Neudopa
(Levodopa + Carbidopa)

نیوڈوپا
(لیوڈوپا+کاربیڈوپا)

Tablets

گولیاں

Each tablet contains:
Levodopa (U.S.P.) 250mg
Carbidopa (U.S.P.) 25mg
Product Complies U.S.P. Specs.

NEUDOPA is a combination of carbidopa, U.S.P., an aromatic amino acid decarboxylase inhibitor, and levodopa, U.S.P., the metabolic precursor of dopamine, for use in the treatment of Parkinson's disease and syndrome.

Levodopa relieves the symptoms of Parkinson's disease by being decarboxylated to dopamine in the brain. Carbidopa, which does not-cross the blood-brain barrier, inhibits the extracerebal decarboxylation of levodopa, making more levodopa available for transport to the brain and subsequent conversion to dopamine.

NEUDOPA improves overall therapeutic response as compared to levodopa.

NEUDOPA provides effective long -lasting levodopa plasma levels at doses that are approximately 80 percent lower than those needed with levodopa alone. While pyridoxine hydrochloride (Vitamin B6) is known to accelerate the peripheral metabolism of levodopa to dopamine, carbidopa prevents this action.

INDICATIONS

Levodopa + Carbidopa (NEUDOPA) is indicated for the treatment of Parkinson's disease and syndrome. It is useful in relieving many of the symptoms of parkinsonism, particularly rigidity and bradykinesia. Levodopa + Carbidopa (NEUDOPA) frequently is helpful in the management of tremor, dysphagia, sialorrhea, and postural instability associated with Parkinson's disease and syndrome.

When therapeutic response to levodopa alone is irregular, and signs and symptoms of Parkinson's disease are not evenly controlled throughout the day, substitution of Levodopa + Carbidopa (NEUDOPA) usually is effective in reducing fluctuations in response.

By reducing certain adverse reactions produced by levodopa alone, Levodopa + Carbidopa (NEUDOPA) permits more patients to obtain adequate relief of the symptoms of Parkinson's disease.

Levodopa + Carbidopa (NEUDOPA) is also indicated for patients with Parkinsonism who are taking vitamin preparations that contain pyridoxine hydrochloride (Vitamin B6).

DOSAGE AND ADMINISTRATION

The optimum daily dosage of Levodopa + Carbidopa (NEUDOPA) must be determined by careful titration in each patient. NEUDOPA tablets are available in a 1:10 ratio of carbidopa to levodopa (NEUDOPA 25/250).
Each tablet of Levodopa + Carbidopa (NEUDOPA) is designed to divide in half with minimal pressure.

General Considerations
Dosage should be titrated to the individual patient needs and this may require adjusting both the individual dose and the frequency of administration.

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

Standard antiparkinson medicines, other than levodopa alone, may be continued while Levodopa + Carbidopa (NEUDOPA) is being administered, although their dosage may have to be adjusted.

Usual Initial Dose
The initial dose of NEUDOPA 25/250mg is one-half tablet taken once or twice daily. However this may not provide the optimal amount of carbidopa needed by many patients. If necessary, add 1/2 tablet every day or every other day until optimal response is reached.

Response has been observed in one day, and sometimes after one dose. Fully effective doses usually are reached within seven days as compared to weeks or months with levodopa alone.

How to Transfer Patients from Levodopa
Because both therapeutic and adverse responses occur more rapidly with NEUDOPA than when levodopa is given, patients should be monitored closely during the dose adjustment period. Specifically, involuntary movements will occur more rapidly with NEUDOPA than with levodopa. The occurrence of involuntary movements may require dosage reduction. Blepharospasm may be a useful early sign of excess dosage in some patients.

Levodopa should be discontinued at least 12 hours before Levodopa + Carbidopa (NEUDOPA) is started (24 hours for slow-release preparations of levodopa). A daily dosage of Levodopa + Carbidopa (NEUDOPA) should be chosen that will provide approximately 20 percent of the previous levodopa daily dosage. The suggested starting dosage for most patients taking more than 1500mg of levodopa is one tablet of NEUDOPA 25/250mg three or four times a day.

Maintenance
Therapy should be individualised and adjusted according to the desired therapeutic response. At least 70 to 100mg of carbidopa per day should be provided for optimal inhibition of extracerebral decarboxylation of levodopa.

If necessary, the dosage of NEUDOPA 25/250mg may be increased by one-half or one tablet every day to a maximum of eight tablets a day. Experience with total daily dosages of carbidopa greater than 200mg is limited.

Maximum Recommended Dose
Eight tablets of NEUDOPA 25/250mg per day (200mg of carbidopa and 2g of levodopa). This is about 3mg/kg of carbidopa, and 30mg/kg of levodopa in a patient weighing 70kg.

