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

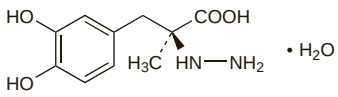
Proprietary Preparations (details are given in Part 3)
Arg.: Cabaser; Caberpar; Cieldom; Dostinex; Lac Stop; Lactamax; Triaspar; ***Austral.:*** Cabaser; Dostinex; ***Austria:*** Cabaseril; Dostinex; ***Belg.:*** Dostinex; Sostilar; ***Braz.:*** Dostinex; ***Canad.:*** Dostinex; ***Chile:*** Dostinex;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

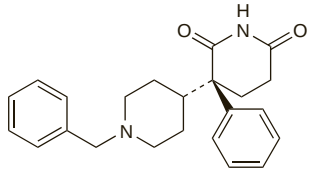
Multi-ingredient: ***Arg.:*** Lebocar; Lecarge; Nervocur; Parkinel; Sinemet; Stalevo; ***Austral.:*** Kinson; Sinemet; Stalevo; ***Austria:*** Levocar; Sinemet; ***Belg.:*** Sinemet; Stalevo; ***Braz.:*** Carbidol; Cronomet; Duodopa; Levocarb; Parkidopa; Parklen; Sinemet; Stalevo; ***Canad.:*** Apo-Levocarb;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

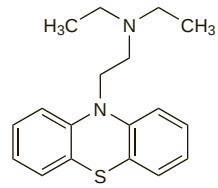
Proprietary Preparations (details are given in Part 3)
Belg.: Tremblex; ***Neth.:*** Tremblex.

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

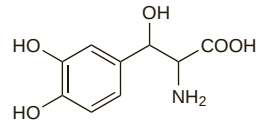
Proprietary Preparations (details are given in Part 3)
Cz.: Deparkin†.

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.

Entacapone *(BAN, USAN, rINN)*

Entacapona; Entacaponum; Entakapon; Entakaponi; OR-611. (*E*)-α-Cyano-*N*,*N*-diethyl-3,4-dihydroxy-5-nitrocinnamamide; (*E*)-2-Cyano-3-(3,4-dihydroxy-5-nitrophenyl)-*N*,*N*-diethylacrylamide.

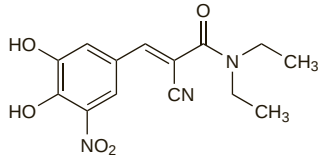
Энтакапон

$C_{14}H_{15}N_3O_5$ = 305.3.

CAS — 130929-57-6.

ATC — N04BX02.

ATC Vet — QN04BX02.



Adverse Effects

The most frequent adverse effects produced by entacapone relate to increased dopaminergic activity and occur most commonly at the start of treatment; reduction of the levodopa dosage may reduce the severity and frequency of such effects. Adverse effects may include nausea, vomiting, abdominal pain, constipation, diarrhoea, colitis, dry mouth, and dyskinesias. Other commonly reported adverse effects include dizziness, insomnia, nightmares, hallucinations, confusion, fatigue, and increased sweating. There have been rare reports of agitation, urticaria, erythematous or maculopapular rash, anorexia, and weight decrease. Increases in liver enzyme values have been reported rarely; there have also been isolated cases of cholestatic hepatitis. Isolated cases of neuroleptic malignant syndrome have been reported after abrupt reduction or withdrawal of entacapone; there have also been isolated cases of rhabdomyolysis. It may produce a harmless reddish-brown discoloration of the urine. Skin, hair, beard, and nail discolorations have been reported.

◊ References.

1. Brooks DJ. Safety and tolerability of COMT inhibitors. *Neurology* 2004; **62** (Suppl 1): S39–S46.

Precautions

Entacapone is contra-indicated in patients with phaeochromocytoma and in patients with a history of neuroleptic malignant syndrome or nontraumatic rhabdomyolysis. It should be avoided in patients with hepatic impairment, and given with caution to patients with biliary obstruction. A general medical evaluation, including liver function, should be considered in those who experience progressive anorexia, asthenia, and weight decrease within a relatively short period of time.Use with levodopa may cause dizziness and orthostatic hypotension; if affected patients should not drive or operate machinery. Excessive daytime sleepiness and sudden onset of sleep may also occur with combination use (see Effects on Mental Function, in Levodopa, p.805) and again, caution is advised when driving or operating machinery; patients who suffer such effects should not drive or operate machinery until the effects have stopped recurring.

Treatment with entacapone should not be stopped abruptly; when necessary withdrawal should be made gradually, increasing the dose of levodopa as required.

Genetic polymorphism. For reference to slow metabolisers being more susceptible to COMT-inhibitor induced hepatotoxicity, see under Tolcapone, p.820.

Interactions

Use of entacapone with a non-selective MAOI is contra-indicated. Entacapone should be used with caution in patients receiving drugs metabolised by catechol-*O*-methyltransferase (COMT) including adrenaline, apomorphine, dobutamine, dopamine, isoprenaline, methyldopa, noradrenaline, paroxetine, and rimiterol. Caution is also advised when used with certain antidepressants including the tricyclics, reversible inhibitors of monoamine oxidase type A, and noradrenaline reuptake inhibitors such as venlafaxine.

