

Dopacone™

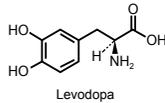
[Levodopa+Carbidopa+Entacapone]

50mg + 12.5mg + 200mg, 75mg + 18.75mg + 200mg, 100mg + 25mg + 200mg, 125mg + 31.25mg + 200mg, 150mg + 37.5mg + 200mg & 200mg + 50mg + 200mg

DESCRIPTION

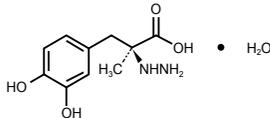
Dopacone is a combination of levodopa, carbidopa and entacapone for the treatment of Parkinson's disease.

Levodopa is an aromatic amino acid. Chemically, it is (-)-L- α -amino- β -(3,4-dihydroxybenzene) propanoic acid. Its molecular formula is $C_9H_9NO_4$ and the structural formula is:



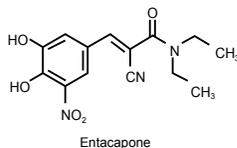
Levodopa

Carbidopa is an inhibitor of aromatic amino acid decarboxylation. Chemically, it is (-)-L-(α -hydrazino-(α -methyl- β -(3,4-dihydroxybenzene) propanoic acid monohydrate. Its molecular formula is $C_{10}H_{14}N_2O_4 \cdot H_2O$ and the structural formula is:



Carbidopa monohydrate

Entacapone, a Catechol-O-Methyl Transferase (COMT) inhibitor, is a nitro-catechol-structured compound. Chemically, it is (E)-2-cyano-3-(3,4-dihydroxy-5-nitrophenyl)-N,N-diethyl-2-propanamide. Its molecular formula is $C_{18}H_{19}N_3O_5$ and the structural formula is:



Entacapone

QUALITATIVE AND QUANTITATIVE COMPOSITION

Dopacone (Levodopa + Carbidopa + Entacapone) Tablets are available for oral administration as:

Dopacone Tablets 50mg + 12.5mg + 200mg

Each film-coated tablet contains:

Levodopa USP... 50mg

Carbidopa monohydrate USP equivalent to Carbidopa... 12.5mg

Entacapone USP... 200mg

Dopacone Tablets 75mg + 18.75mg + 200mg

Each film-coated tablet contains:

Levodopa USP... 75mg

Carbidopa monohydrate USP equivalent to Carbidopa... 18.75mg

Entacapone USP... 200mg

Dopacone Tablets 100mg + 25mg + 200mg

Each film-coated tablet contains:

Levodopa USP... 100mg

Carbidopa monohydrate USP equivalent to Carbidopa... 25mg

Entacapone USP... 200mg

Dopacone Tablets 125mg + 31.25mg + 200mg

Each film-coated tablet contains:

Levodopa USP... 125mg

Carbidopa monohydrate USP equivalent to Carbidopa... 31.25mg

Entacapone USP... 200mg

Dopacone Tablets 150mg + 37.5mg + 200mg

Each film-coated tablet contains:

Levodopa USP... 150mg

Carbidopa monohydrate USP equivalent to Carbidopa... 37.5mg

Entacapone USP... 200mg

Dopacone Tablets 200mg + 50mg + 200mg

Each film-coated tablet contains:

Levodopa USP... 200mg

Carbidopa monohydrate USP equivalent to Carbidopa... 50mg

Entacapone USP... 200mg

CLINICAL PHARMACOLOGY

Mechanism of Action

Levodopa: The symptoms of Parkinson's disease are related to depletion of dopamine in the corpus striatum. Levodopa, the metabolic precursor of dopamine, crosses the blood brain barrier and relieves the symptoms of the disease.

Carbidopa: When levodopa is administered orally, it is rapidly decarboxylated to dopamine in extracerebral tissues so that only a small portion of a given dose is transported unchanged to the central nervous system. Carbidopa inhibits the decarboxylation of peripheral levodopa, making more levodopa available for delivery to the brain.

Entacapone: Entacapone is a selective and reversible inhibitor of catechol-O-methyltransferase (COMT). When decarboxylation of levodopa is prevented by carbidopa, COMT becomes the major metabolizing enzyme for levodopa, catalyzing its metabolism to 3-methoxy-4-hydroxy-L-phenylalanine (3-OMD).

