MedChoice
CNS

Levodopa + Carbidopa

Sinedin

100 mg / 25 mg Tablet • 250 mg / 25 mg Tablet

ANTI-PARKINSONISM

FORMULATION:

Each 100 mg/ 25 mg tablet contains:
Levodopa, USP.....100 mg
Carbidopa, USP..... 25 mg
Each 250 mg/ 25 mg tablet contains:
Levodopa, USP..... 250 mg
Carbidopa, USP..... 25 mg

PRODUCT DESCRIPTION:

Levodopa+Carbidopa 100 mg/ 25 mg Tablet (Sinedin) is a light yellow, mottled, oval shaped biconvex tablet, scored on one side and plain on the other side.
Levodopa+Carbidopa 250 mg/ 25 mg Tablet (Sinedin) is a light blue, mottled, oval shaped, biconvex tablet, scored on one side and plain on the other side.

INDICATION:

Treatment of Parkinson's disease specifically on idiopathic Parkinsonism.

CLINICAL PHARMACOLOGY:

Mechanism of Action:
Levodopa is a metabolic precursor of dopamine that readily crosses blood-brain barrier.

Pharmacodynamics:

Levodopa, when administered orally, is rapidly decarboxylated to dopamine on extracerebral tissues so that only portion of a given dose is transported unchanged to the central nervous system.
Carbidopa inhibits decarboxylation of peripheral levodopa. It does not cross blood-brain barrier and does not affect the metabolism of levodopa within the central nervous system.

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.
Levodopa is rapidly absorbed from the gastrointestinal tract by an active transport system. Most absorption takes place in the small intestine; absorption is very limited from the stomach, and since decarboxylation may take place in the stomach wall, delays in gastric emptying may reduce the amount of levodopa available for absorption.
Levodopa is rapidly decarboxylated by the enzyme aromatic L-amino acid decarboxylase, mostly in the gut, liver, and kidney, to dopamine which is metabolized, principally to dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA). Other routes of metabolism include O-methylation, transamination, and oxidation, producing a variety of minor metabolites including noradrenaline and 3-O-methyldopa; the latter may accumulate in the CNS due to its relatively long half-life. The plasma half-life of levodopa itself is reported to be about 1 to 3 hours.
Unlike dopamine, levodopa is actively transported across the blood-brain barrier, but because of the extent of the peripheral decarboxylation, very little is available to enter the CNS unless it is given in association with a peripheral dopa-decarboxylase inhibitor, the major route of metabolism of levodopa becomes the formation of 3-O-methyldopa by the enzyme cathechol-O-methyltransferase.
About 80% of an oral dose of levodopa is excreted in the urine within 24 hours, mostly as dihydroxyphenylacetic acid and homovanillic acids. Only small amounts of levodopa are excreted unchanged in the feces.

DOSAGE AND ADMINISTRATION:

Dosage depends on patient's response. Optimum daily dosage must be determined by careful titration in each patient.
Usual starting dose: One (1) tablet of 100 mg/ 25 mg of Levodopa+Carbidopa (Sinedin) three times daily to provide 75 mg of carbidopa daily. Dose may be titrated by increasing one tablet every day or every other day, as necessary, until a dosage of eight (8) tablets (2 tablets q.i.d) of 100 mg/ 25 mg of Levodopa+Carbidopa (Sinedin) a day is reached.
Maintenance dose: Dosing should be individualized depending on patient response. As a maintenance dose, at least 70 to 100 mg of carbidopa per day should be provided. If higher dose of levodopa is required, 250 mg/ 25 mg of Levodopa+Carbidopa (Sinedin) should be substituted for 100 mg/ 25 mg doses. If necessary, the 250 mg/ 25 mg dose may be increased by one-half or one tablet every day or every other day to a maximum of eight (8) tablets daily. Maximum dose for carbidopa is 200 mg daily.
Or as prescribed by the physician.

WARNINGS AND PRECAUTIONS:

In patients being treated with levodopa alone, levodopa must be discontinued at least twelve hours before initiating Levodopa+Carbidopa Tablet (Sinedin) therapy to reduce adverse reactions.
This product should not be given in patients with narrow-angle glaucoma, undiagnosed skin lesions or history of melanoma. Patients should be observed carefully for the development of depression with concomitant suicidal tendencies. Caution should be taken when given to patients with severe cardiovascular or pulmonary disease, bronchial asthma, renal, hepatic or endocrine disease. This product should be given cautiously to patients with a history of myocardial infarction who have residual atrial, nodal, or ventricular arrhythmias. It may also increase the risk of upper gastrointestinal hemorrhage in patients with a history of peptic ulcer disease. It should not be given to patients hypersensitive to levodopa, carbidopa, or any of its ingredients.
Effect on ability to drive or operate machinery: Levodopa+Carbidopa Tablet (Sinedin) may cause drowsiness; advice patients to exercise caution while driving or operating machines during treatment.

CONTRAINDICATIONS:

Non-selective Monoamine Oxidase (MAO) inhibitors are contraindicated for use with Levodopa+Carbidopa Tablet (Sinedin). These inhibitors must be discontinued at least two weeks prior to initiating therapy.
Levodopa+Carbidopa Tablet (Sinedin) may be administered concomitantly with the recommended dose of a MAO inhibitor with selectivity for MAO type B (e.g., selegiline HCl) (see DRUG INTERACTIONS). It is contraindicated in patients with known hypersensitivity to any component of this medication, and in patients with narrow-angle glaucoma. Since levodopa may activate a malignant melanoma, it should not be used in patients with suspicious undiagnosed skin lesions or a history of melanoma.

