dose is the equivalent of 1 to 1.25 mg of bromocriptine at night during week 1, increased to 2 to 2.5 mg at night for week 2, 2.5 mg twice daily for week 3, and for week 4, 2.5 mg three times daily; the dose may be increased thereafter by 2.5 mg every 3 to 14 days according to response. The EMEA has recommended a maximum dose of 30 mg daily. In the USA, a usual starting dose is 1.25 to 2.5 mg twice daily increased by 2.5 mg every 14 to 28 days to a maximum dose of 100 mg daily if necessary.

Acromegaly. Dopaminergics can produce a paradoxical reduction in growth hormone secretion and bromocriptine has been used in acromegaly (p.1798) as adjunctive therapy to surgery, radiotherapy, or somatostatin analogues to reduce circulating growth hormone levels. While it is less effective than somatostatin analogues, it can be given orally and is therefore more convenient to administer.

Cushing's syndrome. There have been occasional reports of benefit with the use of bromocriptine in the treatment of Cushing's syndrome (p.2344). Remission of ACTH-dependent Cushing's syndrome was maintained for 6 years by bromocriptine 2.5 mg twice daily in a patient who had initially received pituitary irradiation.[1] However, the same group subsequently reported that they had found that bromocriptine did not effectively reduce ACTH secretion following bilateral adrenalectomy.[2]

1. Atkinson AB, *et al.* Six year remission of ACTH-dependent Cushing's syndrome using bromocriptine. *Postgrad Med J* 1985; **61:** 239–42.
2. Atkinson AB. The treatment of Cushing's syndrome. *Clin Endocrinol (Oxf)* 1991; **34:** 507–13.

Hepatic encephalopathy. For the view that the evidence does not support the use of dopaminergics such as bromocriptine in the management of hepatic encephalopathy see p.1697.

Hyperprolactinaemia and prolactinomas. Prolactinomas (prolactin-secreting pituitary adenomas) are among the commonest causes of hyperprolactinaemia. Raised serum-prolactin concentrations can result in reduced gonadotrophin production, which in turn may suppress gonadal function. Consequences may include oligomenorrhoea or amenorrhoea, and infertility in either sex. Galactorrhoea may also result from high prolactin levels and can occur in men as well as women.

Dopamine is the major inhibitory factor in the hypothalamus and directly inhibits the secretion of prolactin. Bromocriptine, a dopamine agonist, has been the first choice of treatment in many centres for the treatment of hyperprolactinaemia secondary to a prolactinoma although cabergoline is now preferred by some. Bromocriptine is extremely effective in controlling elevated circulating prolactin concentrations and restoring gonadal function; although it is rarely curative, it may produce considerable shrinkage of the adenoma.[1]

The sensitivity of hyperprolactinaemia to bromocriptine therapy can vary considerably between patients and this is reflected in the wide range of oral doses required to reduce prolactin concentrations to normal levels. Although beginning therapy with gradually increasing doses can minimise adverse effects it has been reported that about 5 to 10% of patients are unable to tolerate oral bromocriptine;[2] other dosage routes have therefore been investigated. Bromocriptine is well absorbed from standard oral tablets placed in the vagina and appears to be both effective in lowering prolactin concentrations and well tolerated when given by this route.[3] However, limitations are considered to be the relatively short duration of action and the relatively low dose that can be given.[2] A depot preparation given intramuscularly in a dose of 50 to 250 mg monthly has been found to be effective and well tolerated in long-term studies;[4,5] it is reported to be used in some centres to begin treatment for macroprolactinomas.[2]

For discussions of the management of hyperprolactinaemia and associated disorders see p.2079 (hyperprolactinaemia), p.2078 (amenorrhoea), p.2079 (hypogonadism), p.2179 (erectile dysfunction), and p.2080 (infertility).

1. Molitch ME. Medical management of prolactin-secreting pituitary adenomas. *Pituitary* 2002; **5:** 55–65.
2. Ciccarelli E, Camanni F. Diagnosis and drug therapy of prolactinoma. *Drugs* 1996; **51:** 954–65.
3. Ginsburg J, *et al.* Vaginal bromocriptine. *Lancet* 1991; **338:** 1205–6.
4. Ciccarelli E, *et al.* Long term therapy of patients with macroprolactinoma using repeatable injectable bromocriptine. *J Clin Endocrinol Metab* 1993; **76:** 484–8.
5. Ciccarelli E, *et al.* Double blind randomized study using oral or injectable bromocriptine in patients with hyperprolactinaemia. *Clin Endocrinol (Oxf)* 1994; **40:** 193–8.