Pharmacokinetics

Absorption: Carbidopa is absorbed and eliminated slightly slower compared with levodopa. Both levodopa and entacapone are rapidly absorbed and eliminated. Meals rich in large neutral amino acid may delay & reduce the absorption of levodopa.

Distribution: The distribution volume of both levodopa (V_d 0.36-1.6 l/kg) and entacapone (V_d 0.27 l/kg) is moderately small while no data for carbidopa are available. Levodopa is bound to plasma protein only to a minor extent of about 10-30% and carbidopa is bound approximately 36%, while entacapone is extensively bound to plasma proteins (about 98%) mainly to serum albumin.

Metabolism: Carbidopa is metabolized to two main metabolites which are excreted in the urine as glucuronides and unconjugated compounds. Unchanged carbidopa accounts for 30% of the total urinary excretion.

Levodopa is extensively metabolized to various metabolites: decarboxylation by dopa decarboxylase (DDC) and O-methylation by catechol-O-methyltransferase (COMT) being the most important pathways.

Entacapone is almost completely metabolized prior to excretion via urine (10 to 20%) and bile/faeces (80 to 90%). The main metabolic pathway is glucuronidation of entacapone and its active metabolite, the cis-isomer, which accounts for about 5% of plasma total amount.

Excretion: Total clearance for levodopa is in the range of 0.55-1.38 l/kg/h and for entacapone is in the range of 0.70 l/kg/h. The elimination-half life ($t_{1/2}$) is 0.6-1.3 hours for levodopa, 2-3 hours for carbidopa and 0.4-0.7 hours for entacapone, each given separately.

Special Population

Elderly: After combination of carbidopa with levodopa, the absorption of levodopa is similar between the elderly and the young people, but the AUC is 1.5 fold greater in the elderly due to decreased DDC activity and lower clearance by aging.

Gender: The bioavailability of levodopa is higher in women than in men, primarily due to the difference in body weight, while there is no gender difference with carbidopa and entacapone.

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Patients with Hepatic Impairment: The metabolism of entacapone is slowed in patients with mild to moderate hepatic impairment (Child-Pugh Class A and B) leading to an increased plasma concentration of entacapone both in the absorption and elimination phases. Levodopa + Carbidopa + Entacapone should be administered cautiously to patients with mild or moderate hepatic impairment.

Patients with Renal Impairment: A longer dosing interval of Levodopa + Carbidopa + Entacapone may be considered for patients who are receiving dialysis therapy.

THERAPEUTIC INDICATIONS

Dopacone (Levodopa + Carbidopa + Entacapone) is indicated for the treatment of Parkinson's disease. Dopacone (Levodopa + Carbidopa + Entacapone) can be used:

- To substitute (with equivalent strengths of each of the three components) carbidopa, levodopa and entacapone previously administered as individual products.
- To replace carbidopa/levodopa therapy (without entacapone) when patients experience the signs and symptoms of end-of-dose "wearing-off" and when they have been taking a total daily dose of levodopa of 600mg or less and have not been experiencing dyskinesias.

DOSAGE & ADMINISTRATION

Dopacone (Levodopa + Carbidopa + Entacapone) should be used as a substitute for patients already stabilized on equivalent doses of carbidopa, levodopa and entacapone. Therapy should be individualized and adjusted according to the desired therapeutic response.

Dosing Information

The optimum daily dose must be determined by careful titration of levodopa in each patient. The maximum recommended daily dose of Dopacone (Levodopa + Carbidopa + Entacapone) depends on the strength used. The maximum number of tablets to be used in a 24-hour period is less with the highest strength (Dopacone Tablets 200mg + 50mg + 200mg) than with lower strengths (see Table below).

Maximum Recommended Dose of Dopacone (Levodopa + Carbidopa + Entacapone) in a 24-hour Period

Levodopa + Carbidopa + Entacapone Dosage Strength	Maximum Number of Tablets in a 24-hour Period
Dopacone Tablets 50mg + 12.5mg + 200mg	
Dopacone Tablets 75mg + 18.75mg + 200mg	
Dopacone Tablets 100mg + 25mg + 200mg	8
Dopacone Tablets 125mg + 31.25mg + 200mg	
Dopacone Tablets 150mg + 37.5mg + 200mg	
Dopacone Tablets 200mg + 50mg + 200mg	6

Converting Patients from levodopa, carbidopa and Entacapone to Dopacone (Levodopa + Carbidopa + Entacapone)

Patients currently treated with entacapone 200mg with each dose of non-extended release carbidopa/levodopa tablet, can switch to the corresponding strength of Dopacone (Levodopa + Carbidopa + Entacapone) containing the same amounts of levodopa and carbidopa.

