LEVODOPA + CARBIDOPA

LAVIDA®

100 mg / 25 mg and 250 mg / 25 mg TABLET

ANTIPARKINSONISM

FORMULATION

Each tablet contains:

Levodopa…….…….….....	100 mg	or	Levodopa.....	250 mg
Carbidopa……..	25 mg		Carbidopa.....	25 mg

PRODUCT DESCRIPTIONS

Levodopa 100 mg + Carbidopa 25 mg is a mottled yellow elliptical tablet, bisected on one side, plain on the other side.
Levodopa 250 mg + Carbidopa 25 mg is a mottled blue elliptical tablet, bisected on one side, plain on the other side.

CLINICAL PHARMACOLOGY

Pharmacodynamics

Levodopa, the metabolic precursor of dopamine, crosses the blood-brain barrier and is converted to dopamine in the basal ganglia. It is believed to act principally by increasing dopamine concentration in the brain. This is thought to be the mechanism whereby levodopa relieves symptoms of Parkinson's disease.

Carbidopa inhibits decarboxylation of peripheral levodopa, resulting to more levodopa available for transport to the brain. Carbidopa does not cross the blood-brain barrier and does not affect the metabolism of levodopa within the central nervous system (CNS). In doses that effectively inhibit peripheral decarboxylation of levodopa, carbidopa has little effect on the CNS, cardiovascular or gastrointestinal (GI) systems.

Levodopa + carbidopa improves overall therapeutic response compared with levodopa alone.

Pharmacokinetics

Levodopa is rapidly decarboxylated to dopamine in extracerebral tissues so that only a small portion of a given dose is transported unchanged to the CNS. Thus, large doses of levodopa are required for adequate therapeutic effect.

Carbidopa reduces the amount of levodopa required to produce a given response by about 75%. When administered with levodopa, carbidopa increases both levodopa's plasma levels and half-life, and decreases plasma and urinary dopamine and homovanillic acid (HVA). Levodopa + carbidopa provides effective long lasting levodopa plasma levels at doses that are approximately 70% to 80% lower than those needed with levodopa alone.

The plasma-half-life of levodopa is about 50 minutes; it is increased to 1.5 hours when carbidopa and levodopa are administered together. At steady state, the bioavailability of carbidopa from levodopa + carbidopa is approximately 99% relative to the concomitant administration of levodopa and carbidopa.

Levodopa is widely distributed into most body tissues and the total volume of distribution is about 65% of body weight. There is considerable uptake of levodopa by the pancreas, liver, GI tract, salivary glands, kidneys, and skin. Levodopa is approximately 10% to 30% bound to plasma proteins. Carbidopa crosses the placenta and is distributed into milk.

Substantial amounts of levodopa are metabolized in the lumen of the stomach and intestines and on first pass through the liver. Most absorbed levodopa is decarboxylated to dopamine; more than 95% of the drug is decarboxylated peripherally by aromatic L-amino acid decarboxylase, a widely distributed enzyme. Small amounts of levodopa are metabolized to norepinephrine, epinephrine and 3-methoxytyramine. Dopamine is further metabolized to 3,4-dihydroxyphenylacetic acid (DOPAC) and 3-methoxy-4-hydroxyphenylacetic acid (HVA) and is excreted in urine. HVA, DOPAC and dopamine are the metabolites of levodopa present in cerebrospinal fluid (CSF). Carbidopa is not extensively metabolized; about 30% of an oral dose of carbidopa is excreted in urine unchanged within 24 hours.

When carbidopa and levodopa are administered concurrently, the urinary excretion of dopamine, DOPAC and HVA is substantially diminished, and the amount of unchanged levodopa excreted in urine has been reported to be increased by 6%.

INDICATION

Treatment of Parkinson's disease and syndrome

DOSAGE AND ADMINISTRATION

The optimum daily dosage of levodopa + carbidopa must be determined by careful titration according to individual requirements, response and tolerance. Titration and dosage adjustment should be made in small steps and the dosage ranges recommended should usually not be exceeded. Treatment with levodopa should not be stopped abruptly.

Levodopa + carbidopa tablets are available in a ratio of 4:1 or 10:1 of levodopa to carbidopa to provide facility for fine dosage titration for each patient.

General Dosing Recommendation:

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

Patients should be carefully monitored during the dosage adjustment period since both therapeutic and adverse effects are seen more rapidly with levodopa + carbidopa than with levodopa alone. Involuntary movements, particularly blepharospasm, are a useful early sign of excess dosage in some patients, thus requiring dose reduction.

STATEMENT ON USAGE FOR HIGH RISK GROUPS

Pregnancy and Lactation

Pregnancy Category C. 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. Levodopa + carbidopa should be administered to pregnant women or women who might become pregnant only when the benefits to the mother outweigh the possible risks to the mother and fetus since there are no adequate or well-controlled studies available.

Breastfeeding: Caution should be exercised since excretion of levodopa in human breast milk was reported in a study of one breastfeeding mother with Parkinson's disease and levodopa inhibits prolactin excretion, interfering with breastfeeding.

Pediatric (< 18 years old)

The use of levodopa + carbidopa in patients below 18 years old is not recommended.