PREGNANCY. References to the management of prolactinoma during pregnancy.[1-3] Bromocriptine has been successfully used for management in pregnant women, particularly if there is symptomatic enlargement of the tumour, although there continues to be debate on the appropriateness of continuous therapy in less high-risk individuals.

1. Randeva HS, *et al.* Prolactinoma and pregnancy *Br J Obstet Gynaecol* 2000; **107:** 1064–8.
2. Bronstein MD, *et al.* Medical management of pituitary adenomas: the special case of management of the pregnant woman. *Pituitary* 2002; **5:** 99–107.
3. Chiodini I, Liuzzi A. PRL-secreting pituitary adenomas in pregnancy. *J Endocrinol Invest* 2003; **26:** 96–9.

Lactation inhibition. Because of its effects on prolactin, bromocriptine is a potent suppressor of lactation and has been widely used for the prevention of lactation in women who choose not to breast feed post partum. However, bromocriptine has been associated with severe adverse effects in some women, and its use to suppress a physiological state has been criticised (see p.2003). Consequently, licensed product information from a number of countries recommends that bromocriptine should only be used to suppress puerperal lactation for medical reasons; it is also not recommended for the treatment of postpartum breast pain and engorgement that may be adequately relieved with simple analgesics and breast support.

Mastalgia. Since mastalgia (p.2092) can improve spontaneously, treatment should rarely be considered unless pain has been present for about 6 months. Bromocriptine is one of the drugs that may be used to treat mastalgia.[1,2] It may improve symptoms in up to about 50% of patients with cyclical mastalgia, but is less effective in the non-cyclical form.[3,4] Adverse effects can be severe in some patients.

1. Gateley CA, Mansel RE. Management of the painful and nodular breast. *Br Med Bull* 1991; **47:** 284–94.
2. Anonymous. Cyclical breast pain—what works and what doesn't. *Drug Ther Bull* 1992; **30:** 1–3.
3. Pye JK, *et al.* Clinical experience of drug treatments for mastalgia. *Lancet* 1985; **ii:** 373–7.
4. Mansel RE, Dogliotti L. European multicentre trial of bromocriptine in cyclical mastalgia. *Lancet* 1990; **335:** 190–3.

Neuroleptic malignant syndrome. Bromocriptine has been used in doses of up to 30 mg daily,[1-6] usually alone or with dantrolene, in the treatment of neuroleptic malignant syndrome (p.972) although some workers have not found it to be of use.[7]

1. Mueller PS, *et al.* Neuroleptic malignant syndrome: successful treatment with bromocriptine. *JAMA* 1983; **249:** 386–8.
2. Dhib-Jalbut S, *et al.* Treatment of the neuroleptic malignant syndrome with bromocriptine. *JAMA* 1983; **250:** 484–5.
3. Clarke CE, *et al.* Clinical spectrum of neuroleptic malignant syndrome. *Lancet* 1988; **ii:** 969–70.
4. Guerrero RM, Shifrar KA. Diagnosis and treatment of neuroleptic malignant syndrome. *Clin Pharm* 1988; **7:** 697–701.
5. Lo TCM, *et al.* Neuroleptic malignant syndrome: another medical cause of acute abdomen. *Postgrad Med J* 1989; **65:** 653–5.
6. Chandran GJ, *et al.* Neuroleptic malignant syndrome: case report and discussion. *Can Med Assoc J* 2003; **169:** 439–42.
7. Rosebush PI, *et al.* The treatment of neuroleptic malignant syndrome: are dantrolene and bromocriptine useful adjuncts to supportive care? *Br J Psychiatry* 1991; **159:** 709–12.

Parkinsonism. Dopamine agonists such as bromocriptine are often used to begin treatment of parkinsonism (p.791), particularly in younger patients, in an attempt to delay therapy with levodopa. They also have an adjunctive use when levodopa is no longer effective alone or cannot be tolerated and may sometimes be useful in reducing 'off' periods with levodopa and in ameliorating other fluctuations of mobility in the later stage of the disease. However, in early disease, there is no evidence that adjunctive bromocriptine prevents or delays the onset of motor complications associated with levodopa monotherapy.