Converting Patients from Carbidopa and Levodopa Products to Dopacone (Levodopa + Carbidopa + Entacapone)

Patients with a history of moderate or severe dyskinesias or taking more than 600mg of the levodopa component per day are likely to require a reduction in their daily levodopa dose when entacapone is added. Because dose adjustment of the individual carbidopa or levodopa component is not possible with fixed-dose products, initially titrate patients to a dose that is tolerated and that meets their individual therapeutic need using a separate carbidopa + levodopa tablet (1:4 ratio) plus an entacapone tablet. Once the patient's individual dose of carbidopa + levodopa plus entacapone dose has been established using two separate tablets; switch the patient to a corresponding single tablet of Dopacone (Levodopa + Carbidopa + Entacapone).

When less levodopa is required, reduce the total daily dosage of carbidopa + levodopa either by decreasing the strength of Dopacone (Levodopa + Carbidopa + Entacapone) at each administration or by decreasing the frequency of administration by extending the time between doses.

Concomitant Use with Other Anti-Parkinson's Disease Drugs

Anticholinergic agents, dopamine agonists, monoamine oxidase (MAO) - B inhibitors, amantadine and other standard drugs for Parkinson's disease may be used concomitantly while Dopacone (Levodopa + Carbidopa + Entacapone) is being administered; however, dosage adjustments of the concomitant medication or Dopacone (Levodopa + Carbidopa + Entacapone) may be required.

Decrease or Interruption of Dosing

Avoid interruption of Dopacone (Levodopa + Carbidopa + Entacapone) dosing because hyperpyrexia has been reported in patients who suddenly discontinue or reduce their use of levodopa.

Discontinuation of Dopacone (Levodopa + Carbidopa + Entacapone) therapy

If Dopacone (Levodopa + Carbidopa + Entacapone) treatment is discontinued and the patient is transferred to levodopa/DDC inhibitor therapy without entacapone, it is necessary to adjust the dosing of other antiparkinsonian treatments, especially levodopa, to achieve a sufficient level of control of the parkinsonian symptoms.

Special Population

Patients with Renal Impairment: Dopacone (Levodopa + Carbidopa + Entacapone) therapy should be administered cautiously to patients in severe renal impairment including those receiving dialysis therapy.

Patients with Hepatic Impairment: Dopacone (Levodopa + Carbidopa + Entacapone) should be administered cautiously to patients with biliary obstruction or mild to moderate hepatic impairment since biliary excretion appears to be the major route of excretion of entacapone and hepatic impairment had a significant effect on the pharmacokinetics of entacapone when 200mg entacapone was administered alone.

Method of administration

Each tablet is to be taken orally either with or without food. One tablet contains one treatment dose and the tablet may only be administered as whole tablet.

ADVERSE REACTIONS

Very common: Dyskinesia, diarrhoea, nausea, muscle pain, musculoskeletal and connective tissue pain and chromaturia.

Common: Anaemia, weight decreased, decreased appetite, depression, hallucination, confusional state, abnormal dreams, anxiety, insomnia, parkinsonism aggravated (e.g. bradykinesia), tremor, on and off phenomenon, dystonia, mental impairment (e.g. memory impairment, dementia), somnolence, dizziness, headache, blurred vision, ischemic heart disease events other than myocardial infarction (e.g. angina pectoris), irregular heart rhythm, orthostatic hypotension, hypertension, dyspnea, constipation, vomiting, dyspepsia, abdominal pain and discomfort, dry mouth, rash, hyperhidrosis, muscle spasms, arthralgia, urinary tract infection, chest pain, peripheral oedema, fall, gait disturbance, asthenia and fatigue.

Uncommon: Thrombocytopenia, psychosis, agitation, myocardial infarction, gastrointestinal haemorrhage, colitis, dysphagia, hepatic function test abnormal, discolourations other than urine (e.g. skin, nail, hair, sweat), urinary retention and malaise.

Not known: Suicidal behaviour, dopamine dysregulation syndrome, neuroleptic malignant syndrome, hepatitis with mainly cholestatic features, urticaria and rhabdomyolysis.

Rare: Angioedema.

