Only for the use of Medical Professionals

Tridopa®

Levodopa+Carbidopa+Entacapone

Description

Tridopa® is a combination of levodopa, carbidopa and entacapone for the treatment of Parkinson's disease. Levodopa is the metabolic precursor of dopamine, it crosses the blood-brain barrier and is converted to dopamine in the brain. Carbidopa is a dopa decarboxylase (DDC) inhibitor which reduces the peripheral metabolism of levodopa to dopamine, and thus, more levodopa is available to the brain. Entacapone is a selective inhibitor of catechol-o-methyltransferase. Given concurrently, entacapone results in greater and more sustained plasma levels of levodopa, leading to greater control of parkinsonism symptoms.

Indication and usage

Tridopa® is indicated for the treatment of adult patients with Parkinson's disease and end-of-dose motor fluctuations not stabilized on levodopa/dopa decarboxylase (DDC) inhibitor treatment.

Dose and administration

Adults:
The optimum daily dose must be determined by careful titration of levodopa in each patient. Patients should be instructed to take only 1 (one) Tridopa® tablet per dose administration. The maximum recommended daily dose of entacapone is 2,000 mg and therefore the maximum dose is 10 (ten) tablets/day for Tridopa® 50, Tridopa® 100, Tridopa® 150; and 7 (seven) tablets/day of Tridopa® 200.

Usually Tridopa® is to be used in patients who are currently treated with corresponding doses of standard release levodopa/DDC inhibitor and entacapone.

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 tablets.

How to transfer patients taking levodopa/DDC inhibitor (carbidopa or benserazide) preparations and entacapone tablets to Tridopa®

a. Patients who are currently treated with entacapone and with standard release levodopa/carbidopa in doses equal to Tridopa® tablet strengths can be directly transferred to corresponding Tridopa® tablets.
For example, a patient taking one tablet of 100 mg/25 mg of levodopa/carbidopa with one tablet of entacapone 200 mg four times daily can take one Tridopa® 100 tablet four times daily in place of their usual levodopa/carbidopa and entacapone doses.

b. When initiating Tridopa® therapy for patients currently treated with entacapone and levodopa/carbidopa in doses not equal to Tridopa® 100 (or Tridopa® 50 or Tridopa® 150 or Tridopa® 200) tablets, Tridopa® dosing should be carefully titrated for optimal clinical response. At the initiation, Tridopa® should be adjusted to correspond as closely as possible to the total daily dose of levodopa currently used.

c. When initiating Tridopa® in patients currently treated with entacapone and levodopa/benserazide in a standard release formulation, the dosing of levodopa/benserazide

should be discontinued in the previous night, and Tridopa® should be started in the next morning. The starting dose of Tridopa® should provide either the same amount of levodopa or slightly (5-10%) more.

How to transfer patients not currently treated with entacapone to Tridopa®

Initiation of Tridopa® may be considered at corresponding doses to current treatment in some patients with Parkinson's disease and end-of-dose motor fluctuations, who are not stabilized on their current standard release levodopa/DDC inhibitor treatment. However, a direct switch from levodopa/DDC inhibitor to Tridopa® is not recommended for patients who have dyskinesias or whose daily levodopa dose is above 800 mg. In such patients it is advisable to introduce entacapone treatment as a separate treatment (entacapone tablets) and adjust the levodopa dose if necessary, before switching to Tridopa®.

Entacapone enhances the effects of levodopa. It may therefore be necessary, particularly in patients with dyskinesia, to reduce levodopa dose by 10-30% within the first days to first weeks after initiating Tridopa® treatment. The daily dose of levodopa can be reduced by extending the dosing intervals and/or by reducing the amount of levodopa per dose, according to the clinical condition of the patient.

Dose adjustment during the course of the treatment

When more levodopa is required, an increase in the frequency of doses and/or the use of an alternative strength of Tridopa® should be considered, within the dose recommendations.
When less levodopa is required, the total daily dose of Tridopa® should be reduced either by decreasing the frequency of administration by extending the time between doses, or by decreasing the strength of Tridopa® at an administration.
If other levodopa products are used concomitantly with a Tridopa® tablet, the maximum dose recommendations should be followed.