Entacapone may aggravate levodopa-induced orthostatic hypotension and should be used cautiously in patients who are taking other drugs which may cause orthostatic hypotension.

Entacapone may form chelates with iron preparations in the gastrointestinal tract; the two drugs should be taken at least 2 to 3 hours apart.

Pharmacokinetics

There are large intra- and interindividual variations in the absorption of entacapone. Peak plasma concentrations are achieved about one hour after oral doses. Entacapone undergoes extensive first-pass metabolism and oral bioavailability is about 35%. Absorption is not affected significantly by food. Entacapone is about 98% bound to plasma proteins. It is eliminated mainly in the faeces with about 10 to 20% being excreted in the urine, mainly as glucuronide conjugates. Entacapone is thought to be distributed into breast milk on the basis of studies in *rats*.

◊ Entacapone is rapidly absorbed from the gastrointestinal tract and bioavailability after oral doses has been reported to range from 29 to 46%. It does not cross the blood-brain barrier. Over half of a dose appears in the faeces with smaller amounts being excreted in the urine as glucuronides of entacapone and its (*Z*)-isomer. Elimination half-lives of about 1.6 to 3.4 hours have been reported for entacapone.

References.

1. Wikberg T, *et al.* Identification of major metabolites of the catechol-O-methyltransferase inhibitor entacapone in rats and humans. *Drug Metab Dispos* 1993; **21:** 81–92.
2. Keränen T, *et al.* Inhibition of soluble catechol-O-methyltransferase and single-dose pharmacokinetics after oral and intravenous administration of entacapone. *Eur J Clin Pharmacol* 1994; **46:** 151–7.

Uses and Administration

Entacapone is a selective, reversible, peripheral inhibitor of catechol-*O*-methyltransferase (COMT), an enzyme involved in the metabolism of dopamine and levodopa. It is used as an adjunct to combination preparations of levodopa and dopa-decarboxylase inhibitors, in patients with Parkinson's disease and 'end-of-dose' motor fluctuations who cannot be stabilised on levodopa combinations alone. Entacapone is given orally in a dosage of 200 mg at the same time as each dose of levodopa with dopa-decarboxylase inhibitor, up to a maximum of 200 mg ten times daily. It is often necessary to gradually reduce the dosage of levodopa by about 10 to 30% within the first few weeks after starting treatment with entacapone; this effect may be more marked in the presence of benserazide than of carbidopa.

Entacapone may also be given as a combination preparation with carbidopa and levodopa; for dosage details, see Levodopa, p.808.

Parkinsonism. Entacapone is a selective and reversible inhibitor of catechol-*O*-methyltransferase (COMT), with mainly peripheral actions. It is given as adjunctive therapy to patients with Parkinson's disease (p.791) experiencing fluctuations in disability related to levodopa and dopa-decarboxylase inhibitor combinations. When levodopa is given with a peripheral dopa-decarboxylase inhibitor, *O*-methylation then becomes the predominant form of metabolism of levodopa; therefore adding a peripheral COMT inhibitor such as entacapone potentially extends the duration and effect of levodopa in the brain, and thus allows levodopa to be given less often and in lower doses.

References.

1. Holm KJ, Spencer CM. Entacapone: a review of its use in Parkinson's disease. *Drugs* 1999; **58:** 159–177.
2. Anonymous. Entacapone for Parkinson's disease. *Med Lett Drugs Ther* 2000; **42:** 7–8.
3. Chong BS, Mersfelder TL. Entacapone. *Ann Pharmacother* 2000; **34:** 1056–65.
4. Myllyla VV, *et al.* Twelve-month safety of entacapone in patients with Parkinson's disease. *Eur J Neurol* 2001; **8:** 53–60.
5. Poewe WH, *et al.* Efficacy and safety of entacapone in Parkinson's disease patients with suboptimal levodopa response: a 6-month randomized placebo-controlled double-blind study in Germany and Austria (Celomen study). *Acta Neurol Scand* 2002; **105:** 245–55.
6. Brooks DJ, *et al.* Entacapone is beneficial in both fluctuating and non-fluctuating patients with Parkinson's disease: a randomised, placebo controlled, double blind, six month study. *J Neurol Neurosurg Psychiatry* 2003; **74:** 1071–9.
7. Fenelon G, *et al.* Efficacy and tolerability of entacapone in patients with Parkinson's disease treated with levodopa plus a dopamine agonist and experiencing wearing-off motor fluctuations: a randomized, double-blind, multicentre study. *J Neural Transm* 2003; **110:** 239–51.
8. Olanow CW, Stocchi F. COMT inhibitors in Parkinson's disease: can they prevent and/or reverse levodopa-induced motor complications? *Neurology* 2004; **62** (suppl 1): S72–S81.
9. Deane KHO, *et al.* Catechol-O-methyltransferase inhibitors for levodopa-induced complications in Parkinson's disease. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2004 (accessed 16/02/06).
10. Poewe W. The role of COMT inhibition in the treatment of Parkinson's disease. *Neurology* 2004; **62** (suppl 1): S31–S38.
11. Schrag A. Entacapone in the treatment of Parkinson's disease. *Lancet Neurol* 2005; **4:** 366–70.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Comtan; ***Austral.:*** Comtan; ***Austria:*** Comtan; ***Belg.:*** Comtan; ***Braz.:*** Comtan; ***Canad.:*** Comtan; ***Cz.:*** Comtan; Comtess; ***Denm.:*** Comtess; ***Fin.:*** Comtess; ***Fr.:*** Comtan; ***Ger.:*** Comtess; ***Gr.:*** Comtan; ***Hong Kong:*** Comtan; ***Hung.:*** Comtan; ***Indon.:*** Comtan; ***Irl.:*** Comtess; ***Israel:*** Comtan; ***Ital.:*** Comtan; ***Malaysia:*** Comtan; ***Mex.:*** Comtan; ***Neth.:*** Comtan; Comtess; ***Norw.:*** Comtess; ***NZ:*** Comtan; ***Philipp.:*** Comtan; ***Pol.:*** Comtan; ***Port.:*** Comtan; Comtess; ***S.Afr.:*** Comtan; ***Singapore:*** Comtan; ***Spain:*** Comtan; ***Swed.:*** Comtess; ***Switz.:*** Comtan; ***Thai.:*** Comtan; ***Turk.:*** Comtan; ***UK:*** Comtess; ***USA:*** Comtan; ***Venez.:*** Comtan.