UNDESIRABLE EFFECTS

Body as a whole: *Unknown* - Asthenia, fatigue, malaise, sense of stimulation.
Cardiovascular: *Common* - Orthostatic hypotension. *Uncommon* - Cardiac irregularities and/or palpitation (i.e., sinus tachycardia, ventricular tachycardia or extra systole, atrial flutter or fibrillation, or block of atrioventricular conduction), hypertension. *Rare* - Phlebitis. *Unknown* - Hypotension, syncope, chest pain, myocardial infarction
Dermatologic and Hypersensitivity: *Unknown* - Rash, increased sweating, alopecia, dark sweat, malignant melanoma, angioedema, urticaria, pruritus, Henoch-Schonlein purpura, bullous lesions (including pemphigus-like reactions), flushing, pigmentation of the skin and teeth
Endocrine/Metabolic: *Common* - Anorexia (may be accompanied with weight loss). *Very Rare* - Increased libido including hypersexuality. *Unknown* - Edema, weight gain or loss, priapism, elevated serum glucose, decreased serum potassium, increased uric acid
Gastrointestinal: *Common* - Nausea, vomiting. *Uncommon* - Dark saliva. *Rare* - Epigastric and abdominal pain and distress, diarrhea, constipation. *Unknown* - GI bleeding, development of duodenal ulcer, vomiting, dyspepsia, dry mouth, GI pain, dysphagia, sialorrhea, flatulence, burning sensation of the tongue, hiccups, heartburn, hoarseness, trismus
Hematologic: *Rare* - Leukopenia, agranulocytosis, hemolytic and non-hemolytic anemia, thrombocytopenia, decreased hemoglobin and hematocrit
Musculoskeletal: *Very Common* - Involuntary movements (e.g., grimacing, bruxism, gnawing, chewing, twisting and protrusion of the tongue, rhythmic opening and closing of the mouth, bobbling and wave-like motions of the head with or without gesticulation, slow rhythmic movements of the neck, hands or feet, jerky movements of the shoulder or pelvic girdle, and opisthotonos or ballismus), intermittent myoclonic body jerks during sleep. *Unknown* - Back pain, shoulder pain, muscle cramps, leg pain
Nervous system: *Very Common* - Dyskinesia (e.g., choreiform, dystonic), increased hand tremor,ataxia, agitation, anxiety, euphoria). *Common* - Dream abnormalities including nightmares, insomnia, drowsiness. *Very Rare* - Somnolence (e.g., excessive daytime somnolence and sudden sleep onset episodes, pathological gambling. *Rare* - Headache, paresthesia. *Unknown* - Decreased attention span, insouciance, aggression, psychotic episodes (e.g., delusions, hallucinations, paranoid ideation), NMS, bradykinetic episodes (the “on-off” phenomenon), confusion, dizziness, depression with or without development of suicidal tendencies, dementia, impulse control symptoms (e.g., compulsive spending or buying, binge or compulsive eating), convulsions, extrapyramidal disorder, falling, gait abnormalities, nervousness, decreased mental acuity, memory impairment, disorientation, numbness, activation of latent Horner's syndrome, peripheral neuropathy, faintness, toxic delirium
Respiratory: *Rare* - Stridor, episodic hyperventilation. *Unknown* - dyspnea, upper respiratory infection, pharyngeal pain, cough, bizarre breathing patterns, excessive nasal discharge
Special Senses: *Common* - Blepharospasm. *Rare* - Dilated or constricted pupils, diplopia, blurred vision, precipitation of glaucoma. *Unknown* - Oculogyric crises, taste alterations, widening of the palpebral fissures
Urogenital: *Uncommon* - Polyuria, urinary retention, urinary incontinence, dark urine. *Unknown* - Urinary tract infection, hot flashes, white blood cells, bacteria, and blood in the urine, increased serum creatinine, protein and glucose in urine, postmenopausal bleeding

OVERDOSE AND TREATMENT

Levodopa + carbidopa overdosage requires general supportive measures along with immediate gastric lavage. Intravenous fluids should be given judiciously and an adequate airway maintained. Electrocardiographic monitoring should be instituted and the patient carefully observed for the development of arrhythmias; if necessary, appropriate antiarrhythmic therapy should be given.

The value of hemodialysis in the management of levodopa + carbidopa overdosage is not known. The usefulness of pyridoxine administration during overdosage has not been established, but pyridoxine is not effective in reversing the actions of levodopa + carbidopa combination.

The possibility that the patient may have taken drugs other than levodopa + carbidopa should be taken into consideration.

ADVERSE DRUG REACTION REPORTING STATEMENT

For suspected adverse drug reaction, seek medical attention immediately and report to the FDA at www.fda.gov.ph **AND** Unilab at (+632) 858-1000 or productsafety@unilab.com.ph. By reporting undesirable effects, you can help provide more information on the safety of this medicine.

AVAILABILITY

Levodopa + Carbidopa (Lavida) 100 mg / 25 mg Tablet - Aluminum flex foil x 10’s (Box of 30’s) - DR-XY37524
Levodopa + Carbidopa (Lavida) 250 mg / 25 mg Tablet - Aluminum flex foil x 10’s (Box of 30’s) - DR-XY37438

STORAGE CONDITION

Store at temperatures not exceeding 30°C.
Keep the product out of sight and reach of children.

CAUTION

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

Trusted Quality Healthcare

Manufactured by
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