References.

1. Temlett JA, *et al.* Adjunctive therapy with bromocriptine in Parkinson's disease. *S Afr Med J* 1990; **78:** 680–5.
2. Hely MA, *et al.* The Sydney Multicentre Study of Parkinson's disease: a randomised, prospective five year study comparing low dose bromocriptine with low dose levodopa-carbidopa. *J Neurol Neurosurg Psychiatry* 1994; **57:** 903–10.
3. Montastruc JL, *et al.* A randomised controlled study comparing bromocriptine to which levodopa was later added, with levodopa alone in previously untreated patients with Parkinson's disease: a five year follow up. *J Neurol Neurosurg Psychiatry* 1994; **57:** 1034–8.
4. Giménez-Roldán S, *et al.* Early combination of bromocriptine and levodopa in Parkinson's disease: a prospective randomized study of two parallel groups over a total follow-up period of 44 months including an initial 8-month double-blind stage. *Clin Neuropharmacol* 1997; **20:** 67–76.
5. Ogawa N, *et al.* Nationwide multicenter prospective study on the long-term effects of bromocriptine for Parkinson's disease: final report of a ten-year follow-up. *Eur Neurol* 1997; **38** (suppl 2): 37–49.
6. Lees AJ, *et al.* Ten-year follow-up of three different initial treatments in de-novo PD: a randomized trial. *Neurology* 2001; **57:** 1687–94.
7. van Hilten JJ, *et al.*. Bromocriptine versus levodopa in early Parkinson's disease. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2007 (accessed 30/05/08).
8. van Hilten JJ, *et al.* Bromocriptine/levodopa combined versus levodopa alone for early Parkinson's disease. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2007 (accessed 30/05/08).

Polycystic ovary syndrome. Bromocriptine has been tried in women with the polycystic ovary syndrome (p.2080) who have mild basal hyperprolactinaemia without evidence of a pituitary tumour.

Restless legs syndrome. The aetiology of restless legs syndrome (see Sleep-associated Movement Disorders, p.958) is obscure and treatment has largely been empirical but dopaminergic therapy has emerged as a common first-line choice. Bromocriptine showed some benefit in a small study.[1]

1. Walters AS, *et al.* A double-blind randomized crossover trial of bromocriptine and placebo in restless legs syndrome. *Ann Neurol* 1988: **24:** 455–8.

Withdrawal syndromes. ***ALCOHOL.*** Studies of the efficacy of bromocriptine as an aid in the maintenance of abstinence from alcohol (p.1626) have yielded conflicting results.[1-4] However, it has been suggested[3] that response to bromocriptine might be linked to a specific genotype of the D_2 dopamine receptor.

1. Dongier M, *et al.* Bromocriptine in the treatment of alcohol dependence. *Alcohol Clin Exp Res* 1991; **15:** 970–7.
2. Naranjo CA, *et al.* Long-acting bromocriptine (B) does not reduce relapse in alcoholics. *Clin Pharmacol Ther* 1995; **57:** 161.
3. Lawford BR, *et al.* Bromocriptine in the treatment of alcoholics with the D dopamine receptor A1 allele. *Nat Med* 1995; **1:** 337–41.
4. Powell BJ, *et al.* A double-blind, placebo-controlled study of nortriptyline and bromocriptine in male alcoholics subtyped by comorbid psychiatric disorders. *Alcohol Clin Exp Res* 1995; **19:** 462–8.

Preparations

BP 2008: Bromocriptine Capsules; Bromocriptine Tablets;
USP 31: Bromocriptine Mesylate Capsules; Bromocriptine Mesylate Tablets.

