Carbidopa is used with carbidopa-levodopa or with levodopa to permit the administration of lower doses of levodopa with reduced nausea and vomiting, more rapid onset of action, and with a somewhat smoother doser response. However, patients with markedly irregular (“on-off”) responses to levodopa have not been shown to benefit from carbidopa.

Since carbidopa prevents the reversal of levodopa effects caused by pyridoxine, supplemental pyridoxine (vitamin B₆) can be given to patients when they are receiving carbidopa-levodopa or levodopa with pyridoxine.

Although the administration of carbidopa permits control of parkinsonism and Parkinson’s disease with much lower doses of levodopa, there is no conclusive evidence that this is beneficial other than in reducing nausea and vomiting, permitting more rapid titration, and providing a more even levodopa effect over time when compared with levodopa alone.

Certain patients who responded poorly to levodopa alone have improved when carbidopa and levodopa were given concurrently. This was most likely due to decreased activity of carbidopa on the peripheral nervous system. Carbidopa has not been shown to enhance the intrinsic efficacy of levodopa.

In deciding whether to give carbidopa-levodopa or levodopa to patients who have nausea and/or vomiting, the physician should be aware that, while many patients may be expected to improve, some may not. Since one cannot predict which patients are likely to improve, this can only be determined by a trial of therapy. It should be further noted that many patients who respond to the combination initially have nausea and vomiting spontaneously or despite being maintained on the same dose of levodopa during the control period.

**CONTRAINDICATIONS**

Carbidopa is contraindicated in patients with known hypersensitivity to any component of this drug.

Nonselective monoamine oxidase (MAO) inhibitors are contraindicated for use with levodopa or carbidopa-levodopa combination products with or without carbidopa. These inhibitors must be discontinued at least two weeks prior to initiating therapy with levodopa. Carbidopa-levodopa, or levodopa may be administered concomitantly with the manufacturer’s recommended dose of MAO inhibitor if otherwise indicated (see PRECAUTIONS, Drug Interactions).

Levodopa or carbidopa-levodopa products, with or without carbidopa, are contraindicated in patients with narrow-angle glaucoma.

**WARNINGS**

Carbidopa has no antiparkinsonian effect when given alone. It is indicated for use with carbidopa-levodopa or levodopa does not alter the adverse reactions of levodopa; however, carbidopa does not decrease the adverse reactions due to the central effects of levodopa. Because carbidopa permits more rapid onset of levodopa action, the incidence of carbidopa-induced nausea and vomiting is less when carbidopa is used with levodopa than when levodopa is used without carbidopa. In patients this redution in nausea and vomiting will permit more rapid dosage titration.

Carbidopa inhibits decarboxylase of peripheral levodopa. Carbidopa has not been shown to inhibit dopamine release or dopamine receptors or dopamine actions in the recommended doses. It does not appear to cross the blood-brain barrier readily and does not affect the metabolism of levodopa within the central nervous system at doses of carbidopa that are recommended for maximum effective inhibition of peripheral decarboxylation of levodopa.

Since its decarboxylase-inhibiting activity is limited primarily to extrarenal tissues, administration of carbidopa with levodopa makes levodopa more useful for patients with renal failure. Levodopa and carbidopa compete with certain amino acids for transport across the gut wall. The addition of carbidopa to levodopa therapy, which inhibits decarboxylase, may be accompanied by nausea and other adverse reactions, some of which are attributable to dopamine formed in extrarenal tissues.

In clinical pharmacologic studies, simultaneous administration of separate tablets of carbidopa and levodopa produced primary renal excretion of levodopa in proportion to the excretion of dopamine when compared to the two drugs administered at separate times.

Pseudobulbar palsy (vitamin B₆) can be given to patients when they are receiving levodopa and carbidopa concurrently or the fixed combination carbidopa-levodopa. However, levodopa, the metabolic precursor of dopamine, does cross the blood-brain barrier, and presumably it is concentrated in the brain. This is thought to be the mechanism whereby levodopa relieves symptoms of Parkinson’s disease.

**Pharmacodynamics**

When levodopa is administered orally it is rapidly decarboxylated to dopamine in extrarenal tissues. Administration of decarboxylase inhibition is ineffective in the treatment of Parkinson’s disease apparently because it does not reduce the brain levels of levodopa. The levodopa monoamine precursor of dopamine, does cross the blood-brain barrier, and presumably it is concentrated in the brain. This is thought to be the mechanism whereby levodopa relieves symptoms of Parkinson’s disease.

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The introduction of carbidopa to levodopa therapy, which inhibits decarboxylase, may be accompanied by nausea and other adverse reactions, some of which are attributable to dopamine formed in extrarenal tissues.

**Pharmacokinetics**

Carbidopa reduces the amount of levodopa required to produce a given response by about 75% and, when administered with levodopa, increases both plasma levels of levodopa and its bioavailability, and decreases plasma and urinary dopamine and homovanillic acid.

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**INDICATIONS AND USAGE**

Carbidopa tablets are indicated for use with carbidopa-levodopa or with levodopa in the treatment of the symptoms of parkinsonism by improving the mobility and control of the extrapyramidal muscle system. Its characteristic features include resting tremor, rigidity, and bradykinetic movements. Symptomatic treatments, such as levodopa therapies, may permit the patient better mobility.

**Mechanism of Action**

Current evidence indicates that symptoms of Parkinson’s disease are related to the substantia nigra’s lack of dopaminergic neurons. Administration of dopamine, 3-4 times normal dose, is effective in the treatment of Parkinson’s disease apparently because it does not cross the blood-brain barrier and presumably it is concentrated in the brain. This is thought to be the mechanism whereby levodopa relieves symptoms of Parkinson’s disease.

**Pharmacokinetics**

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Carbidopa inhibits decarboxylase of peripheral levodopa. Carbidopa has not been shown to inhibit dopamine release or dopamine receptors or dopamine actions in the recommended doses. It does not appear to cross the blood-brain barrier readily and does not affect the metabolism of levodopa within the central nervous system at doses of carbidopa that are recommended for maximum effective inhibition of peripheral decarboxylation of levodopa.

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The introduction of carbidopa to levodopa therapy, which inhibits decarboxylase, may be accompanied by nausea and other adverse reactions, some of which are attributable to dopamine formed in extrarenal tissues.
Contraindications

The combination products, is started, dosage adjustment of the antihypertensive drug may be required.

Caution should be exercised when the following drugs are administered concomitantly with carbidopa and carbidopa-levodopa preparations.

Dopamine D2 receptor antagonists (e.g., phenothiazines, butyrophenones, metoclopramide, antipsychotic agents), and other dopamine D2 receptor antagonists may be associated with severe orthostatic hypotension not attributable to carbidopa-levodopa alone (see CONTRAINDICATIONS).

There have been rare reports of adverse reactions, including hypotension and dizziness, resulting from the concomitant use of tyrocarbazine and levodopa preparations.

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