PREGNANCY AND LACTATION:

Pregnancy Category C: Either study in animals has revealed adverse effects on the fetus and there are no controlled studies in women or studies in women and animals are not available. Drugs should be given only if the potential benefit justifies the potential risk to the fetus. Levodopa has been detected in human milk. Caution should be exercised when Levodopa+Carbidopa Tablet (Sinedin) is administered to a nursing woman.

DRUG-DRUG INTERACTIONS:
Caution should be exercised when the following drugs are administered concomitantly with Levodopa+Carbidopa Tablet (Sinedin).

Antihypertensive agents: Symptomatic postural hypotension may occur when added to the treatment of patients receiving some antihypertensive drugs. Therefore, when therapy with Levodopa+Carbidopa Tablet (Sinedin) is started, dosage adjustment of the antihypertensive drug may be required.
Antidepressants: For patients receiving monoamine oxidase inhibitors, see CONTRAINDICATIONS. Potential risk for hypertension and dyskinesia may result from concomitant use of tricyclic antidepressants and Levodopa+Carbidopa Tablet (Sinedin).
Other drugs: Dopamine D2 receptor antagonists (e.g., 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 Levodopa+Carbidopa Tablet (Sinedin) should be observed carefully for loss of therapeutic response. Concomitant therapy with selegiline may be associated with severe orthostatic hypotension not attributable to Levodopa+Carbidopa Tablet (Sinedin) alone.

DRUG-FOOD INTERACTION:
Since levodopa competes with certain amino acids, the absorption of levodopa may be impaired in some patients on a high protein diet. Cautiously administer Levodopa+Carbidopa Tablet (Sinedin) with iron salts or multivitamin containing iron salts. Iron salts can form chelates with levodopa and carbidopa and consequently reduce the bioavailability of carbidopa and levodopa.

ADVERSE EFFECTS:
Effects on gastrointestinal system: Nausea, vomiting, and anorexia are common early in the treatment, particularly if the dosage is increased too rapidly. Potential risk of gastrointestinal bleeding in patients with history of peptic ulcer disease.
Effects on cardiovascular system: Orthostatic hypotension, which is usually asymptomatic, but may be associated with faintness and dizziness. Cardiac arrhythmias and hypertension may also occur.
Effects on nervous system: May occur in a high proportion of patients, especially the elderly, and include agitation, anxiety, euphoria, nightmares, and insomnia, or sometimes drowsiness and depression. More serious effects usually requiring a reduction in dosage or withdrawal, includes aggression, paranoid delusions, hallucinations, delirium, severe depression, with or without suicidal behavior, and unmasking of psychoses. Psychotic reactions are more likely in patients with post-encephalitic Parkinsonism or a history of mental disorders.
Effects on musculoskeletal system: Abnormal involuntary movements or dyskinesias are the most serious dose-limiting adverse effects and are very common at the optimum dose required to control Parkinsonism; their frequency increases with the duration of treatment. Involuntary movements of the face, tongue, lip, and jaw often appear first and those of the trunk and extremities later. Severe generalized choreoathetoid and dystonic movements may occur after prolonged administration. Muscle twitching and blepharospasm may be early signs of excessive dosage.
Effects on respiratory system: Exaggerated respiratory movements and exacerbated oculogyric crises have been reported in patients with post-encephalitic Parkinsonism. Re-emergence of bradykinesia and akinesia, in the form of end-of-dose deterioration and the on-off phenomenon, in patients with Parkinsonism is a complication of long-term treatment, but may be due to the progression of the disease rather than to levodopa.
Effects on laboratory tests: A positive response to the direct Coombs' test may occur, usually without evidence of hemolysis although autoimmune hemolytic anemia has occasionally being reported. Transient leucopenia has occurred rarely. The effects of levodopa on liver and kidney function are generally slight. Levodopa may cause discoloration of the urine; reddish at first then darkening on standing. Other body fluids may also be discolored.

"For suspected adverse drug reaction, report to FDA: www.fda.gov.ph.
Seek medical attention immediately at first sign of any adverse drug reaction."

OVERDOSE AND MANAGEMENT:
Pyridoxine is not effective in reversing the actions of Levodopa+Carbidopa Tablet (Sinedin). General supportive measures should be employed, along with immediate gastric lavage. Intravenous fluids should be administered judiciously and an adequate airway maintained. Electrocardiographic monitoring should be instituted and the patient carefully observed 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 Levodopa+Carbidopa Tablet (Sinedin) should be taken into consideration. To date, no experience has been reported with dialysis; hence, its value in overdosage is not known.

CAUTION:
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

STORAGE CONDITION:
Store at temperatures not exceeding 30ºC.
Keep out of reach of children.

AVAILABILITY:
Levodopa+Carbidopa
100 mg/ 25 mg Tablet (Sinedin)…….... In Alu-PVC White Opaque Blister x 10's (Box x 100's)
Registration No.: DR-XY41871
Date of First Authorization: March 2013

Levodopa+Carbidopa
250 mg/ 25 mg Tablet (Sinedin)…….... In Alu-PVC White Opaque Blister x 10's (Box x 100's)
Registration No.: DR-XY41327
Date of First Authorization: November 2012

Date of Revision of Package Insert: April 2017

Manufactured for:
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