AUSTRALIAN PRODUCT INFORMATION
SINEMET® (levodopa and carbidopa) Tablet

1 NAME OF THE MEDICINE

Levodopa and carbidopa

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Carbidopa
Carbidopa, an inhibitor of aromatic amino acid decarboxylase, is a white, crystalline compound, slightly soluble in water.

Levodopa
Levodopa, an aromatic amino acid, is a white, crystalline compound, slightly soluble in water.

SINEMET 250/25 tablets contain levodopa 250 mg and carbidopa 25 mg and SINEMET 100/25 tablets contain levodopa 100 mg and carbidopa 25 mg.

For the full list of excipients, see **Section 6.1 List of Excipients**.

3 PHARMACEUTICAL FORM

SINEMET is supplied as tablets for oral administration.

SINEMET 250/25: light dapple blue oval tablet with 654 and a score line on one side and plain on the other.

SINEMET 100/25: yellow oval tablet with 650 and a score line on one side and plain on the other.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

SINEMET is indicated for the treatment of Parkinson's disease and syndrome. It is useful in relieving many of the symptoms of parkinsonism, particularly rigidity and bradykinesia. SINEMET frequently is helpful in the management of tremor, dysphagia, sialorrhoea and postural instability associated with Parkinson's disease and syndrome.

4.2 DOSE AND METHOD OF ADMINISTRATION

The optimum daily dosage of SINEMET must be determined by careful titration in each patient. SINEMET tablets are available in a 1:4 ratio of carbidopa to levodopa (SINEMET 100/25) as well as a 1:10 ratio (SINEMET 250/25). Tablets of the two ratios may be given separately or combined as needed to provide the optimum dosage.

The tablet score-line for SINEMET 100/25 is only to facilitate breaking for ease of swallowing and not to divide into equal doses. If subdivided, the tablet should be consumed as a whole dose.

The tablet score-line for SINEMET 250/25 can be divided into equal doses.

General Considerations
Dosage should be titrated to individual patient needs and this may require adjusting both the individual dose and the frequency of administration.

Studies show that peripheral dopa decarboxylase is saturated by carbidopa at approximately 70 to 100 mg a day. Patients receiving less than this amount of carbidopa are more likely to experience nausea and vomiting.

Standard antiparkinson drugs, other than levodopa alone, may be continued while SINEMET is being administered, although their dosage may have to be adjusted.

Usual Initial Dosage
Dosage is best initiated with one tablet of SINEMET 100/25 three times a day. This dosage schedule provides 75 mg of carbidopa per day. Dosage may be increased by one tablet every day or every other day, as necessary, until a dosage equivalent of eight tablets of SINEMET 100/25 a day is reached.

For patients starting with SINEMET 25/250, the initial dose is one-half tablet taken once or twice daily. However, this may not provide the optimal amount of carbidopa needed by many patients. If necessary, add 1/2 tablet every day or every other day until optimal response is reached.

Response has been observed in one day, and sometimes after one dose. Fully effective doses usually are reached within seven days as compared to weeks or months with levodopa alone.

How to Transfer Patients from Levodopa
Because both therapeutic and adverse responses occur more rapidly with SINEMET than when levodopa is given, patients should be monitored closely during the dose adjustment period. Specifically, involuntary movements will occur more rapidly with SINEMET than with levodopa. The occurrence of involuntary movements may require dosage reduction. Blepharospasm may be a useful early sign of excess dosage in some patients.

Levodopa should be discontinued at least 12 hours before SINEMET is started (24 hours for slow-release preparations of levodopa). A daily dosage of SINEMET should be chosen that will provide approximately 20% of the previous levodopa daily dosage.

Patients who are taking less than 1500 mg of levodopa a day should be started on one tablet of SINEMET 100/25 three or four times a day. The suggested starting dosage for most patients taking more than 1500 mg of levodopa is one tablet of SINEMET 250/25 three or four times a day.

Maintenance
Therapy should be individualised and adjusted according to the desired therapeutic response. At least 70 to 100 mg of carbidopa per day should be provided for optimal inhibition of extracerebral decarboxylation of levodopa.

When more levodopa is required, SINEMET 250/25 should be substituted for SINEMET 100/25. If necessary, the dosage of SINEMET 250/25 may be increased by one-half or one tablet every day or every other day to a maximum of eight tablets a day. Experience with total daily dosages of carbidopa greater than 200 mg is limited.