Discontinuation of Tridopa® therapy:

If Tridopa® treatment (levodopa/carbidopa/entacapone) 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.

Children:

Safety and effectiveness in pediatric patients have not been established.

Elderly:

No dose adjustment is required for elderly patients.

Hepatic impaired patients:

Should be administered cautiously to patients with mild to moderate hepatic impairment. Dose reduction may be needed.

Renally impaired patients:

Should be administered cautiously to patients in severe renal impairment including those receiving dialysis therapy

Use in pregnancy and lactation
Pregnancy category C. The combination of levodopa/carbidopa/entacapone should not be used during pregnancy unless the potential benefit justifies the potential risk to the fetus. The safety of this combination in the infant is not known. Women should not breast-feed during treatment with this combination.

Side effects
Common side effects include dyskinesia, nausea, hyperkinesia, change in urine color, diarrhea and stomach pain. Other side effects may include diarrhea, sometimes severe; colitis; hallucinations; other mental disturbances; orthostatic hypotension; rhabdomyolysis; and symptoms resembling neuroleptic malignant syndrome (a condition characterized by high fever, muscle stiffness, and confusion); fibrosis; skin cancer, etc.

Precautions
Levodopa, carbidopa and entacapone together may cause dizziness and symptomatic orthostatism. Therefore, caution should be exercised when driving or using machines. As with levodopa, periodic evaluations of hepatic, hematopoietic, cardiovascular and renal function are recommended during extended therapy.

Drug interactions
Symptomatic postural hypotension may occur when levodopa is added to the treatment of patients already receiving antihypertensive. Dose adjustment of the antihypertensive agent may be required. 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 combination should be carefully observed for loss of therapeutic response. Since levodopa competes with certain amino acids, the absorption of Tridopa® may be impaired in some patients on high protein diet.

Contraindications
Levodopa/carbidopa/entacapone combination is contraindicated in patients with severe hepatic impairment, narrow-angle glaucoma, pheochromocytoma, coadministration with non-selective monoamine oxidase (MAO-A and MAO-B) inhibitors (e.g. phenelzine, tranylcypromine), a previous history of Neuroleptic Malignant Syndrome (NMS) and/or non-traumatic rhabdomyolysis and known hypersensitivity to the active substances or to any of the excipients.

Overdose
The acute symptoms and signs of overdose include agitation, confusional state, coma, bradycardia, ventricular tachycardia, Cheyne-Stokes respiration, discolorations of skin, tongue and conjunctiva, and chromaturia. Management of acute overdose with levodopa/carbidopa/entacapone combination is similar to acute overdose with levodopa. Pyridoxine, however, is not effective in reversing the actions of levodopa/carbidopa/entacapone combination. Hospitalization is advised and general supportive measures should be employed with immediate gastric lavage and repeated doses of charcoal over time.

Pharmaceutical precautions
Store in a cool and dry place. Protect from light.

Presentation

Tridopa® 50 tablet : Each coated tablet contains Levodopa BP 50 mg, Carbidopa 12.5 mg as Monohydrate USP & Entacapone INN 200 mg

Tridopa® 100 tablet : Each coated tablet contains Levodopa BP 100 mg, Carbidopa 25 mg as Monohydrate USP & Entacapone INN 200 mg

Tridopa® 150 tablet : Each coated tablet contains Levodopa BP 150 mg, Carbidopa 37.5 mg as Monohydrate USP & Entacapone INN 200 mg

Tridopa® 200 tablet : Each coated tablet contains Levodopa BP 200 mg, Carbidopa 50 mg as Monohydrate USP & Entacapone INN 200 mg

Packaging

Tridopa® 50 tablet : Carton of 20 tablets in blister pack
Tridopa® 100 tablet : Carton of 20 tablets in blister pack
Tridopa® 150 tablet : Carton of 20 tablets in blister pack
Tridopa® 200 tablet : Carton of 20 tablets in blister pack

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