10 mg daily for about 3 months.[1]

1. Giampietro O, *et al*. Severe leukopenia and mild thrombocytopenia after chronic bromocriptine (CB-154) administration. *Am J Med Sci* 1981; **281:** 169–72.

Effects on the cardiovascular system. An early review noted that asymptomatic **hypotension** occurred in many subjects given bromocriptine.[1] However, faintness and dizziness, sometimes accompanied by *nausea* and *vomiting*, were common at the start of treatment with bromocriptine and these symptoms rather than an anaphylactic type of reaction were likely to account for the collapse that occurred in a few sensitive patients. Two of 53 patients with Parkinson's disease fainted after an initial dose of 1.25 or 2.5 mg, but the exact incidence of shock-like syndromes was difficult to assess; the manufacturers had stated that 22 of over 10 000 subjects given bromocriptine had had hypotension and collapse, mainly at the start of treatment.

- All patients starting treatment should be warned of the possibility of fainting. The initial dose should not exceed 1.25 to 2.5 mg and should be taken with food and in bed.

If fainting does occur recovery is usually rapid and spontaneous. Tolerance to adverse effects such as hypotension and nausea may develop rapidly.

Hypertension, *seizures*, *stroke*, and *myocardial infarction* have been associated with bromocriptine therapy, notably in postpartum women.[2-4] A study involving 1813 women suggested that the risk of **postpartum hypertension** was increased in women who had pregnancy-induced hypertension and that this risk was further increased in those who took bromocriptine for suppression of lactation.[5] A case-controlled study[6] involving 43 of the women who had had postpartum seizures while taking bromocriptine found that while the initial risk of seizures appeared to be lower in patients taking bromocriptine there was a small positive association with seizures occurring more than 72 hours after delivery.

- Although a causal relationship between the use of bromocriptine and these adverse effects in postpartum women has not been established, licensed product information recommends that bromocriptine should not be used post partum or in the puerperium in women with high blood pressure, coronary artery disease or other severe cardiovascular disorders, or symptoms or history of serious psychiatric disorders.
- It is also recommended that when bromocriptine is used in postpartum women blood pressure should be carefully monitored, especially during the first few days and if hypertension, unremitting headache, or signs of CNS toxicity develop, treatment should be discontinued immediately.

Severe dilated **cardiomyopathy** has been reported in a patient being treated with bromocriptine for microprolactinoma.[7]

For details of **fibrotic reactions** resulting in cardiovascular adverse effects, see Fibrosis, below.

1. Parkes D. Side effects of bromocriptine. *N Engl J Med* 1980; **302:** 749–50.
2. Anonymous. Postpartum hypertension, seizures, strokes reported with bromocriptine. *FDA Drug Bull* 1984; **14:** 3.
3. Ruch A, Duhring JL. Postpartum myocardial infarction in a patient receiving bromocriptine. *Obstet Gynecol* 1989; **74:** 448–51.
4. Larrazet F, *et al*. Possible bromocriptine-induced myocardial infarction. *Ann Intern Med* 1993; **118:** 199–200.
5. Watson DL, *et al*. Bromocriptine mesylate for lactation suppression: a risk for postpartum hypertension? *Obstet Gynecol* 1989; **74:** 573–6.
6. Rothman KJ, *et al*. Bromocriptine and puerperal seizures. *Epidemiology* 1990; **1:** 232–8.
7. Kaushik P, *et al*. Acute onset of severe dilated cardiomyopathy during bromocriptine therapy. *Ann Pharmacother* 2004; **38:** 1219–21.

Effects on the ears. Audiometric evidence of bilateral sensorineural hearing loss was reported in 3 patients receiving bromocriptine 15 or 20 mg daily for chronic hepatic encephalopathy.[1] Hearing improved when the dose was reduced to 10 mg daily.

1. Lanthier PL, *et al*. Bromocriptine-associated ototoxicity. *J Laryngol Otol* 1984; **98:** 399–404.

Effects on electrolytes. There have been isolated reports of severe hyponatraemia associated with the use of bromocriptine.[1,2]

1. Marshall AW, *et al*. Bromocriptine-associated hyponatraemia in cirrhosis. *BMJ* 1982; **285:** 1534–5.
2. Damase-Michel C, *et al*. Hyponatraemia in a patient treated with bromocriptine. *Drug Invest* 1993; **5:** 285–7.