Maximum Recommended Dose
Eight tablets of SINEMET 250/25 per day (200 mg of carbidopa and 2 g of levodopa). This is about 3 mg/kg of carbidopa, and 30 mg/kg of levodopa in a patient weighing 70 kg.

4.3 CONTRAINDICATIONS

Monoamine oxidase inhibitors and SINEMET should not be given concomitantly. These inhibitors must be discontinued at least two weeks prior to initiating therapy with SINEMET. SINEMET may be administered concomitantly with the manufacturer's recommended dose of an MAO inhibitor with selectivity for MAO type B, eg selegiline (see **Section 4.5 Interactions with Other Medicines and Other Forms of Interactions, Other Drugs**).

SINEMET is contraindicated in patients with known hypersensitivity to any component of this medication and in patients with narrow angle glaucoma.

Because levodopa may activate a malignant melanoma it should not be used in patients with suspicious undiagnosed skin lesions or history of melanoma.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

SINEMET may be given to patients already receiving levodopa alone; however, the levodopa alone must be discontinued 12 hours before SINEMET is started. SINEMET should be substituted at a dosage that will provide approximately 20 percent of the previous levodopa dosage (see **Section 4.2 Dose and Method of Administration**). Patients taking SINEMET should be instructed not to take additional levodopa unless prescribed.

SINEMET is not recommended for the treatment of drug-induced extrapyramidal reactions.

All patients should be monitored carefully for the development of mental changes, depression with suicidal tendencies, or other serious antisocial behaviour.

Dyskinesias may occur in patients previously treated with levodopa alone because carbidopa permits more levodopa to reach the brain and, thus more dopamine to be formed. The occurrence of dyskinesias may require dosage reduction.

Patients with a history of severe involuntary movements or psychotic episodes when treated with levodopa alone should be observed carefully when SINEMET is substituted. These reactions are thought to be due to increased brain dopamine following administration of levodopa and use of SINEMET may cause a recurrence.

If concomitant administration of psychoactive drugs is necessary, such drugs should be administered with caution and patients carefully observed for loss of antiparkinsonian effect. Patients with a history of convulsions should be treated with caution.

Levodopa has been associated with somnolence and episodes of sudden sleep onset. Sudden onset of sleep during daily activities, in some cases without awareness or warning signs, has been reported very rarely. Patients must be informed of this and advised to exercise caution while driving or operating machines during treatment with levodopa. Patients who have experienced somnolence and/or an episode of sudden sleep onset must refrain from driving or operating machines. Furthermore, a reduction of dosage or termination of therapy may be considered.

Patients with chronic wide angle glaucoma may be treated cautiously with SINEMET, provided the intraocular pressure is well controlled and the patient monitored carefully for changes in intraocular pressure during therapy.

Care should be exercised in administering SINEMET to patients who have atrial, nodal or ventricular arrhythmia. In such patients, cardiac function should be monitored continuously during the period of initial dosage adjustment.

Symptomatic postural hypotension has been reported occasionally. For this reason, SINEMET should be given cautiously to patients on anti-hypertensive drugs. When SINEMET is started, dosage adjustment of the antihypertensive drug may be required. (For patients receiving pargyline, see **Section 4.3 Contraindications**, monoamine oxidase inhibitors.)

A symptom complex resembling the neuroleptic malignant syndrome including muscular rigidity, elevated body temperature, mental changes, and increased serum creatine phosphokinase has been reported when antiparkinsonian agents were withdrawn abruptly. Therefore, patients should be observed carefully when the dosage of SINEMET is reduced abruptly or discontinued, especially if the patient is receiving neuroleptics.

If general anaesthesia is required, therapy with SINEMET may be continued as long as the patient is permitted to take fluids and medication by mouth. If therapy is interrupted temporarily, the usual daily dosage may be administered as soon as the patient is able to take oral medication.

SINEMET should be administered cautiously to patients with severe cardiovascular or pulmonary disease, bronchial asthma, renal, hepatic or endocrine disease. Periodic evaluations of hepatic, haematopoietic, cardiovascular and renal function are recommended during extended therapy.

As with levodopa there is a possibility of upper gastrointestinal haemorrhage in patients with a history of peptic ulcer.

