# 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.

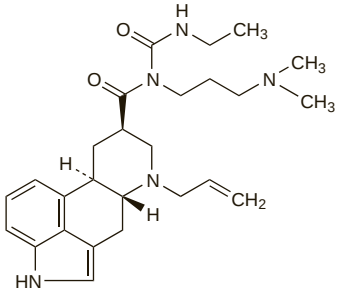
Каберголин

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

**Restless legs syndrome.** The aetiology of restless legs syndrome (RLS—see Sleep-associated Movement Disorders, p.958) is obscure and treatment has been largely empirical but dopaminergic therapy has emerged as a common first-line choice. Long-acting drugs such as cabergoline may be preferred in order to avoid the complications associated with levodopa therapy. Results from a 12-week open-label pilot study[1] in 9 patients with idiopathic RLS given cabergoline after insufficient response to levodopa therapy were promising; doses of cabergoline ranged from 1 to 4 mg. A later randomised multicentre study[2] in 85 patients concluded that a single evening dose of cabergoline for 5 weeks markedly reduced symptoms during the night and the next day compared with placebo. Results from the follow-up analysis of 66 patients after 1 year of treatment suggested that cabergoline at a median dose of 2 mg daily has a high rate of remission and is well tolerated. The authors recommended an initial dose of cabergoline 500 micrograms in the evening increased in increments of 500 micrograms weekly according to response.

1. Stiasny K, *et al*. Treatment of idiopathic restless legs syndrome (RLS) with the D2-agonist cabergoline—an open clinical trial. *Sleep* 2000; **23:** 349–54.
2. Stiasny-Kolster K, *et al.* Effective cabergoline treatment in idiopathic restless legs syndrome. *Neurology* 2004; **63:** 2272–9.

## Preparations

**Proprietary Preparations** (details are given in Part 3)
***Arg.:*** Cabaser; Caberpar; Cieldom; Dostinex; Lac Stop; Lactamax; Triaspar; ***Austral.:*** Cabaser; Dostinex; ***Austria:*** Cabaseril; Dostinex; ***Belg.:*** Dostinex; Sostilar; ***Braz.:*** Dostinex; ***Canad.:*** Dostinex; ***Chile:*** Dostinex; ***Cz.:*** Cabera; Dostinex; ***Denm.:*** Cabaser; Dostinex; ***Fin.:*** Cabaser; Dostinex; ***Fr.:*** Dostinex; ***Ger.:*** Cabaseril; Dostinex; ***Gr.:*** Dostinex; ***Hong Kong:*** Dostinex; ***India:*** Caberlin; Camforte†; ***Irl.:*** Cabaser; Dostinex; ***Israel:*** Cabaser; Dostinex; ***Ital.:*** Actualene; Cabaser; Dostinex; ***Malaysia:*** Dostinex; ***Mex.:*** Dostinex; ***Neth.:*** Dostinex; ***Norw.:*** Cabaser; Dostinex; ***NZ:*** Dostinex; ***Pol.:*** Dostinex; ***Port.:*** Dostinex; ***Rus.:*** Dostinex (Достинекс); ***S.Afr.:*** Dostinex; ***Singapore:*** Dostinex; ***Spain:*** Dostinex; Sogilen; ***Swed.:*** Cabaser; Dostinex; ***Switz.:*** Cabaser; Dostinex; ***Turk.:*** Cabaser; Dostinex; ***UK:*** Cabaser; Dostinex; ***USA:*** Dostinex†; ***Venez.:*** Dostinex.

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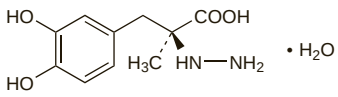
## Carbidopa *(BAN, USAN, rINN)*

Carbidopum; Carbidopum Monohydricum; Karbidopa; Karbidopa monohydrát; α-Methyldopa Hydrazine; MK-486. (+)-2-(3,4-Dihydroxybenzyl)-2-hydrazinopropionic acid monohydrate; (−)-L-α-Hydrazino-3,4-dihydroxy-α-methylhydrocinnamic acid monohydrate.

Карбидопа

$C_{10}H_{14}N_2O_4,H_2O$ = 244.2.
*CAS — 28860-95-9 (anhydrous); 38821-49-7 (monohydrate).*



NOTE. The synonym MK-485 has been used for the racemic mixture.
Compounded preparations of carbidopa and levodopa may be represented by the following names:

- Co-careldopa *x/y* (*BAN*)—where *x* and *y* are the strengths in milligrams of carbidopa and levodopa respectively
- Co-careldopa (*PEN*)—carbidopa and levodopa

**Pharmacopoeias.** In *Chin., Eur.* (see p.vii), *Int., Jpn,* and *US.*
**Ph. Eur. 6.2** (Carbidopa). A white or yellowish-white powder. Slightly soluble in water; very slightly soluble in alcohol; practically insoluble in dichloromethane; dissolves in dilute solutions of mineral acids. Protect from light.
**USP 31** (Carbidopa). A white to creamy-white, odourless or practically odourless powder. Slightly soluble in water and in methyl alcohol; practically insoluble in alcohol, in acetone, in chloroform, and in ether; freely soluble in 3N hydrochloric acid. Protect from light.