CONTRAINDICATIONS

Nonselective monoamine oxidase (MAO) inhibitors are contraindicated for use with Levodopa + Carbidopa (NEUDOPA). These inhibitors must be discontinued at least two weeks prior to initiating therapy with Levodopa + Carbidopa (NEUDOPA). Levodopa + Carbidopa (NEUDOPA) may be administered concomitantly with the manufacturer's recommended dose of a MAO inhibitor with selectivity for MAO type B (e.g., selegiline HCl) (See Drug Interactions, Other Medicines).

Levodopa + Carbidopa (NEUDOPA) is contraindicated in patients with known hypersensitivity to any component of this medication, and in patients with narrow-angle glaucoma.

Since levodopa may activate a malignant melanoma, Levodopa + Carbidopa (NEUDOPA) should not be used in patients with suspicious undiagnosed skin lesions or a history of melanoma.

PRECAUTIONS

Levodopa + Carbidopa (NEUDOPA) is not recommended for the treatment of drug-induced extrapyramidal reactions.

Levodopa + Carbidopa (NEUDOPA) may be given to patients already receiving levodopa alone; however, the levodopa alone must be discontinued at least 12 hours before Levodopa + Carbidopa (NEUDOPA) is started. Levodopa + Carbidopa (NEUDOPA) should be substituted at a dosage that will provide approximately 20 percent of the previous levodopa dosage. (See Dosage and Administration).

Dyskinesias may occur in patients previously treated with levodopa alone because carbidopa permits more levodopa to reach the brain and, thus, more dopamine to be formed. The occurrence of dyskinesias may require dosage reduction.

As with levodopa, Levodopa + Carbidopa (NEUDOPA) may cause involuntary movements and mental disturbances. These reactions are thought to be due to increased brain dopamine following administration of levodopa, and use of Levodopa + Carbidopa (NEUDOPA) may cause a recurrence. Dosage reduction may be required. All patients should be observed carefully for the development of depression with concomitant suicidal tendencies. Patients with past or current psychoses should be treated with caution.

Caution should be exercised with concomitant administration of psychoactive medicines and Levodopa + Carbidopa (NEUDOPA) (see DRUG ADMINISTRATIONS).

Levodopa + Carbidopa (NEUDOPA) should be administered cautiously to patients with severe cardiovascular or pulmonary disease, bronchial asthma, renal, hepatic or endocrine disease, or a history of peptic ulcer disease (because of the possibility of upper gastrointestinal haemorrhage) or of convulsions.

As with levodopa, care should be exercised in administering Levodopa + Carbidopa (NEUDOPA) to patients with a history of myocardial infarction who have residual atrial, nodal, or ventricular arrhythmia. In such patients, cardiac function should be monitored with particular care during the period of initial dosage administration and titration.

Patients with chronic wide-angle glaucoma may be treated cautiously with Levodopa + Carbidopa (NEUDOPA), provided the intraocular pressure is well controlled and the patient monitored carefully for changes in intraocular pressure during therapy.

A symptom complex resembling the neuroleptic malignant syndrome including muscular rigidity, elevated body temperature, mental changes, and increased

serum creatine phosphokinase has been reported when antiparkinsonian agents were withdrawn abruptly. Therefore, patients should be observed carefully when the dosage of Levodopa + Carbidopa (NEUDOPA) is reduced abruptly or discontinued, especially if the patient is receiving neuroleptics.

As with levodopa, periodic evaluations of hepatic, haematopoietic, cardiovascular and renal function are recommended during extended therapy.

If general anaesthesia is required, Levodopa + Carbidopa (NEUDOPA) may be continued as long as the patient is permitted to take fluids and medication by mouth. If therapy is interrupted temporarily, the usual daily dosage may be administered as soon as the patient is able to take oral medication.

Pregnancy
Although the effects of **NEUDOPA** on human pregnancy are unknown both levodopa and combinations of carbidopa and levodopa have caused visceral and skeletal malformations in rabbits. Therefore, use of Levodopa + Carbidopa (NEUDOPA) in women of childbearing potential requires that the anticipated benefits of the medicine be weighed against possible hazards should pregnancy occur.

Nursing Mothers
It is not known whether carbidopa or levodopa is excreted in human milk. Because many medicines are excreted in human milk and because of the potential for serious adverse reactions in infants, a decision should be made whether to discontinue nursing or to discontinue the use of Levodopa + Carbidopa (NEUDOPA), taking into account the importance of the medicine to the mother.

Use in Children
Safety and effectiveness of Levodopa + Carbidopa (NEUDOPA) in infants and children have not been established, and its use in patients below the age of 18 years is not recommended.

SIDE EFFECTS

Adverse effects that occur frequently in patients receiving Levodopa + Carbidopa (NEUDOPA) are those due to the central neuropharmacologic activity of dopamine. These reactions usually can be diminished by dosage reduction. The most common adverse effects are dyskinesias including choreiform, dystonic, and other involuntary movements and nausea. Muscle twitching and blepharospasm may be taken as early signs to consider dosage reduction.

Other adverse effects reported in clinical trials or in post-marketing experience include:

Body as a whole: syncope, chest pain, anorexia.