Melanoma: Epidemiological studies have shown that patients with Parkinson's disease have a higher risk (2- to approximately 6-fold higher) of developing melanoma than the general population. Whether the increased risk observed was due to Parkinson's disease or other factors, such as drugs used to treat Parkinson's disease, is unclear.

For the reasons stated above, patients and providers are advised to monitor for melanomas frequently and on a regular basis when using SINEMET for any indication. Ideally, periodic skin examinations should be performed by appropriately qualified individuals (e.g. dermatologists).

Compulsive behaviour

Patients should be regularly monitored for the development of impulse control disorders. Patients and caregivers should be made aware that behavioural symptoms of impulse control disorders (such as pathological gambling, hypersexuality, increased libido, compulsive spending/buying, and binge/compulsive eating, medication use and punding (repetitive purposeless activity)) have been reported in patients treated with dopamine agonists and/or other dopaminergic treatment for Parkinson's disease, especially at high doses. Review of treatment is recommended if such symptoms develop. Prescribers, patients and caregivers should be alert to the possibility of such behaviour, which may have serious financial and social consequences.

Use in hepatic impairment

SINEMET should be administered cautiously to patients with hepatic disease. Periodic evaluation of hepatic function is recommended during extended therapy.

Use in renal impairment

SINEMET should be administered cautiously to patients with renal disease. Periodic evaluation of renal function is recommended during extended therapy.

Use in the elderly

There is wide experience in the use of levodopa and carbidopa in elderly patients. The recommendations set out above reflect the clinical data derived from this experience (see section 4.2 **Dose and method of administration**).

Paediatric use

Safety and effectiveness of SINEMET in infants and children have not been established, and its use in patients below the age of 18 is not recommended.

Effects on laboratory tests

Abnormalities in laboratory tests may include elevations of blood urea nitrogen, creatinine, SGOT (AST), SGPT (ALT), lactic dehydrogenase (LDH), bilirubin, alkaline phosphatase or protein bound iodine. More commonly, levels of blood urea nitrogen and uric acid are lower during the administration of SINEMET than with levodopa.

Decreased haemoglobin and haematocrit; elevated serum glucose, and white blood cells, bacteria and blood in the urine have been reported.

Levodopa-carbidopa preparations may cause a false positive reaction for urinary ketone bodies when a test tape is used for determination of ketonuria. This reaction will not be altered by boiling the urine specimen. False-negative tests may result with the use of glucose-oxidase methods of testing for glycosuria.

Positive Coombs' tests have been reported both with SINEMET and with levodopa alone, but haemolytic anaemia is rare.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Caution should be exercised when the following drugs are administered concomitantly with SINEMET:

Antihypertensive agents:
Symptomatic postural hypotension has occurred when SINEMET is added to the treatment of patients receiving some antihypertensive drugs. Therefore, when therapy with SINEMET is started, dosage adjustment of the antihypertensive drug may be required.

Antidepressants:
For patients receiving monoamine oxidase inhibitors, see **Section 4.3 Contraindications**.

There have been rare reports of adverse reactions, including hypertension and dyskinesia, resulting from the concomitant use of tricyclic antidepressants and SINEMET.

Iron:
Studies demonstrate a decrease in the bioavailability of carbidopa and/or levodopa when it is ingested with ferrous sulfate or ferrous gluconate.

Other drugs:
Dopamine D_2 receptor antagonists (eg., phenothiazines, butyrophenones and risperidone) and isoniazid may reduce the therapeutic effects of levodopa. The beneficial effects of levodopa in Parkinson's disease have been reported to be reversed by phenytoin and papaverine. Patients taking these drugs with SINEMET should be observed carefully for loss of therapeutic response.

Use of SINEMET with dopamine-depleting agents (e.g., reserpine and tetrabenazine) or other drugs known to deplete monoamine stores is not recommended.

Concomitant therapy with selegiline and carbidopa-levodopa may be associated with severe orthostatic hypotension not attributable to carbidopa-levodopa alone (see **Section 4.3 Contraindications**).

Since levodopa competes with certain amino acids the absorption of levodopa may be impaired in some patients on a high protein diet.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

In reproduction studies with levodopa and carbidopa, no effects on fertility were found in rats receiving doses of approximately two times the maximum daily human dose of carbidopa and four times the maximum daily human dose of levodopa.