### Adverse Effects

**Hypersensitivity.** Henoch-Schönlein purpura that developed in a 68-year-old patient being treated for Parkinson's disease appeared to be due to either carbidopa or an excipient of the carbidopa preparation (*Sinemet*).[1]

1. Niedermaier G, Briner V. Henoch-Schönlein syndrome induced by carbidopa/levodopa. *Lancet* 1997; **349:** 1071–2.

### Pharmacokinetics

Carbidopa is rapidly but incompletely absorbed from the gastrointestinal tract. It is rapidly excreted in the urine both unchanged and in the form of metabolites. It does not cross the blood-brain barrier. In *rats*, carbidopa has been reported to cross the placenta and to be distributed into breast milk.

### Uses and Administration

Carbidopa is a peripheral dopa-decarboxylase inhibitor with little or no pharmacological activity when given alone in usual doses. It inhibits the peripheral decarboxylation of levodopa to dopamine and as, unlike levodopa, it does not cross the blood-brain barrier, effective brain concentrations of dopamine are produced with lower doses of levodopa. At the same time reduced peripheral formation of dopamine reduces peripheral adverse effects, notably nausea and vomiting, and cardiac arrhythmias, although the dyskinesias and adverse mental effects associated with levodopa therapy tend to develop earlier. Contrary to its effect in patients on levodopa alone, pyridoxine does not inhibit the response to levodopa in patients also receiving a peripheral dopa-decarboxylase inhibitor.

In the treatment of parkinsonism (p.791) carbidopa is given with levodopa to enable a lower dosage of the latter to be used, a more rapid response to be obtained, and to decrease adverse effects. For details of administration and dosage, see Levodopa, p.808.

Carbidopa also inhibits the peripheral decarboxylation of the serotonin precursor oxitriptan (p.414).

◊ General references.

1. Pinder RM, *et al*. Levodopa and decarboxylase inhibitors: a review of their clinical pharmacology and use in the treatment of parkinsonism. *Drugs* 1976; **11:** 329–77.
2. Boshes B. Sinemet and the treatment of parkinsonism. *Ann Intern Med* 1981; **94:** 364–70.

## Preparations

***BP 2008:*** Co-careldopa Tablets;
***USP 31:*** Carbidopa and Levodopa Tablets.

**Proprietary Preparations** (details are given in Part 3)
***Arg.:*** Prikap; ***Pol.:*** Nakom; ***USA:*** Lodosyn.

**Multi-ingredient:** ***Arg.:*** Lebocar; Lecarge; Nervocur; Parkinel; Sinemet; Stalevo; ***Austral.:*** Kinson; Sinemet; Stalevo; ***Austria:*** Levocar; Sinemet; ***Belg.:*** Sinemet; Stalevo; ***Braz.:*** Carbidol; Cronomet; Duodopa; Levocarb; Parkidopa; Parklen; Sinemet; Stalevo; ***Canad.:*** Apo-Levocarb; Novo-Levocarbidopa; Nu-Levocarb; Sinemet; ***Chile:*** Grifoparkin; Levofamil†; Protonis; Saniter Compuesto; Sinemet; Stalevo; ***Cz.:*** Dopalux; Duodopa; Isicom; Lecardop; Nakom; Sinemet; Stalevo; ***Denm.:*** Duodopa; Sinemet; Stalevo; ***Fin.:*** Kardopal; Sinemet; Stalevo; ***Fr.:*** Duodopa; Sinemet; Stalevo; ***Ger.:*** Dopadura C; Isicom; Levo-C; Levobeta C; Levocarb; Levocomp; Levodop; Levodopa Comp; Levodopa comp C; Levodopa-Carbi†; Nacom; Stalevo; Striaton; Tremopar†; ***Gr.:*** Sinemet; Sinemet-CR; Stalevo; Zimox; ***Hong Kong:*** Apo-Levocarb; Levomed; Levomet; Sinedopa; Sinemet; Stalevo; ***Hung.:*** Duellin; Sinemet; Stalevo; ***India:*** Levopa-C†; Syndopa; ***Indon.:*** Stalevo; ***Irl.:*** Half Sinemet; Sinemet; Stalevo; ***Israel:*** Dopicar; Sinemet; Stalevo; ***Ital.:*** Duodopa; Sinemet; Sirio; Stalevo; ***Malaysia:*** Apo-Levocarb; Levomed; Sinemet; Stalevo; ***Mex.:*** Cloisone; Lemdopa; Racovel; Sinemet; Stalevo; Ternovag; ***Neth.:*** Duodopa; Sinemet; Stalevo; ***Norw.:*** Duodopa; Sinemet; Stalevo; ***NZ:*** Apo-Levocarb; Sindopa; Sinemet; ***Philipp.:*** Ledocar; Sinemet; Stalev; Tidomet; ***Pol.:*** Sinemet; Stalevo; ***Port.:*** Duodopa; Ledopsan; Sinemet; Stalevo; ***Rus.:*** Duellin (Дуэллин); Nakom (Наком); Stalevo (Сталево); Syndopa (Синдопа); Tidomet (Тидомет); Tremonorm (Тремонорм); ***S.Afr.:*** Carbilev; Sinemet; ***Singapore:*** Cardopar; Levomet; Sinemet; Stalevo; Tidomet; ***Spain:*** Duodopa; Ledopsan; Sinemet; Stalevo; ***Swed.:*** Duodopa; Sinemet; Stalevo; ***Switz.:*** Sinemet; Stalevo; ***Thai.:*** Levomed†; Levomet; Sinemet; Stalevo; Syndopa; ***Turk.:*** Sinemet; Stalevo; ***UK:*** Duodopa; Half Sinemet; Sinemet; Stalevo; Tilolec†; ***USA:*** Atamet; Parcopa; Sinemet; Stalevo; ***Venez.:*** Sinemet; Stalevo.