"To report SUSPECTED ADVERSE REACTIONS to Getz Pharma's pharmacovigilance Section, please contact at dsafety@getzpharma.com or +92-21-38636363"

CONTRAINDICATIONS

Levodopa + Carbidopa + Entacapone is contraindicated in patients:

- With known hypersensitivity to the active substances or to any of the excipient of the product.
- With severe hepatic impairment.
- With narrow-angle glaucoma.
- With pheochromocytoma.
- Taking concomitantly non-selective monoamine oxidase (MAO-A and MAO-B) inhibitors (e.g. phenelzine, tranylcypromine) & selective MAO-A inhibitor and selective MAO-B inhibitor.
- With a previous history of Neuroleptic Malignant Syndrome (NMS) and/or non-traumatic rhabdomyolysis.
- With suspicious undiagnosed skin lesions or a history of malignant melanoma, because levodopa may activate malignant melanoma.
- With clinical or laboratory evidence of uncompensated cardiovascular, endocrine, hematologic, pulmonary (including bronchial asthma) or renal disease.

PRECAUTIONS

- Patients with Parkinson's disease treated with Levodopa + Carbidopa + Entacapone or other carbidopa/levodopa products have reported suddenly falling asleep without prior warning of sleepiness while engaged in activities of daily living (including the operation of motor vehicles). Some of these events have been reported to occur up to one year after initiation of treatment.
- Levodopa + Carbidopa + Entacapone is not recommended for the treatment of drug-induced extrapyramidal reactions.
- Levodopa + Carbidopa + Entacapone therapy should be administered cautiously to patients with history of peptic ulcer disease or history of convulsions.
- In patients with a history of myocardial infarction who have residual atrial nodal or ventricular arrhythmias; cardiac function should be monitored with particular care during the period of initial dose adjustments.
- All patients treated with Levodopa + Carbidopa + Entacapone should be monitored carefully for the development of mental changes, depression with suicidal tendencies and other serious antisocial behaviour. Patients with past or current psychosis should be treated with caution.
- Concomitant administration of antipsychotics with dopamine receptor-blocking properties, particularly D2 receptor antagonists should be carried out with caution and the patient carefully observed for loss of antiparkinsonian effect or worsening of parkinsonian symptoms.
- Patients with chronic wide-angle glaucoma may be treated with Levodopa + Carbidopa + Entacapone with caution, provided the intra-ocular pressure is well controlled and the patient is monitored carefully for changes in intra-ocular pressure.
- Levodopa + Carbidopa + Entacapone may induce orthostatic hypotension. Therefore, Levodopa + Carbidopa + Entacapone should be given cautiously to patients who are taking other medicinal products which may cause orthostatic hypotension.
- Dopaminergic adverse reactions, e.g. dyskinesia, were more common in patients who received entacapone and dopamine agonists (such as bromocriptine), selegiline or amantadine. Dyskinesia may occur or be exacerbated at lower dosages and sooner with Levodopa + Carbidopa + Entacapone than with preparations containing only carbidopa and levodopa. The occurrence of dyskinesias may require dosage reduction.
- Any abrupt dose reduction or withdrawal of levodopa should be carefully observed, particularly in patients who are also receiving neuroleptics. When considered necessary, the replacement of Levodopa + Carbidopa + Entacapone with levodopa and DDC inhibitor without entacapone or other dopaminergic treatment should proceed slowly and an increase in levodopa dose may be necessary.
- If general anaesthesia is required, therapy with Levodopa + Carbidopa + Entacapone may be continued for as long as the patient is permitted to take fluids and medicinal products by mouth. If therapy has to be stopped temporarily, Levodopa + Carbidopa + Entacapone may be restarted as soon as oral medicinal products can be taken at the same daily dose as before.
- Periodic evaluation of hepatic, haematopoietic, cardiovascular and renal function is recommended during extended therapy with Levodopa + Carbidopa + Entacapone.
- Prolonged or persistent diarrhoea appearing during use of entacapone may be a sign of colitis. In the event of prolonged or persistent diarrhoea, the drug should be discontinued and appropriate medical therapy and investigations considered.
- Patients treated with anti-Parkinson medications can experience intense urges to gamble, increased sexual urges, intense urges to spend money uncontrollably and other intense urges. Patients may be unable to control these urges while taking one or more of the medications generally used for the treatment of Parkinson's disease and which increase central dopaminergic tone, including entacapone taken with levodopa and carbidopa. In some cases, although not all, these urges were reported to have stopped when the dose of anti-Parkinson medications was reduced or discontinued. Physicians should consider dose reduction or stopping Levodopa + Carbidopa + Entacapone if a patient develops such urges while taking medicine.