Therefore, the use of SINEMET in women of childbearing potential requires that the anticipated benefits of the drug be weighed against possible hazards should pregnancy occur.

Use in pregnancy (Category B3)

Although the effect of SINEMET on human pregnancy is unknown, levodopa caused visceral and skeletal malformations in rabbits at doses of 125 and 250 mg/kg/day. With combinations of levodopa and carbidopa in doses ranging from 250/50 to 500/100 mg/kg/day there was no evidence of teratogenicity in mice, but in rabbits visceral and skeletal malformations occurred similar to those seen with levodopa alone. Carbidopa alone showed no evidence of teratogenicity in mice and rabbits at doses up to 120 mg/kg/day.

Use in lactation

It is not known whether carbidopa is excreted in human milk. In a study of one nursing mother with Parkinson's disease, excretion of levodopa in human breast milk was reported. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in infants, SINEMET should not be used in nursing mothers. A decision should be made either to discontinue nursing or discontinue SINEMET.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

See **Section 4.4 Special Warnings and Precautions for Use.**

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Side effects that occur frequently in patients receiving SINEMET are those due to the central neuropharmacologic activity of dopamine. These reactions usually can be diminished by dosage reduction. The most common side effects are dyskinesias, including choreiform, dystonic, and other involuntary movements. Muscle twitching and blepharospasm may be taken as early signs to consider dosage reduction.

Other serious side effects are: mental changes, including paranoid ideation and psychotic episodes including delusions, hallucinations; depression with or without development of suicidal tendencies; and dementia. A common but less serious side effect is nausea.

Less frequent side effects are cardiac irregularities and/or palpitation, orthostatic effects including hypotensive episodes, bradykinetic episodes (the "on-off" phenomenon), anorexia, vomiting, dizziness, and somnolence.

Gastrointestinal bleeding, development of duodenal ulcer, hypertension, phlebitis, leucopoenia, haemolytic and non-haemolytic anaemia, thrombocytopenia, agranulocytosis, chest pain, dyspnoea, and paraesthesia have occurred rarely.

Rarely convulsions have occurred; however, a causal relationship with SINEMET has not been established.

Haemolytic anaemia is extremely rare.

Other side effects that have been reported include:

Body as a whole: syncope.

Nervous system: ataxia, numbness, increased hand tremor, muscle twitching, muscle cramps, trismus, activation of latent Horner's syndrome, oculogyric crises, peripheral neuropathy.

Psychiatric: confusion, insomnia, nightmares and dream abnormalities, hallucinations, delusions, agitation, anxiety, euphoria, lethargy, sedation, increased libido. Levodopa is associated with somnolence and has been associated very rarely with excessive daytime somnolence and sudden sleep onset episodes.

Gastrointestinal: dry mouth, bitter taste, sialorrhoea, dysphagia, bruxism, hiccups, epigastric and abdominal pain and distress, constipation, diarrhoea, flatulence, burning sensation of the tongue, difficulty in swallowing, dark saliva.

Hypersensitivity: angioedema, urticaria, pruritus, Henoch-Schönlein purpura.

Investigations: weight gain, weight loss.

Metabolism and nutrition disorders: oedema, anorexia.

Integumentary: flushing, increased sweating, dark sweat, rash, hair loss, bad odour.

Genitourinary: urinary retention, urinary incontinence, dark urine, priapism, haematuria.

Special senses: diplopia, blurred vision, dilated pupils.

Miscellaneous: weakness, faintness, fatigue, headache, hoarseness, malaise, hot flushes, sense of stimulation, bizarre breathing patterns, neuroleptic malignant syndrome (see **Section 4.4 Special Warnings and Precautions for Use**), malignant melanoma (see **Section 4.3 Contraindications**).

OTHER SIDE EFFECTS THAT HAVE BEEN REPORTED WITH SINEMET CR AND MAY BE POTENTIAL SIDE EFFECTS WITH SINEMET are listed below:

Gastrointestinal: dyspepsia.

Nervous system/psychiatric: asthenia, decreased mental acuity, disorientation, falling, gait abnormalities.

In post-marketing use, pathological (compulsive) gambling, increased libido, hypersexuality, compulsive spending/buying, and binge/compulsive eating have been reported with dopamine agonists and/or other dopaminergic treatments, and in patients treated with levodopa, including SINEMET (see **Section 4.4 Special Warnings and Precautions for Use**).