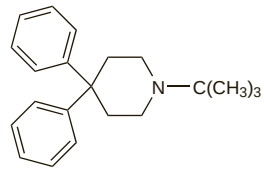
Proprietary Preparations (details are given in Part 3)
Arg.: Parlodel; Serocryptin†; ***Austral.:*** Bromohexal; Bromolactin†; Kripton; Parlodel; ***Austria:*** Bromed; Cehapark; Parlodel; Umprel; ***Belg.:*** Parlodel; ***Braz.:*** Bagren; Parlodel; ***Canad.:*** Parlodel; ***Chile:*** Criten; Grifocriptina; Kriptonal; Parlodel; Prigost; ***Cz.:*** Medocriptine; Parlodel; Serocryptin†; ***Denm.:*** Bromergon†; Parlodel; ***Fin.:*** Parlodel; ***Fr.:*** Bromo-Kin; Parlodel; ***Ger.:*** Bromocrel†; kirim; kirim gyn; Pravidel; ***Gr.:*** Parlodel; ***Hong Kong:*** Bromtine; Medocriptine; Parlodel; Serocryptin†; ***Hung.:*** Serocryptin†; ***India:*** Sicriptin; ***Indon.:*** Cripsa; Parlodel; ***Irl.:*** Parlodel; ***Israel:*** Parilac; Parlodel; ***Ital.:*** Parlodel; ***Malaysia:*** Butin†; Criptamine†; Medocriptine; Parlodel; Zolac†; ***Mex.:*** Broptin; Crilem; Cryocriptina; Kriptiser; Mesiken; Parlodel; Serocryptin†; ***Neth.:*** Parlodel; ***Norw.:*** Parlodel; ***Philipp.:*** Parlodel; Provasyn; ***Pol.:*** Bromergon; Bromocorn; Ergolaktyna; Parlodel; ***Port.:*** Parlodel; ***Rus.:*** Bromergon (Бромэргон); Parlodel (Парлодел); ***S.Afr.:*** Parlodel; ***Singapore:*** Butin†; Parlodel; Suplac†; ***Spain:*** Parlodel; ***Swed.:*** Pravidel; ***Switz.:*** Parlodel; ***Thai.:*** Brocaden; Bromergon; Parlodel; Suplac; ***Turk.:*** Gynodel; Parlodel; ***UAE:*** Antiprotin; ***UK:*** Parlodel; ***USA:*** Parlodel; ***Venez.:*** Parlodel; Serocryptin†.

Budipine *(rINN)*

Budipino; Budipinum. 1-*tert*-Butyl-4,4-diphenylpiperidine.

Будипин

$C_{21}H_{27}N$ = 293.4.
CAS — 57982-78-2.
ATC — N04BX03.
ATC Vet — QN04BX03.



Profile

Budipine is a phenylpiperidine derivative used as an adjunct in the treatment of parkinsonism (p.791). It is given orally as the hydrochloride in daily doses of up to 60 mg.

◊ References.

1. Spieker S, *et al.* Tremorlytic activity of budipine: a quantitative study with long-term tremor recordings. *Clin Neuropharmacol* 1995; **18:** 266–72.
2. Groen H, *et al.* A study to investigate the pharmacokinetics and metabolism of budipine after administration of a single oral dose of [C]-B757-01 to six healthy volunteers. *Br J Clin Pharmacol* 1999; **48:** 771P–772P.
3. Malsch U, *et al.* Monotherapie der Parkinsonschen Erkrankung mit Budipin: ein randomisierter Doppelblindvergleich mit Amantadin. *Fortschr Neurol Psychiatr* 2001; **69:** 86–9.
4. Przuntek H, *et al.* Budipine provides additional benefit in patients with Parkinson disease receiving a stable optimum dopaminergic drug regimen. *Arch Neurol* 2002; **59:** 803–6.

Preparations

Proprietary Preparations (details are given in Part 3)
Ger.: Parkinsan.

Cabergoline *(BAN, USAN, rINN)*

Cabergolina; Cabergolinum; FCE-21336; Kabergoliini; Kabergolin; Kabergolina. 1-[(6-Allylergolin-8β-yl)carbonyl]-1-[3-(dimethylamino)propyl]-3-ethylurea; (8*R*)-6-Allyl-*N*-[3-(dimethylamino)propyl]-*N*-(ethylcarbamoyl)ergoline-8-carboxamide.

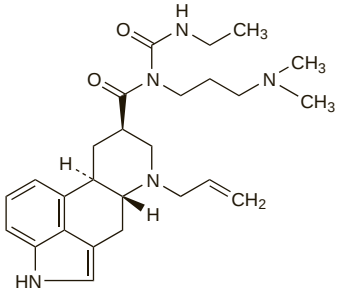
Каберголин

$C_{26}H_{37}N_5O_2$ = 451.6.

CAS — 81409-90-7.

ATC — G02CB03; N04BC06.

ATC Vet — QG02CB03; QN04BC06.