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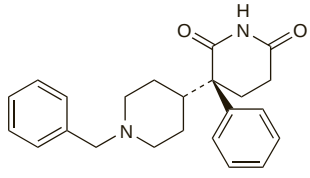
## Dexetimide *(BAN, USAN, rINN)*

Dexetimida; Dexétimide; Dexetimidum. (*S*)-2-(1-Benzyl-4-piperidyl)-2-phenylglutarimide; (*S*)-3-Phenyl-1′-(phenylmethyl)-(3,4′-bipiperidine)-2,6-dione.

Дексэтимид

$C_{23}H_{26}N_2O_2$ = 362.5.
*CAS — 21888-98-2.*
*ATC — N04AA08.*
*ATC Vet — QN04AA08.*



## Dexetimide Hydrochloride *(BANM, rINNM)*

Dexbenzetimide Hydrochloride; Dexétimide, Chlorhydrate de; Dexetimidi Hydrochloridum; Hidrocloruro de dexetimida; R-16470.

Дексэтимида Гидрохлорид

$C_{23}H_{26}N_2O_2$,HCl = 398.9.
*CAS — 21888-96-0.*
*ATC — N04AA08.*
*ATC Vet — QN04AA08.*

### Profile

Dexetimide is a tertiary antimuscarinic with actions similar to those of trihexyphenidyl (p.820). It has been used to alleviate drug-induced extrapyramidal symptoms (see under Chlorpromazine, p.971), but, like other antimuscarinics, is of no value against tardive dyskinesias. Dexetimide is given as the hydrochloride although doses are expressed in terms of the base; dexetimide hydrochloride 1.1 mg is equivalent to about 1 mg of dexetimide. A usual oral dose is 0.5 to 1 mg once daily; it has also been given by intramuscular injection.

### Preparations

**Proprietary Preparations** (details are given in Part 3)
***Belg.:*** Tremblex; ***Neth.:*** Tremblex.

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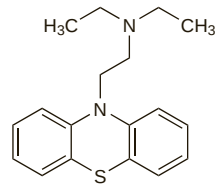
## Diethazine Hydrochloride *(BANM, rINNM)*

Diaethazinium Chloratum; Diéthazine, Chlorhydrate de; Diethazini Hydrochloridum; Eazamine Hydrochloride; Hidrocloruro de dietazina; RP-2987. 10-(2-Diethylaminoethyl)phenothiazine hydrochloride.

Диэтазина Гидрохлорид

$C_{18}H_{22}N_2S$,HCl = 334.9.
*CAS — 60-91-3 (diethazine); 341-70-8 (diethazine hydrochloride).*



*(diethazine)*

### Profile

Diethazine hydrochloride is an antimuscarinic with actions similar to those of profenamine hydrochloride (p.815), but it is more toxic and bone-marrow depression may occur. It has been used in the treatment of parkinsonism.

### Preparations

**Proprietary Preparations** (details are given in Part 3)
***Cz.:*** Deparkin†.

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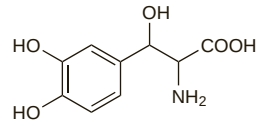
## Droxidopa *(USAN, rINN)*

L-*threo*-3,4-Dihydroxyphenylserine; DOPS; Droxidopum; L-DOPS; L-*threo*-DOPS. (−)-*threo*-3-(3,4-Dihydroxyphenyl)-L-serine.

Дроксидопа

$C_9H_{11}NO_5$ = 213.2.
*CAS — 23651-95-8.*



### Profile

Droxidopa is a precursor of noradrenaline that is used in the treatment of parkinsonism (p.791) and some forms of orthostatic hypotension (p.1530). The usual oral maintenance dose is 600 mg daily for the treatment of parkinsonism and 300 to 600 mg daily in orthostatic hypotension; daily doses should be divided.

The racemic form (DL-*threo*-3,4-dihydroxyphenylserine) has also been studied for orthostatic hypotension.

◊ References.

1. Iida N, *et al.* Treatment of dialysis-induced hypotension with -threo-3, 4-dihydroxyphenylserine. *Nephrol Dial Transplant* 1994; **9:** 1130–5.
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### Preparations

**Proprietary Preparations** (details are given in Part 3)
***Jpn:*** Dops.

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