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

Management of acute overdosage with SINEMET is basically the same as management of acute overdosage with levodopa; however, pyridoxine is not effective in reversing the actions of SINEMET.

In the event of overdosage, general supportive measures should be employed. Intravenous fluids should be administered judiciously and an adequate airway maintained. Electrocardiographic monitoring should be instituted and the patient observed carefully for the development of arrhythmias; if required, appropriate antiarrhythmic therapy should be given. The possibility that the patient may have taken other drugs as well as SINEMET should be taken into consideration. To date, no experience has been reported with dialysis, hence its value in overdosage is not known.

For information on the management of overdose, contact the Poisons Information Centre on 131126 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

Symptoms of Parkinson's disease have been related to depletion of dopamine in the corpus striatum of the brain. Levodopa, the metabolic precursor of dopamine, relieves the symptoms of Parkinson's disease presumably by being converted to dopamine in the brain.

Following oral administration, levodopa is rapidly decarboxylated and converted to dopamine in extracerebral tissues and only a small amount of unchanged levodopa reaches the central nervous system. Thus, large doses of levodopa are required at frequent intervals for adequate therapeutic effect and are often attended by many adverse reactions, some of which are attributable to dopamine being formed in extracerebral tissue.

Carbidopa, which does not cross the blood-brain barrier, inhibits only extracerebral decarboxylation of levodopa, making more levodopa available for transport to the brain and conversion to dopamine. The lower dosage reduces or eliminates certain adverse reactions attributable to dopamine being formed in extracerebral tissues.

Following coadministration of levodopa and carbidopa in man, plasma levels of levodopa were markedly increased over those found when the same dosage of levodopa was given alone, while plasma levels of dopamine and homovanillic acid, two principal metabolites of levodopa, were markedly reduced.

Pyridoxine hydrochloride (Vitamin B6) in oral doses of 10 mg to 25 mg has been noted to rapidly reverse the antiparkinsonian effect of levodopa. Carbidopa prevents this action of pyridoxine. In a study in which patients received 100 mg - 500 mg of pyridoxine a day whilst being treated with levodopa and carbidopa in combination, there was no reversal of therapeutic effect.

Clinical trials

SINEMET is well established in medical use (see **Section 4.2 Dose and Method of Administration** and **Section 4.8 Adverse Effects (Undesirable Effects)**).

5.2 PHARMACOKINETIC PROPERTIES

Carbidopa

Absorption

Following an oral dose of radioactive labelled carbidopa to healthy subjects and to patients with Parkinson's disease, maximum plasma levels of radioactivity were reached in two to four hours in the subjects and in one and one-half to five hours in the patients.

Metabolism and Excretion

Following an oral dose of radioactive labelled carbidopa to healthy subjects and to patients with Parkinson's disease, approximately equal quantities were excreted in the urine and the faeces by both groups. Comparison of urinary metabolites in healthy subjects and patients indicated that the drug is metabolised to the same degree in both. Urinary excretion of unchanged drug was essentially complete in seven hours and represented 35 percent of the total urinary radioactivity. Only metabolites were present thereafter.

Among the metabolites excreted by man are α-methyl-3-methoxy-4-hydroxy-phenylpropionic acid and α-methyl-3,4 dihydroxyphenylpropionic acid. These accounted for approximately 14 and 10 percent, respectively, of the radioactive metabolites excreted. Two minor metabolites were found. One was identified as 3,4 dihydroxyphenylacetone and the other tentatively identified as N-methylcarbidopa. They each accounted for less than five percent of the urinary metabolites. Unchanged carbidopa is also present in the urine. No conjugates were found.

Levodopa

Absorption

Levodopa is rapidly absorbed from the gastro-intestinal tract.

Metabolism and Excretion

Levodopa is extensively metabolised. Although more than 30 metabolites may be formed, it is converted mainly to dopamine and in lesser amounts, to adrenaline and noradrenaline. These are ultimately metabolised to the principal excretion products, dopacetic acid, homovanillic acid and vanillylmandelic acid.

When single test doses of radioactive levodopa are given to fasting patients with Parkinson's disease, plasma levels of radioactivity peak in one-half to two hours and remain measurable for four to six hours. At peak levels, about 30 percent of the radioactivity appears as catecholamines, 15 percent as dopamine and 10 percent as dopa.