Effects on the eyes. Blurred vision and diplopia has been reported in several patients receiving bromocriptine.[1] Reversible myopia also developed in a patient with hyperprolactinaemia given bromocriptine.[2]

Licensed product information states that visual field impairment associated with macroprolactinoma usually resolves with bromocriptine treatment. However, in a patient with progressive visual loss due to compression of the optic chiasm by a large pituitary tumour, bromocriptine caused total visual loss within hours.[3] Vision slowly returned to normal when the patient was placed in the supine position; the most likely cause of the visual loss was thought to be orthostatic hypotension with resultant decrease in perfusion pressure to the visual system. Monitoring of visual fields is recommended in patients with macroprolactinoma.

Bromocriptine has been reported to cause visual cortical disturbances.[4] In some cases blurred vision and transient cortical blindness have preceded seizures and strokes.

1. Calne DB, *et al*. Long-term treatment of parkinsonism with bromocriptine. *Lancet* 1978; **i:** 735–7.
2. Manor RS, *et al*. Myopia during bromocriptine treatment. *Lancet* 1981; **i:** 102.
3. Couldwell WT, Weiss MH. Visual loss associated with bromocriptine. *Lancet* 1992; **340:** 1410–11.
4. Lane RJM, Routledge PA. Drug-induced neurological disorders. *Drugs* 1983; **26:** 124–47.

Effects on mental function. High doses of bromocriptine are well known to cause **psychotic reactions** in patients with parkinsonism.[1] However, mania has also been associated with the use of bromocriptine post partum[2,3] and it has been stated that psychological symptoms can occur with doses of only 2.5 to 5 mg daily.[4] It was also noted that, unlike the relatively mild and transient symptoms associated with levodopa, bromocriptine produces a severe psychosis in which the patient is violent and aggressive, suffering from intense delusions which are often hostile and violent; complete withdrawal of bromocriptine may still leave a residue of severe psychotic illness persisting for 1 to 3 weeks. Psychosis associated with low doses of bromocriptine has often occurred in patients with a history of psychotic illness or disturbances in behaviour and mood prior to treatment.[5-7] Drug-related psychotic reactions have also been reported in patients with no psychiatric history;[8,9] of 600 patients given bromocriptine or lisuride for the treatment of acromegaly or prolactinoma, 8 developed symptoms including anxiety, depression, auditory hallucinations, delusions, hyperactivity, disinhibition, euphoria, and insomnia and 4 had received doses only previously associated with psychosis in susceptible patients.[9]

For reference to **disturbed behaviour** including **excessive gambling** reported in patients with Parkinson's disease receiving dopamine agonists, see under Levodopa, p.805.

For reports of **daytime somnolence** occurring in patients receiving dopamine agonists including bromocriptine, see under Levodopa, p.805.

1. Calne DB, *et al*. Long-term treatment of parkinsonism with bromocriptine. *Lancet* 1978; **i:** 735–7.
2. Vlissides DN, *et al*. Bromocriptine-induced mania? *BMJ* 1978; **1:** 510.
3. Brook NM, Cookson IB. Bromocriptine-induced mania? *BMJ* 1978; **1:** 790.
4. Pearce I, Pearce JMS. Bromocriptine in parkinsonism. *BMJ* 1978; **1:** 1402–4.
5. Pearson KC. Mental disorders from low-dose bromocriptine. *N Engl J Med* 1981; **305:** 173.
6. Le Feuvre CM, *et al*. Bromocriptine-induced psychosis in acromegaly. *BMJ* 1982; **285:** 1315.
7. Procter AW, *et al*. Bromocriptine induced psychosis in acromegaly. *BMJ* 1983; **286:** 50. Correction. *ibid.*; 311.
8. Einarson TR, Turchet EN. Psychotic reaction to low-dose bromocriptine. *Clin Pharm* 1983; **2:** 273–4.
9. Turner TH, *et al*. Psychotic reactions during treatment of pituitary tumours with dopamine agonists. *BMJ* 1984; **289:** 1101–3.

Effects on the nervous system. CSF rhinorrhoea has been associated with bromocriptine therapy in patients with invasive prolactinomas. A report of 3 cases found 13 further cases on re-