xxxxxxxx-5343

LEVODOPA + CARBIDOPA

TIDOMET

250 mg / 25 mg Tablet
ANTIPARKINSONISM

FORMULATION
Each tablet contains:
Levodopa, B.P. ..... 250 mg
Carbidopa ..... 25 mg

PRODUCT DESCRIPTION
Levodopa + Carbidopa (Tidomet) 250 mg / 25 mg is a white to off white, round, flat uncoated tablet with break line on one side.

CLINICAL PHARMACOLOGY

Pharmacodynamics
Levodopa, a naturally occurring amino acid, is the immediate precursor of the neurotransmitter dopamine. The actions of levodopa are mainly those of dopamine.
Unlike dopamine, levodopa readily enters the CNS and is used in the treatment of conditions, such as Parkinson's disease, that are associated with depletion of dopamine in the brain. Levodopa is rapidly decarboxylated by peripheral enzymes so that very little unchanged drug is available to cross the blood-brain barrier for central conversion into dopamine.
Consequently, levodopa is usually given with a peripheral dopa-decarboxylase inhibitor such as carbidopa to increase the proportion of levodopa that can enter the brain. This enables the dosage of levodopa to be reduced and may diminish peripheral adverse effects, such as nausea and vomiting and cardiac arrhythmias, by blocking the peripheral production of dopamine. It may also provide a more rapid response at the start of therapy.

Pharmacokinetics
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. Peak plasma concentrations are achieved within 2 hours of oral doses. Levodopa is about 10 to 30% bound to plasma proteins. Levodopa is rapidly decarboxylated by the enzyme aromatic L-amino acid decarboxylase, mostly in the gut, liver, and kidney, to dopamine, which is metabolized in turn, 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 elimination half-life of levodopa itself is reported to be about 30 to 60 minutes.
Unlike dopamine, levodopa is actively transported across the blood-brain barrier, but because of the extent of peripheral decarboxylation very little is available to enter the CNS unless it is given with a peripheral dopa-decarboxylase inhibitor. In the presence of a peripheral dopa-decarboxylase inhibitor the major route of metabolism of levodopa becomes the formation of 3-O-methyldopa by the enzyme catechol-O-methyltransferase.
About 80% of an oral dose of levodopa is excreted in the urine within 24 hours, mainly as dihydroxyphenylacetic and homovanillic acids. Only small amounts of levodopa are excreted unchanged in the faeces.
Levodopa crosses the placenta and is distributed into breast milk.

INDICATIONS
Symptoms of idiopathic Parkinson's disease (paralysis agitans), postencephalitic parkinsonism, which may follow injury to the nervous system by carbon monoxide intoxication and manganese intoxication.

DOSAGE AND ADMINISTRATION
Carefully titrate dosage in each patient. Initiate treatment with 1 tablet of co-careldopa. Plus 3 times a day. Dosage may be increased by 1 tablet a day or every other day as necessary until a dosage of 8 tablets of co-careldopa plus per day is reached. If co-careldopa LS is used, initiate 1 tablet 3 or 4 times a day and increased by 1 tablet every day or every other day until a total 8 tablets i.e. 2 tablets 4 times a day is reached. Transferring patients from levodopa to co-careldopa, levodopa must be discontinued at least before 8 hours. 1/4 th of the previous levodopa dosage may be started as co-careldopa. Patients taking less than 1500 mg of levodopa per day should be started on one tablet of co-careldopa. Plus 3-4 times a day. Maintenance therapy should be individualized and adjusted according to the desired therapeutic response.
When a greater proportion of carbidopa is required, one tablet of co-careldopa plus may be substituted for each tablet of co-careldopa LS. When more levodopa is required co-careldopa forte should be substituted at a dosage of 1 tablet 3 or 4 times a day. If necessary the dosage may be increased by 1/2 or 1 tablet everyday or every other day to a maximum of 8 tablets a day. The occurrence of involuntary movements may require dosage reduction; Blepharospasm may be a useful early sign of excess dosage in some patients.

CONTRAINDICATIONS
Known hypersensitivity to any of the components, narrow angle glaucoma, patients with suspicious undiagnosed skin lesions or a history of melanoma. MAO inhibitors must be discontinued at least 2 weeks prior to initiating therapy because of likelihood of development of high blood pressure if both the drugs are given concomitantly.

WARNINGS AND PRECAUTIONS
Levodopa is contraindicated in patients with angle closure glaucoma and should be used with caution in open-angle glaucoma. Caution is also required in patients with cardiovascular disease, pulmonary disease, endocrine disorders, psychiatric disturbances, osteomalacia, hepatic or renal disease, or a history of peptic ulceration. Periodic evaluations of hepatic, psychiatric, haematological, renal, and cardiovascular functions have been advised.
Since an association between levodopa and activation of malignant melanoma has been suspected (although not confirmed), it is generally recommended that levodopa should not be given to patients with (or with a history of) the disease or with skin disorders suggestive of it.
Parkinsonian patients who benefit from levodopa therapy should be warned to resume normal activities gradually to avoid the risk of injury. Treatment with levodopa should not be stopped abruptly. Excessive daytime sleepiness and sudden onset of sleep may occur with levodopa and caution is advised when driving or operating machinery; patients who suffer such effects should not drive or operate machinery until the effects have stopped recurring.
Levodopa inhibits prolactin secretion and may therefore interfere with lactation. Food interferes with the absorption of levodopa, though levodopa is usually given with or immediately after meals to reduce nausea and vomiting. However, patients experiencing the 'on-off' phenomenon may benefit from dosage on an empty stomach.