Multi-ingredient: ***Arg.:*** Stalevo; ***Austral.:*** Stalevo; ***Belg.:*** Stalevo; ***Braz.:*** Stalevo; ***Chile:*** Stalevo; ***Cz.:*** Stalevo; ***Denm.:*** Stalevo; ***Fin.:*** Stalevo; ***Fr.:*** Stalevo; ***Ger.:*** Stalevo; ***Gr.:*** Stalevo; ***Hong Kong:*** Stalevo; ***Hung.:*** Stalevo; ***Indon.:*** Stalevo; ***Irl.:*** Stalevo; ***Israel:*** Stalevo; ***Ital.:*** Stalevo; ***Malaysia:*** Stalevo; ***Mex.:*** Stalevo; ***Neth.:*** Stalevo; ***Norw.:*** Stalevo; ***Philipp.:*** Stalev; ***Pol.:*** Stalevo; ***Port.:*** Stalevo; ***Rus.:*** Stalevo (Сталево); ***Singapore:*** Stalevo; ***Spain:*** Stalevo; ***Swed.:*** Stalevo; ***Switz.:*** Stalevo; ***Thai.:*** Stalevo; ***Turk.:*** Stalevo; ***UK:*** Stalevo; ***USA:*** Stalevo; ***Venez.:*** Stalevo.

Levodopa *(BAN, USAN, rINN)*

Dihydroxyphenylalanine; L-Dopa; 3-Hydroxy-L-tyrosine; Laevodopa; Lévodopa; Levodopum. (–)-3-(3,4-Dihydroxyphenyl)-L-alanine.

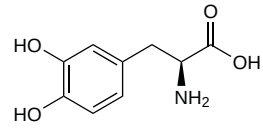
Леводопа

$C_9H_{11}NO_4$ = 197.2.

CAS — 59-92-7.

ATC — N04BA01.

ATC Vet — QN04BA01.



NOTE. Compounded preparations of levodopa may be represented by the following names:

- Co-beneldopa (*BAN*)—benserazide 1 part and levodopa 4 parts (w/w)
- 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 (Levodopa). A white or slightly cream-coloured, crystalline powder. Slightly soluble in water; freely soluble in 1M hydrochloric acid but sparingly soluble in 0.1M hydrochloric acid; practically insoluble in alcohol. A 1% suspension in water has a pH of 4.5 to 7.0. Protect from light.

USP 31 (Levodopa). A white to off-white, odourless, crystalline powder. In the presence of moisture, it is rapidly oxidised by atmospheric oxygen and darkens. Slightly soluble in water; freely soluble in 3N hydrochloric acid; insoluble in alcohol. Store in a dry place in airtight containers at a temperature not exceeding 40°. Protect from light.

Stability. Extemporaneously prepared oral liquid dosage forms may be unstable and manufacturers' formulations should be used where possible.[1] Water dispersible formulations of levodopa with benserazide are available in some countries but a method that can be used by patients to prepare daily solutions of levodopa with carbidopa has been suggested:[2] one litre of a solution in potable water may be prepared with ten crushed standard tablets of levodopa 100 mg with carbidopa 25 mg and 2 g of ascorbic acid added to stabilise the levodopa.

1. Walls TJ, *et al.* Problems with inactivation of drugs used in Parkinson's disease. *BMJ* 1985; **290:** 444–5.
2. Giron LT, Koller WC. Methods of managing levodopa-induced dyskinesias. *Drug Safety* 1996; **14:** 365–74.

Adverse Effects

Gastrointestinal effects, notably nausea, vomiting, and anorexia are common early in treatment with levodopa, particularly if the dosage is increased too rapidly. Gastrointestinal bleeding has been reported in patients with a history of peptic ulcer disease.