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

Ph. Eur. 6.2 (Cabergoline). A white or almost white, crystalline powder. It exhibits polymorphism. Practically insoluble in water; freely soluble in alcohol; very slightly soluble in *n*-hexane. It is slightly soluble in 0.1M hydrochloric acid. Protect from light.

Adverse Effects and Precautions

As for Bromocriptine, p.798, although patients unable to tolerate bromocriptine may tolerate cabergoline (and *vice versa*).

Licensed product information states that conception should be avoided for at least one month after treatment.

Effects on mental function. For reports of **daytime somnolence** occurring in patients receiving dopamine agonists including cabergoline, see under Levodopa, p.805.

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

Fibrosis. For reports of fibrotic reactions occurring in patients with Parkinson's disease receiving ergot derivative dopamine agonists including cabergoline, see under Bromocriptine, p.799.

In 2007, based on further evidence from 3 studies,[1-3] the UK MHRA[4] considered the risk of cardiac valvulopathy to be high and clinically significant with cabergoline and pergolide, and the risks of treatment with these 2 drugs to be similar. This resulted in the following changes to UK labelling for cabergoline products in Parkinson's disease:

- restricted to second-line treatment in patients intolerant of, or who do not respond to, non-ergot drug treatment
- contra-indicated in patients with a history of pulmonary, pericardial, and retroperitoneal fibrotic disorders, or in those with anatomical evidence of cardiac valvulopathy
- monitoring for development of valvular disease or fibrosis recommended: echocardiography should be performed within 3 to 6 months of starting treatment and every 6 to 12 months thereafter

In June 2008 the EMEA further recommended that the maximum dose should be 3 mg daily.[5]

1. Yamamoto M, *et al.* Dopamine agonists and cardiac valvulopathy in Parkinson disease: a case-control study. *Neurology* 2006; **67:** 1225–9.
2. Schade R, *et al.* Dopamine agonists and the risk of cardiac-valve regurgitation. *N Engl J Med* 2007; **356:** 29–38.
3. Zanettini R, *et al.* Valvular heart disease and the use of dopamine agonists for Parkinson's disease. *N Engl J Med* 2007; **356:** 39–46.
4. MHRA/CHM. Cabergoline: cardiovalvulopathy. *Drug Safety Update* 2007: **1** (1): 5. Available at: http://www.mhra.gov.uk/Publications/Safetyguidance/DrugSafetyUpdate/CON2031802 (accessed 30/05/08)
5. EMEA. EMEA recommends new warnings and contraindications for ergot-derived dopamine agonists (issued 26th June, 2008). Available at: http://www.emea.europa.eu/pdfs/human/press/pr/32239508en.pdf (accessed 08/08/08)

Oedema. Three cases of lower limb oedema after chronic treatment with cabergoline have been reported.[1] In one case the oedema was severe enough to necessitate withdrawal of therapy.

1. Geminiani G, *et al.* Cabergoline in Parkinson's disease complicated by motor fluctuations. *Mov Disord* 1996; **11:** 495–500.

Interactions

As for Bromocriptine, p.800.

Pharmacokinetics

Cabergoline is absorbed from the gastrointestinal tract and mean peak plasma concentrations are achieved within 2 to 3 hours. It is subject to first-pass metabolism and is extensively metabolised to several metabolites that do not appear to contribute to its pharmacological activity. Plasma protein binding has been estimated to be about 40%. Cabergoline is mainly eliminated via the faeces; a small proportion is excreted in the urine. In *rats*, cabergoline has been reported to cross the placenta and to be distributed into breast milk.

◊ General references.

1. Del Dotto P, Bonuccelli U. Clinical pharmacokinetics of cabergoline. *Clin Pharmacokinet* 2003; **42:** 633–45.

Half-life. Pharmacokinetic studies of cabergoline have been hampered by lack of an assay method sensitive enough to detect plasma concentrations of cabergoline after therapeutic doses. However, the plasma elimination half-life of cabergoline has been estimated indirectly to be 63 to 68 hours in healthy subjects and 79 to 115 hours in patients with hyperprolactinaemia.[1]

1. Rains CP, *et al.* Cabergoline: a review of its pharmacological properties and therapeutic potential in the treatment of hyperprolactinaemia and inhibition of lactation. *Drugs* 1995; **49:** 255–79.

