xxxxxxxx-5343

LEVODOPA + CARBIDOPA

TIDOMET CR

200 mg / 50 mg Controlled-Release Tablet
ANTIPARKINSONISM

FORMULATION
Each controlled-release tablet contains:
Levodopa ..... 200 mg
Carbidopa ..... 50 mg

PRODUCT DESCRIPTION
Levodopa + Carbidopa (Tidomet CR) 200 mg / 50 mg Controlled-Release Tablet is a white to off-white, round, flat beveled edge, uncoated tablet with break line on one side.

CLINICAL PHARMACOLOGY

Pharmacodynamics
The symptoms of Parkinson's disease are related to depletion of dopamine in the corpus striatum. Administration of dopamine is ineffective in such patients because of dopamine does not cross the blood brain barrier. However, levodopa, the precursor of dopamine, does cross the blood brain barrier and is converted to dopamine in the brain.
When levodopa is administered orally, it is rapidly decarboxylated to dopamine in extracerebral tissues so that only small portion of a given dose is transported unchanged in the central nervous system. Since levodopa competes with certain amino acids for transport across the gut wall, the absorption of levodopa may be impaired in some patients on a high protein diet.
Carbidopa inhibits decarboxylation of peripheral levodopa. It does not cross the blood brain barrier and does not affect the metabolism of levodopa within the central nervous system. Decarboxylase inhibiting activity of Carbidopa is limited to extracerebral tissues; hence the administration of carbidopa with levodopa makes more levodopa available to transport to the brain.
Controlled release preparation is designed to release Carbidopa 50 mg and Levodopa 200mg over 4 to 6 hours period, there is a less variation in plasma levodopa levels than with the conventional formulation.

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 and the plasma half-life of levodopa, and decreases plasma and urinary dopamine and homovanillic acid.
Elimination half-life of levodopa in the presence of carbidopa is about 1.5 hours. Tidomet in controlled release preparation have an apparent half-life of levodopa may be prolonged because of continuous absorption. The mean time to peak concentration of levodopa after a single dose of co-careldopa controlled release preparation is about 2 hours as compared to 0.5 hours after conventional administration. The maximum concentration and extent availability of levodopa after a single dose of co-careldopa controlled release is about 35% and 70-75% respectively compared to conventional formulation. At steady state, carbidopa bioavailability from co-careldopa controlled release is approximately 58% relative to that from conventional formulation.

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
For Patients already receiving levodopa therapy and for those currently receiving levodopa alone - Initial dose is 1 tablet twice daily adjusted according to response at intervals of not less than 3 days. It is recommended that for patients whose are not already receiving initial dosages should not exceed 600 mg of levodopa. Or as prescribed by the physician.
For patients already receiving a conventional preparation - Initial dose similar to that of the conventional preparation but the dosing intervals should be prolonged and are normally between 4 to 12 hours. The initial substitution of the controlled release preparation should provide not more than 10% more levodopa than was previously given for doses greater than 900 mg daily. Doses and intervals may then be altered according to clinical response, allowing at least 3 days between adjustments. Up to 30% more levodopa may be required in the controlled release preparation than was previously administered in the conventional preparation. Or as prescribed by the physician.
Average maintenance dose of controlled release preparation lies between the range of Carbidopa 100 mg with Levodopa 400 mg to Carbidopa 400 mg with Levodopa 1.6 g.
SWALLOW WHOLE TABLET, DO NOT CRUSH OR CHEW.

CONTRAINDICATIONS
Known hypersensitivity to any of the components, arrow 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
Tidomet CR must be used in women of child bearing age group after weighing the possible hazard to the mother and the child.
Tidomet CR should not be given to nursing mothers.

DRUG INTERACTIONS
Symptomatic postural hypotension may occur. If co-careldopa is added to the treatment of patient receiving antihypertensive drugs. Hypertension and dyskinesia results from the concomitant use of tricyclics and Tidomet CR. Phenothiazines and butyrophenones may reduce the therapeutic effects of Tidomet CR. Phenytoin and papaverine reverse beneficial effects 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 dopadecarboxylase 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°C.

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

AVAILABILITY
Levodopa + Carbidopa (Tidomet CR) 200 mg / 50 mg Controlled-Release Tablet – Aluminum Foil Strip of 10's (Box of 30's) - DRP-2769

DATE OF FIRST AUTHORIZATION
April 24, 2008

DATE OF REVISION
February 2017

torrent PHARMA

Manufactured by :
TORRENT PHARMACEUTICALS LTD.
Village: Bhud & Makhnu Majra,
Tehsil: Baddi-173 205, Dist.: Solan (H.P.), INDIA.

Imported and Distributed by :
TORRENT PHARMA PHILIPPINES INC.
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Makati Avenue corner Paseo de Roxas
Makati City, PHILIPPINES

PRODUCT NAME	:	TIDOMET CR	**COUNTRY :** Philippines	**LOCATION :** Baddi		**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 220		Prepared By	**Pkg.Dev**			
ART WORK SIZE	:	S/S		Reviewed By	**Pkg.Dev**			
DATE	:	12-01-2018		Approved By	**Quality**			