- Dopamine Dysregulation Syndrome (DDS) is an addictive disorder resulting in excessive use of the product seen in some patients treated with carbidopa/levodopa. Before initiation of treatment, patients and caregivers should be warned of the potential risk of developing DDS.
- For patients who experience progressive anorexia, asthenia and weight decrease within a relatively short period of time, a general medical evaluation including liver function should be considered.
- Levodopa + carbidopa may cause false positive result when a dipstick is used to test for urinary ketone and this reaction is not altered by boiling the urine sample. The use of glucose oxidase methods may give false negative results for glycosuria.
- Patients with Parkinson's disease have a higher risk (2 to approximately 6 fold higher) of developing melanoma. Advise patients to have their skin examined on a regular basis by a qualified individuals (e.g., dermatologist) and to monitor for melanomas frequently and on a regular basis when using Levodopa + Carbidopa + Entacapone.
- Prostate Cancer has been reported in elderly males during the use of entacapone in combination with levodopa/carbidopa in clinical trials. Physicians are advised to adhere to the routine examination schedule for all male patients for symptoms and risk factors of prostate cancer, including evaluation prior to initiating treatment with Levodopa + Carbidopa + Entacapone.
- Drugs known to be metabolized by COMT, such as isoproterenol, epinephrine, norepinephrine, dopamine, dobutamine, alpha-methyldopa, apomorphine, isotherine and bitolterol should be administered with caution in patients receiving entacapone regardless of the route of administration (including inhalation), as their interaction may result in increased heart rates, possibly arrhythmias and excessive changes in blood pressure.
- Caution should be exercised when administering Levodopa + Carbidopa + Entacapone to patients with biliary obstruction, as entacapone is excreted mostly via the bile.
- Levodopa + Carbidopa + Entacapone should be used cautiously in patients who have a history of seizures or have conditions associated with seizure or have a lowered seizure threshold.
- Levodopa is known to depress prolactin secretion & increase growth hormone level. Cases of severe rhabdomyolysis have been reported with entacapone when used in combination with carbidopa and levodopa. Most of the cases were manifested by myalgia and increased values of creatine phosphokinase (CPK) and myoglobin.
- Cases of hyperpyrexia and confusion resembling neuroleptic malignant syndrome (NMS) have been reported in association with dose reduction or withdrawal of therapy with carbidopa, levodopa and entacapone. However, in some cases, hyperpyrexia and confusion were reported after initiation of treatment with entacapone. If a patient needs to discontinue or reduce their daily dose of Levodopa + Carbidopa + Entacapone, the dose should be decreased slowly, with supervision from a health care provider.
- Abnormalities in laboratory tests may include elevations of liver function tests such as alkaline phosphatase, SGOT (AST), SGPT (ALT), lactic dehydrogenase and bilirubin. Abnormalities in blood urea nitrogen and positive Coombs test have also been reported. Commonly, levels of blood urea nitrogen, creatinine and uric acid are lower during administration of Levodopa + Carbidopa + Entacapone than with levodopa.
- Dopaminergic therapy in patients with Parkinson's disease has been associated with hallucinations.
- Cases of falsely diagnosed pheochromocytoma in patients on carbidopa/levodopa therapy have been reported very rarely. Caution should be exercised when interpreting the plasma and urine levels of catecholamines and their metabolites in patients on carbidopa/levodopa therapy.

Pregnancy

There are no adequate data from the use of the combination of Levodopa + Carbidopa + Entacapone in pregnant women. Levodopa + Carbidopa + Entacapone should not be used during pregnancy unless the benefits for the mother outweigh the possible risks to the foetus.

Nursing Mothers

Levodopa is excreted in human breast milk. Women should not breast-feed during treatment with Levodopa + Carbidopa + Entacapone.

DRUG INTERACTIONS

Antidepressants: Rarely, reactions including hypertension and dyskinesia have been reported with the concomitant use of tricyclic antidepressants and levodopa + carbidopa.

Drugs metabolized by COMT: Drugs metabolized by COMT, such as isoproterenol, epinephrine, norepinephrine, dopamine, dobutamine, alpha-methyldopa, apomorphine, isotherine and bitolterol should be administered with caution in patients receiving entacapone regardless of the route of administration (including inhalation), as their interaction may result in increased heart rates, possibly arrhythmias and excessive changes in blood pressure.

