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

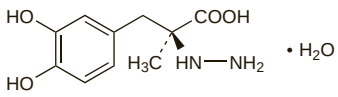
Proprietary Preparations (details are given in Part 3)
Arg.: Cabaser; Caberpar; Cieldom; Dostinex; Lac Stop; Lactamax; Triaspar; ***Austral.:*** Cabaser; Dostinex; ***Austria:*** Cabaseril; Dostinex; ***Belg.:*** Dostinex; Sostilar; ***Braz.:*** Dostinex; ***Canad.:*** Dostinex; ***Chile:*** Dostinex; ***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.

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.

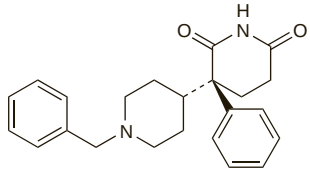
Multi-ingredient: ***Arg.:*** Lebocar; Lecarge; Nervocur; Parkinel; Sinemet; Stalevo; ***Austral.:*** Kinson; Sinemet; Stalevo; ***Austria:*** Levocar; Sinemet; ***Belg.:*** Sinemet; Stalevo; ***Braz.:*** Carbidol; Cronomet; Duodopa; Levocarb; Parkidopa; Parklen; Sinemet; Stalevo; ***Canad.:*** Apo-Levocarb; 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.

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

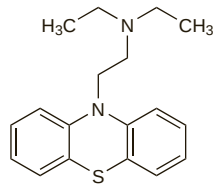
Proprietary Preparations (details are given in Part 3)
Belg.: Tremblex; ***Neth.:*** Tremblex.

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

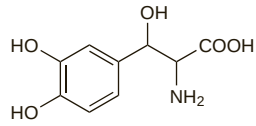
Proprietary Preparations (details are given in Part 3)
Cz.: Deparkin†.

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.
2. Freeman R, *et al.* The treatment of neurogenic orthostatic hypotension with 3,4-DL-threo-dihydroxyphenylserine: a randomized, placebo-controlled, crossover trial. *Neurology* 1999; **10:** 2151–7.
3. Akizawa T, *et al.* Clinical effects of L-threo-3,4-dihydroxyphenylserine on orthostatic hypotension in hemodialysis patients. *Nephron* 2002; **90:** 384–90.
4. Kaufmann H, *et al.* Norepinephrine precursor therapy in neurogenic orthostatic hypotension. *Circulation* 2003; **108:** 724–8.
5. Goldstein DS, *et al.* Clinical pharmacokinetics of the norepinephrine precursor L-threo-DOPS in primary chronic autonomic failure. *Clin Auton Res* 2004; **14:** 363–8.

Preparations

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