Uses and Administration

Cabergoline, an ergot derivative, is a dopamine D_2-agonist with actions and uses similar to those of bromocriptine (p.800). It is a potent and long-lasting inhibitor of prolactin secretion used in the management of disorders associated with hyperprolactinaemia. It is also used to suppress puerperal lactation for medical reasons; it is not recommended for the routine suppression of physiological lactation or for the treatment of postpartum breast pain and engorgement that may be adequately relieved with simple analgesics and breast support. Cabergoline is also used in the management of Parkinson's disease as monotherapy, or as an adjunct to levodopa therapy to reduce 'end-of-dose' or 'on-off' fluctuations in response; in the UK cabergoline is restricted to patients who are intolerant of, or who do not respond to, non-ergot drug treatment.

Cabergoline is given orally and should be taken with food.

To **inhibit physiological lactation**, cabergoline is given as a single 1-mg dose on the first day post partum. For **suppression of established lactation**, the dose is 250 micrograms every 12 hours for 2 days.

In the treatment of **disorders associated with hyperprolactinaemia**, the initial dose of cabergoline is 500 micrograms weekly. The dose is then increased at monthly intervals in increments of 500 micrograms weekly according to response. The weekly dose may be given on a single occasion or divided into 2 or more doses on separate days; doses over 1 mg should be given as divided doses. The usual dose is 1 mg weekly but up to 4.5 mg weekly has been used.

In **Parkinson's disease**, cabergoline should be introduced gradually and during this period the dose of levodopa may be reduced gradually until an optimal response is achieved. A suggested initial dose of cabergoline given as a single daily dose is 0.5 mg in monotherapy or 1 mg in adjunctive therapy. The dose may be increased in increments of 0.5 or 1 mg at intervals of 7 or 14 days. The EMEA has recommended a maximum dose of 3 mg daily.

Doses of cabergoline may need to be reduced in patients with severe hepatic impairment (see below).

Administration in hepatic impairment. Licensed drug information recommends caution in patients with severe hepatic impairment (Child-Pugh category C), and doses of cabergoline should be adjusted accordingly.

Acromegaly. Dopaminergics can produce a paradoxical reduction in growth hormone secretion and may be used in the treatment of acromegaly as adjunctive therapy to surgery, radiotherapy, or somatostatin analogues to reduce circulating growth hormone concentrations, although they are less effective than somatostatin analogues (p.1798). Although a small study comparing cabergoline with depot bromocriptine and quinagolide failed to find evidence of its effectiveness (see p.2377), in a later open study[1] there was a good response in about 40% of patients treated with cabergoline, which is better than the response usually reported for bromocriptine. The addition of cabergoline has also been beneficial in acromegaly that is resistant to somatostatin analogue therapy.[2]

1. Abs R, *et al.* Cabergoline in the treatment of acromegaly: a study in 64 patients. *J Clin Endocrinol Metab* 1998; **83:** 374–8.
2. Cozzi R, *et al.* Cabergoline addition to depot somatostatin analogues in resistant acromegalic patients: efficacy and lack of predictive value of prolactin status. *Clin Endocrinol (Oxf)* 2004; **61:** 209–15.

Hyperprolactinaemia and prolactinomas. Dopamine agonists are widely used for the treatment of hyperprolactinaemia secondary to a prolactinoma (see p.2079). Although bromocriptine has been the first choice for this indication, some now prefer cabergoline,[1] which appears to be more effective and better tolerated.[2,3]

Further references.[4-9]

