When carbidopa is to be given to carbidopa-naive patients who are being treated with levodopa, the two drugs should be given at the same time, starting with either levodopa or carbidopa alone. The addition of levodopa when given without carbidopa. At least twelve hours should elapse between the last dose of levodopa and initiation of therapy with carbidopa and levodopa in combination. With start with no more than one-fifth (25%) to one-fourth (25%) of the previous daily dosage of levodopa when initiating therapy with carbidopa, carbidopa-levodopa tablets. See the WARNINGS and DOSE AND ADMINISTRATION sections before initiating therapy.

When carbidopa tablets contain 25 mg of carbidopa. Inactive ingredients are cellulose, silicon dioxide, FDC Red 40, yellow, and magnesium stearate and purified water. Tablet content is expressed in terms of its active component, a molecular weight of 231.5.

**CLINICAL PHARMACOLOGY**

Parkinson’s disease is a progressive, neurodegenerative disorder of the extrapontinal nervous system affecting the mobility and control of the skeletal muscular system. Its characteristic features include resting tremor, rigidity, and bradykinesia movements. Symptomatic treatments, such as levodopa therapy, only can permit the patient better mobility.

**Mechanism of Action**

Current evidence indicates that symptoms of Parkinson’s disease are related to depletion of dopamine in the corpus striatum. Administration of dopamine is ineffective in the treatment of Parkinson’s disease apparently because it does not cross the blood-brain barrier. However, levodopa, the metabolic precursor of dopamine, does cross the blood-brain barrier, and presumably is converted to dopamine 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 extrapontinal tissues so that only a small portion of a given dose is transported unchanged to the central nervous system. For this reason, large doses of levodopa or its analogues are required to achieve therapeutic levels of dopamine in the brain. Carbidopa, which is a competitive inhibitor of dopa decarboxylase may therefore be used to diminish this peripheral decarboxylation and thus increase the amount of levodopa that reaches the central nervous system. The addition of carbidopa with levodopa or carbidopa-levodopa reduces the peripheral effects (effects, nausea) due to levodopa. However, carbidopa does not decrease the adverse reactions due to the central effects of levodopa. Because carbidopa permits more levodopa to reach the brain and more dopamine to be formed from levodopa, adverse effects, e.g., dyskinesia (involuntary movements), may occur at lower doses and sooner with levodopa in combination with carbidopa than with levodopa alone.

**Falling Asleep**

Patients taking carbidopa-levodopa products alone or with other dopaminergic drugs have reportedly suddenly falling asleep without prior warning of sleepiness when engaged in activities of daily living (includes operation of indoor vehicles). Some of these episodes resulted in automobile accidents. Although many of these patients reported sleepiness while on dopaminergic medications, some did report that they had no warning signs, such as excessive drowsiness, and believed that they were alert immediately prior to the event. Some patients reported these events were associated with fluctuations of levodopa dose, others with the addition of another medication for levodopa. Falling asleep while engaged in activities of daily living usually occurs in patients experiencing pre-existing sleepiness, although some patients may note a such history. For this reason, prescribers should continually reassess patients for drowsiness associated with levodopa, especially since some of those who fall asleep may occur the day after the start of treatment. Prescribers should be aware that patients may not acknowledge drowsiness or sleepiness until directly questioned about their ability to work or drive while taking carbidopa-levodopa. Patients who have already experienced sleepiness or an episode of sudden sleep onset should not participate in these activities during treatment with carbidopa when taking with other carbidopa-levodopa products.

**Impulse Control/Compulsive Behaviors**

Postmarketing reports suggest that patients treated with anti-Parkinson medications can experience intense urges to gamble, increase sexual urges, engage in excessive eating, and other intense urges. Patients may be unable to control these urges while taking one or more of the medications that are used for the treatment of Parkinson’s disease, including dopamine and clozapine, antipsychotics, and other dopamine-related agents. Carbidopa tablets are for use with levodopa in the occasional patient whose dosage requirement of levodopa is greater than can be maintained with levodopa alone. Carbidopa tablets are used with levodopa-levodopa or with levodopa to permit the administration of the dosage of levodopa with reduced nausea and vomiting, more rapid dosage titration, and with a somewhat smoother response to therapy. Patients with marked visual inaccuracy (“on-off”) responses to levodopa have not been shown to benefit from the addition of carbidopa.

**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 products without discontinuation of the MAO inhibitor. These inhibitors must be discontinued at least two weeks prior to initiating therapy with levodopa. Carbidopa-levodopa or levodopa may be administered concurrently with other MAO inhibitors. One MAO inhibitor with selectivity for MAO type B (e.g., selegiline HCl) (see PRECAUTIONS, Drug Interactions). Levodopa or carbidopa-levodopa products, or 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. Carbidopa does not decrease adverse reactions due to central effects of levodopa. When carbidopa is to be given to carbidopa-naive patients who are being treated with levodopa, the two drugs should be given at the same time.
Carbidopa and iron salts or multivitamins containing iron salts should be co-administered with caution.

Somnia and/or sudden sleep onset, they must refrain from these activities. (See WARNINGS, Falling Asleep During Activities of Daily Living and Somnolence General.)

There were no significant differences between treated and control rats with respect to mortality or mutagenicity studies have not been performed with either carbidopa or the combination of carbidopa and levodopa.

There are no adequate and well-controlled studies with carbidopa in pregnant women. It has been reported from individual cases that levodopa crosses the human placental barrier enters the fetus, and is metabolized. Carbidopa concentrations in fetal tissue appeared to be minimal. Carbidopa should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Carbidopa is given as high as 125 mg/day, was without teratogenic effects in the mouse or rat. In the mouse, carbidopa produced only incidental anomalies, similar to those seen with levodopa alone, at approximately 7 times the maximum recommended human dose. The teratogenic effects of levodopa in rabbits was unchanged by the concurrent administration of carbidopa.