Radioactive compounds are rapidly excreted in the urine, one-third of the dose appearing in two hours. Eighty to ninety percent of urinary metabolites are phenylcarboxylic acids, principally homovanillic acid. Over 24 hours, one to two percent of recovered radioactivity is dopamine and less than one percent is adrenaline, noradrenaline and unchanged levodopa.

Effect of carbidopa on levodopa metabolism
Carbidopa consistently increased plasma levels of levodopa by statistically significant amounts, as measured against placebo, in healthy subjects. This has been demonstrated when carbidopa is given before levodopa and when the two drugs are given simultaneously. In one study, pretreatment with carbidopa increased plasma levels of a single dose of levodopa about five times and extended the duration of measurable plasma concentrations of levodopa from four hours to eight hours. When the two drugs were given simultaneously in other studies, similar results were obtained.

In a study in which a single dose of stem-labelled levodopa was given to patients with Parkinson's disease who had been pretreated with carbidopa, there was an increase in the half-life of total plasma radioactivity derived from the levodopa from 3 hours to 15 hours. The proportion of radioactivity remaining as unmetabolised levodopa was increased at least three times by carbidopa. Plasma and urinary dopamine and homovanillic acid were both decreased by carbidopa pretreatment.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

Please see **Carcinogenicity** subsection below.

Carcinogenicity

In a two-year bioassay with levodopa and carbidopa, no evidence of carcinogenicity was found in rats receiving doses of approximately two times the maximum daily human dose of carbidopa and four times the maximum daily human dose of levodopa.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPENTS

In addition to the active ingredients carbidopa and levodopa, each tablet contains the following inactive ingredients: microcrystalline cellulose, magnesium stearate, pregelatinised maize starch, maize starch, indigotine (250/25 mg tablet), quinoline yellow (100/25 mg tablet).

6.2 INCOMPATIBILITIES

Not applicable.

6.3 SHELF LIFE

The expiry date can be found on the packaging. In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG).

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 30°C. Keep in tightly closed container, protected from light and moisture.

6.5 NATURE AND CONTENTS OF CONTAINER

SINEMET 250/25. Supplied in bottles of 100 - AUST R 319331.

SINEMET 100/25. Supplied in bottles of 100 - AUST R 319330.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

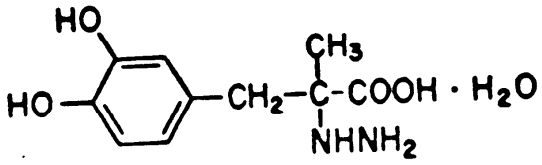
SINEMET is a combination of levodopa, the metabolic precursor of dopamine, and carbidopa, an aromatic amino acid decarboxylase inhibitor, for the treatment of Parkinson's disease and syndrome.

Carbidopa
The empirical formula is $C_{10}H_{14}N_2O_4.H_2O$ with a molecular weight of 244.3. It is designated chemically as (-)-L-alpha-hydrazino-alpha-methyl-beta-(3,4-dihydroxy-benzene) propanoic acid monohydrate. Tablet content is expressed in terms of anhydrous carbidopa, which has a molecular weight of 226.3.

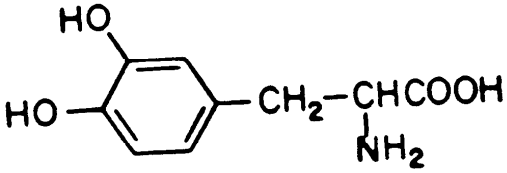
Levodopa
The empirical formula is $C_9H_{11}NO_4$ with a molecular weight of 197.2. It is designated chemically as (-)-L-alpha-amino-beta-(3,4-dihydroxybenzene) propanoic acid.

Chemical structure

Carbidopa
The structural formula is:



Levodopa
The structural formula is:



CAS number

Carbidopa
28860-95-9

Levodopa
59-92-7

7 MEDICINE SCHEDULE (POISONS STANDARD)

Prescription Only Medicine (S4)

8 SPONSOR

Organon Pharma Pty Ltd
Building A, 26 Talavera Road
Macquarie Park NSW 2113

9 DATE OF FIRST APPROVAL

13 April 2011

10 DATE OF REVISION

9 April 2021

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
4.2	Clarifying safety information regarding scoreline of tablet

S-IPC-MK0295B-T-082020

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