1. Webster J. A comparative review of the tolerability profiles of dopamine agonists in the treatment of hyperprolactinaemia and inhibition of lactation. *Drug Safety* 1996; **14:** 228–38. Correction. *ibid*., 342.
2. Pascal-Vigneron V, *et al.* Amenorrhée hyperprolactinémique: traitement par cabergoline versus bromocriptine. *Presse Med* 1995; **24:** 753–7.
3. di Sarno A, *et al.* Resistance to cabergoline as compared with bromocriptine in hyperprolactinemia: prevalence, clinical definition, and therapeutic strategy. *J Clin Endocrinol Metab* 2001; **86:** 5256–61.
4. Webster J, *et al.* The efficacy and tolerability of long-term cabergoline therapy in hyperprolactinaemic disorders: an open, uncontrolled, multicentre study. *Clin Endocrinol (Oxf)* 1993; **39:** 323–9.
5. Webster J, *et al.* A comparison of cabergoline and bromocriptine in the treatment of hyperprolactinemic amenorrhea. *N Engl J Med* 1994; **331:** 904–9.
6. Verhelst J, *et al.* Cabergoline in the treatment of hyperprolactinaemia: a study in 455 patients. *J Clin Endocrinol Metab* 1999; **84:** 2518–22.
7. Colao A, *et al.* Macroprolactinoma shrinkage during cabergoline treatment is greater in naive patients than in patients pretreated with other dopamine agonists: a prospective study in 110 patients. *J Clin Endocrinol Metab* 2000; **85:** 2247–52.
8. Colao A, *et al.* Withdrawal of long-term cabergoline therapy for tumoral and nontumoral hyperprolactinemia. *N Engl J Med* 2003; **349:** 2023–33.
9. Colao A, *et al.* Outcome of cabergoline treatment in men with prolactinoma: effects of a 24-month treatment on prolactin levels, tumor mass, recovery of pituitary function, and semen analysis. *J Clin Endocrinol Metab* 2004; **89:** 1704–11.

Lactation inhibition. A single 1-mg dose of cabergoline was found to be as effective as bromocriptine 2.5 mg given twice daily for 14 days for preventing puerperal lactation in a double-blind multicentre study involving 272 women.[1] It has been suggested that cabergoline would be a better choice than bromocriptine for lactation inhibition.[2] However, as discussed on p.2003, the routine use of dopaminergics such as bromocriptine or cabergoline is not recommended for the suppression of physiological lactation.

1. European Multicentre Study Group for Cabergoline in Lactation Inhibition. Single dose cabergoline versus bromocriptine in inhibition of puerperal lactation: randomised, double blind, multicentre study. *BMJ* 1991; **302:** 1367–71.
2. Webster J. A comparative review of the tolerability profiles of dopamine agonists in the treatment of hyperprolactinaemia and inhibition of lactation. *Drug Safety* 1996; **14:** 228–38. Correction. *ibid*.; 342.

Parkinsonism. Cabergoline is used as a long-acting dopamine agonist in Parkinson's disease (p.791). Dopamine agonists are often used to begin treatment in an attempt to delay therapy with levodopa, particularly in younger patients. They also have an adjunctive use when levodopa is no longer effective alone or cannot be tolerated, and may sometimes be useful in reducing 'off' periods with levodopa and in ameliorating other fluctuations of mobility in the later stages of the disease.

References.

1. Inzelberg R, *et al.* Double-blind comparison of cabergoline and bromocriptine in Parkinson's disease patients with motor fluctuations. *Neurology* 1996; **47:** 785–8.
2. Geminiani G, *et al.* Cabergoline in Parkinson's disease complicated by motor fluctuations. *Mov Disord* 1996; **11:** 495–500.
3. Hutton JT, *et al.* Multicenter, placebo-controlled trial of cabergoline taken once daily in the treatment of Parkinson's disease. *Neurology* 1996; **46:** 1062–5.
4. Marsden CD. Clinical experience with cabergoline in patients with advanced Parkinson's disease treated with levodopa. *Drugs* 1998; **55** (suppl 1): 17–22.
5. Rinne UK, *et al.* Early treatment of Parkinson's disease with cabergoline delays the onset of motor complications: results of a double-blind levodopa controlled trial. *Drugs* 1998; **55** (suppl 1): 23–30.
6. Clarke CE, Deane KHO. Cabergoline for levodopa-induced complications in Parkinson's disease. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2001 (accessed 16/02/06).
7. Clarke CE, Deane KHO. Cabergoline versus bromocriptine for levodopa-induced complications in Parkinson's disease. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2001 (accessed 16/02/06).
8. Bracco F, *et al.* The long-acting dopamine receptor agonist cabergoline in early Parkinson's disease: final results of a 5-year, double-blind, levodopa-controlled study. *CNS Drugs* 2004; **18:** 733–46. Correction. *ibid.* 2005; **19:** 633.
9. Curran MP, Perry CM. Cabergoline: a review of its use in the treatment of Parkinson's disease. *Drugs* 2004; **64:** 2125–41.
10. Odin P, *et al.* Efficacy and safety of high-dose cabergoline in Parkinson's disease. *Acta Neurol Scand* 2006; **113:** 18–24.