It is not known whether carbidopa is excreted in human milk. Because many drugs are excreted in human milk, especially because of the high concentration of levodopa, caution should be exercised when carbidopa is administered to a nursing woman.

Carbidopa has demonstrated that it has no ovulation pharmacodynamic actions in the recommended doses. The only adverse reactions that may have been observed have been with concurrent use of carbidopa with other drugs such as levodopa, and levodopa-combination products.

Contraindications: Levodopa and carbidopa-levodopa combination products 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 the use of urine strips. False-negative tests may result with the use of glucose-oxidase methods of testing for glucose.

Drug Interactions: Caution should be exercised when the following drugs are administered concomitantly with carbidopa/levodopa (See PRECAUTIONS, Impulse Control/Compulsive Behaviors).

ADVERSE REACTIONS

Cardiovascular: orthostatic hypotension, palpitation, phlebitis, syncope.

Symptomatic postural hypotension has occurred when carbidopa, given with levodopa or carbidopa-levodopa combination products, was added to the treatment of a patient receiving antiparkinsonian drugs.

There have been reports of patients experiencing intense urges to gamble, increased sexual urges, and other intense urges, and the inability to control those urges while taking one or more of the medications that are generally used for the treatment of Parkinson’s disease, including carbidopa and levodopa. Although it is not proven that the medications caused these events, the medications were stopped in some cases when the dose was reduced or medication was stopped. Prescribers should ask patients about the development of new or increased carbidopa and levodopa. Physicians should consider dose reduction or stopping carbidopa and levodopa if a patient develops such urges while taking carbidopa with carbidopa-levodopa (See PRECAUTIONS, Impulse Control/Compulsive Behaviors).

Hypersensitivity: flushing, increased sweating, malignant melanosis (see also CONTRAINDICATIONS), rash, alopecia, dark sweat.

Special senses: oculogyric crises, diplopia, blurred vision, dilated pupils.

Uncommon: dark urine, priapism, urinary function, urinary incontinence, urinary retention, urinary tract infection.

DOSAGE AND ADMINISTRATION

Whether given with levodopa-levodopa or with levodopa, the optimal daily dose of carbidopa must be determined by careful titration. Most patients require 100 mg of levodopa equivalent of carbidopa on an average of 6 to 10 times a day to achieve the desired therapeutic effect.

Some patients taking carbidopa-levodopa may not have adequate reduction in nausea and vomiting when levodopa is given without carbidopa. The occurrence of involuntary movements may require dosage reduction. Blepharospasm may be a useful early sign of excess dosage insome patients.

Sporadic cases of hyperpyrexia and confusion have been associated with dose reductions and withdrawal of carbidopa-levodopa or carbidopa-levodopa extended release tablets. Patients should be observed carefully if abrupt reduction or discontinuation of carbidopa-levodopa or carbidopa-levodopa extended release tablets is required, especially if the patient is receiving neuroleptics. (See WARNINGS.)

If general anesthesia is required, therapy may be continued as long as the patient is permitted to take fluids and medication by mouth. When anesthesia is interrupted, the patient should be observed for symptoms resembling MMS, and the usual daily dosage may be resumed as soon as the patient is able to take medication readily.

HOW SUPPLIED

Carbidopa Tablets 25 mg, are light pink, round, standard coneshaped tablets with '323' embossed over the functional scoring on one side and plain on the other side.

They are supplied as:

MDC: 42379/120-65 bottles of 10 tablets

MDC: 42379/120-100 bottles of 10 tablets

Storage: Store at 25°C (77°F), excursions permitted to 15°C to 30°C (59°F to 86°F) (see USP Controlled Temperature).

Manufactured for: EdmontPharmaceuticals, LLC

Pemberton, NS B0N 1N0

877-381-3336

Rev 03/15

ADVERSE REACTIONS

Cardiovascular: orthostatic hypotension, palpitation, phlebitis, syncope.

Gastrointestinal: nausea, vomiting, diarrhea, constipation, changes in appetite or weight, increased hunger.

Hypersensitivity: angioneurotic, urticaria, pruritus, Henoch-Schönlein purpura, bullous lesions (including pemphigoid and epidermolysis.)

Metabolic: edema, weight gain, weight loss.

Miscellaneous: back pain, leg pain, muscle cramps, shoulder pain.

Nervous System: insomnia, mental depression, including delusions, hallucinations and paranoid ideation, neurologic malignant syndrome (MMS, see WARNINGS), brainstem-opioidic spinoff phenomenon, confusion, agitation, dizziness, somnolence, dream abnormalities including nightmares, insomnia, paresthesia, headache, depression with or without development of suicidal tendencies, dementia, pathological gambling, increased libido including hypersexuality, impulse control symptoms. Convulsions also have occurred; however, a causal relationship with carbidopa and levodopa has not been established.

Respiratory: upper respiratory infection, dyspnea, pharyngitis, cough.

Skin: flushing, increased sweating, malignant melanosis (see also CONTRAINDICATIONS), rash, atopic dermatitis.

Hematologic: hemolytic and non-hemolytic anemia, leucopenia, thrombocytopenia, agranulocytosis.

Psychotic episodes including delusions, hallucinations and paranoid ideation, neurologic malignant syndrome (MMS, see WARNINGS), brainstem-opioidic spinoff phenomenon, confusion, agitation, dizziness, somnolence, dream abnormalities including nightmares, insomnia, paresthesia, headache, depression with or without development of suicidal tendencies, dementia, pathological gambling, increased libido including hypersexuality, impulse control symptoms. Convulsions also have occurred; however, a causal relationship with carbidopa and levodopa has not been established.