USE IN PREGNANCY, NURSING MOTHERS AND CHILDREN
Co-careldopa must be used in women of child bearing age group after weighing the possible hazard to the mother and the child.
Co-careldopa should not be given to nursing mothers.

DRUG INTERACTIONS
The therapeutic or adverse effects of levodopa may be affected by interactions with a variety of drugs. Mechanisms may include effects on catecholamine metabolizing enzymes, neurotransmitters, or receptor sites, effects on the endocrine system, and effects on gastrointestinal absorption. Drugs that modify gastric emptying may affect the absorption of levodopa.

ADVERSE REACTIONS
Gastrointestinal effects, notably nausea, vomiting, and anorexia are common early in treatment with levodopa, particularly if the dosage is increased too rapidly. Gastrointestinal bleeding has been reported in patients with a history of peptic ulcer disease.
The commonest cardiovascular effect is orthostatic hypotension, which is usually asymptomatic, but may be associated with faintness and dizziness. Cardiac arrhythmias have been reported and hypertension has occasionally occurred.
Psychiatric symptoms occur in a high proportion of patients, especially the elderly, and include agitation, anxiety, euphoria, nightmares, insomnia or sometimes drowsiness, and depression.
More serious effects, usually requiring a reduction in dosage or withdrawal of levodopa, include aggression, paranoid delusions, hallucinations, delirium, severe depression, with or without suicidal behaviour, and unmasking of psychoses. Psychotic reactions are more likely in patients with postencephalitic parkinsonism or a history of mental disorders. Excessive daytime sleepiness and sudden onset of sleep have been reported very rarely.
Abnormal involuntary movements or dyskinesias are the most serious dose-limiting adverse effects of levodopa and are very common at the optimum dose required to control parkinsonism; their frequency increases with duration of treatment. Involuntary movements of the face, tongue, lips, and jaw often appear first and those of the trunk and extremities later.
Severe generalized choreoathetoid and dystonic movements may occur after prolonged use. Muscle twitching and blepharospasm may be early signs of excessive dosage. Exaggerated respiratory movements and exacerbated oculogyric crises have been reported in patients with postencephalitic parkinsonism. Bradykinesia and akinesia, in the form of 'end-of-dose' deterioration and the 'on-off' phenomenon, may reemerge in patients with parkinsonism as a complication of long-term treatment, but may be due to progression of the disease rather than to levodopa.
A positive response to the direct Coombs' test may occur, usually without evidence of haemolysis although auto-immune haemolytic anaemia has occasionally been reported. Transient leucopenia and thrombocytopenia have occurred rarely. The effects of levodopa on liver and kidney function are generally slight; transient increases in liver enzymes, and in blood-urea nitrogen and serum-uric acid concentrations, have been reported. Levodopa may cause discoloration of the urine; reddish at first then darkening on standing. Other body fluids may also be discoloured.
Some of the adverse effects reported may not be attributable directly to levodopa, but rather to the use of antimuscarinics, to increased mobility, or to the unmasking of underlying conditions as parkinsonism improves. Use with a peripheral dopa-decarboxylase inhibitor may reduce the severity of peripheral symptoms such as gastrointestinal and cardiovascular effects, but central effects such as dyskinesias and mental disturbances may occur earlier in treatment.
"For suspected adverse drug reaction, report to FDA: www.fda.gov.ph or to TORRENT: www.torrentpharma.com".
Patient to seek medical attention immediately at the first sign of any adverse drug reaction shall appear.

OVERDOSAGE AND TREATMENT
Reduction in dosage reverses most of the adverse effects of levodopa. Nausea and vomiting may be diminished by increasing the dose of levodopa gradually, and/or by taking with or after meals, although taking levodopa on a full stomach may lead to lower plasma concentrations. Gastrointestinal effects may also be reduced by giving an antiemetic such as cyclizine or domperidone but not a phenothiazine. Use with a peripheral dopa-decarboxylase inhibitor reduces peripheral but not central adverse effects. Orthostatic hypotension may respond to the use of elastic stockings.
The benefits of gastric decontamination are uncertain. However, activated charcoal should be considered in adults who have ingested more than 2 g (or more than the total daily dose, whichever is greater), and in children who have taken more than 200 mg, if they present within 1 hour of ingestion. Supportive measures should also be instituted. Pyridoxine may increase the metabolism of levodopa but its value in overdosage has not been established; it does not reduce the effects of levodopa given with a peripheral dopa-decarboxylase inhibitor.

STORAGE AND CONDITION
Store at temperatures not exceeding 30^{o}C. Protect from light.

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

AVAILABILITY
Levodopa + Carbidopa (Tidomet) 250 mg / 25 mg Tablet - Foil Strip of 10's (Box of 100's) - DRP-2770

DATE OF FIRST AUTHORIZATION
May 16, 2005

DATE OF REVISION
January 2018

torrent PHARMA

Manufactured by :
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Makati City, PHILIPPINES

PRODUCT NAME	:	Tidomet	**COUNTRY :** Philippines	**LOCATION :** INDRAD		**Supersedes A/W No.:**		
ITEM / PACK	:	Insert	**NO. OF COLORS:** 1	**REMARK :**				
DESIGN STYLE	:	Front/Back	**PANTONE SHADE NOS.:**	**SUBSTRATE :**				
CODE	:	xxxxxxxxx-5343	Black	**Activities**	**Department**	**Name**	**Signature**	**Date**
DIMENSIONS (MM)	:	150 x 240		Prepared By	**Pkg.Dev**			
ART WORK SIZE	:	S/S		Reviewed By	**Pkg.Dev**			
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