Other active substances: Dopamine receptor antagonists (e.g. some antipsychotics and antiemetics), phenytoin and papaverine may reduce the therapeutic effect of levodopa. Patients taking these medicinal products with Levodopa + Carbidopa + Entacapone should be carefully observed for loss of therapeutic response.

Antihypertensive Agents: Symptomatic postural hypotension has occurred when carbidopa + levodopa was added to the treatment of patients receiving antihypertensive drugs. When starting therapy with Levodopa + Carbidopa + Entacapone, dosage adjustment of antihypertensive drug may be required.

Dopamine D2 Receptor Antagonists & Phenytoin: Dopamine D2 receptor antagonists (e.g., metoclopramide, phenothiazines, butyrophenones, risperidone) & Phenytoin may reduce the therapeutic effects of levodopa.

Isoniazid: Isoniazid may reduce the therapeutic effects of levodopa, a dose increase may be necessary.

Phenytoin: The beneficial effects of levodopa in Parkinson's disease have been reported to be reversed by phenytoin. Patients taking phenytoin with carbidopa/levodopa should be carefully observed for loss of therapeutic response. Levodopa + Carbidopa + Entacapone dosage should be increased as clinically needed in patients receiving phenytoin.

Papaverine: The beneficial effects of levodopa in Parkinson's disease have been reported to be reversed by papaverine. Patients taking papaverine with carbidopa/levodopa should be carefully observed for loss of therapeutic response. Levodopa + Carbidopa + Entacapone dosage should be increased as clinically needed in patients receiving papaverine.

Drugs Known to Interfere with Biliary Excretion, Glucuronidation and Intestinal Beta-glucuronidase: Caution should be exercised when drugs known to interfere with biliary excretion, glucuronidation and intestinal beta-glucuronidase are given concurrently with entacapone.

Drugs Metabolized via CYP2C9 (e.g., coumadin): The dosage of Levodopa + Carbidopa + Entacapone should be adjusted as clinically needed in patients using other drugs metabolized via CYP2C9. Monitoring of INR is recommended when Levodopa + Carbidopa + Entacapone treatment is initiated for patients receiving warfarin.

Other forms of interactions: Since levodopa competes with certain amino acids, the absorption of Levodopa + Carbidopa + Entacapone may be impaired in some patients on high protein diet.

Levodopa and entacapone may form chelates with iron in the gastrointestinal tract. Therefore, Levodopa + Carbidopa + Entacapone and iron preparations should be taken at least 2-3 hours apart.

OVERDOSAGE

Symptoms: The acute symptoms and signs in cases of overdose included agitation, confusion, state, coma, bradycardia, ventricular tachycardia, Cheyne-Stokes respiration, discolourations of skin, tongue and conjunctiva and chromaturia.

Management: Management of acute overdose with Levodopa + Carbidopa + Entacapone therapy is similar to acute overdose with levodopa. Hospitalisation is advised and general supportive measures should be employed with immediate gastric lavage and repeated doses of charcoal over time. This may hasten the elimination of entacapone in particular by decreasing its absorption/reabsorption from the gastrointestinal tract. The adequacy of the respiratory, circulatory and renal systems should be carefully monitored and appropriate supportive measures employed. ECG monitoring should be started and the patient carefully monitored for the possible development of arrhythmias. If required, appropriate anti-arrhythmic therapy should be given. The possibility that the patient has taken other active substances in addition to Levodopa + Carbidopa + Entacapone should be taken into consideration.

STORAGE

Do not store above 30°C.
Protect from sunlight and moisture.

The expiration date refers to the product correctly stored at the required conditions.

HOW SUPPLIED

Dopacone (Levodopa + Carbidopa + Entacapone) Tablets 50mg + 12.5mg + 200mg are available in pack of 30's.
Dopacone (Levodopa + Carbidopa + Entacapone) Tablets 75mg + 18.75mg + 200mg are available in pack of 14's.
Dopacone (Levodopa + Carbidopa + Entacapone) Tablets 100mg + 25mg + 200mg are available in pack of 10's.
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Keep out of reach of children.

To be sold on prescription of a registered medical practitioner only.

**Please read the contents carefully before use.
This package insert is continually updated from time to time.**

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