Cardiovascular: cardiac irregularities and/or palpitation, orthostatic effects including hypotensive episodes, hypertension, phlebitis.

Gastrointestinal: vomiting, gastrointestinal bleeding, development of duodenal ulcer, diarrhoea, dark saliva.

Haemotologic: leukopenia, haemolytic and non-haemolytic anaemia, thrombocytopenia, agranulocytosis.

Hypersensitivity: angioedema, urticaria, pruritus, Henoch-Schonlein purpura.
Nervous System/Psychiatric: neuroleptic malignant syndrome (see Warnings and Precautions), bradykinetic episodes (the "on-off' phenomenon), dizziness, somnolence paresthesia, psychotic episodes including delusions, hallucinations and paranoid ideation, depression with or without development of suicidal tendencies, dementia, dream abnormalities, agitation, confusion, increased libido.

Respiratory: dyspnea.

Skin: alopecia, rash, dark sweat.

Urogenital: dark urine.

Rarely convulsions have occurred; however a causal relationship with NEUDOPA has not been established.

Laboratory Tests
Abnormalities in various laboratory tests have occurred with carbidopa-levodopa preparations and may occur with NEUDOPA. These include elevations of liver function tests such as alkaline phosphatase, SGOT (AST), SGPT (ALT), lactic dehydrogenase, bilirubin, blood urea nitrogen, creatinine, uric acid, and positive Coombs' test.

Decreased haemoglobin, haematocrit, elevated serum glucose, and white blood cells, bacteria and blood in the urine have been reported.

Carbidopa-levodopa preparations may cause a false-positive reaction for urinary ketone bodies when a test tape is used for determination of ketonuria. This reaction will not be altered by boiling the urine specimen. False-negative tests may result with the use of glucose-oxidase methods of testing for glycosuria.

OTHER SIDE EFFECTS THAT HAVE BEEN REPORTED WITH LEVODOPA OR LEVODOPA/CARBIDOPA COMBINATIONS AND MAY BE POTENTIAL ADVERSE EFFECTS WITH NEUDOPA are listed below:

Nervous System/Psychiatric: asthenia, decreased mental acuity, disorientation, ataxia, numbness, increased hand tremor, muscle cramps, trismus, activation of latent Horner's syndrome, insomnia, anxiety, euphoria, falling and gait abnormalities.

Gastrointestinal: dyspepsia, dry mouth, bitter taste, sialorrhea, dysphagia, bruxism, hiccups, abdominal pain and distress, constipation, flatulence, burning sensation of tongue.

Metabolic: weight gain or loss, oedema.

Skin: flushing, increased sweating.

Urogenital: urinary retention, urinary incontinence, priapism.

Special senses: diplopia, blurred vision, dilated pupils, oculogyric crises.

Miscellaneous: weakness, faintness, fatigue, headache, hoarseness, malaise, hot flashes, sense of stimulation, bizarre breathing patterns, malignant melanoma (see Contraindications).

DRUG INTERACTIONS

Caution should be exercised when the following medicines are administered concomitantly with NEUDOPA:

Antihypertensive agents: Symptomatic postural hypotension has occurred when NEUDOPA is added to the treatment of patients receiving antihypertensive medicines. Therefore, when therapy with NEUDOPA is started, dosage adjustment of the antihypertensive medicine may be required.

Antidepressants: For patients receiving monoamine oxidase inhibitors, see Contraindications.

There have been rare reports of adverse reactions, including hypertension and dyskinesia, resulting from the concomitant use of tricyclic antidepressants and NEUDOPA.

Other medicines: Dopamine D2 receptor antagonists (e.g., phenothiazines, butyrophenones and risperidone) and isoniazid may reduce the therapeutic effects of levodopa. In addition, the beneficial effects of levodopa in Parkinson's disease have been reported to be reversed by phenytoin and papaverine. Patients taking these medicines with NEUDOPA should be carefully observed for loss of therapeutic response.

Concomitant therapy with selegiline and carbidopa-levodopa may be associated with severe orthostatic hypotension not attributable to carbidopa-levodopa alone (see CONTRAINDICATIONS).

Since levodopa competes with certain amino acids, the absorption of levodopa may be impaired in some patients on a high protein diet.

OVERDOSAGE

Management of acute overdosage with NEUDOPA is basically the same as management of acute overdosage with levodopa; however, pyridoxine is not effective in reversing the actions of NEUDOPA.

Electrocardiographic monitoring should be instituted and the patient carefully observed for the possible development of arrhythmias; if required, appropriate antiarrhythmic therapy should be given. The possibility that the patient may have taken other medicines as well as NEUDOPA should be taken into consideration. To date, no experience has been reported with dialysis; hence, its value in overdosage is not known.

HOW SUPPLIED

NEUDOPA scored tablets containing 25mg of carbidopa (U.S.P.) + 250mg of levodopa (U.S.P.) supplied in blister pack of 100's (10 x 10's blister)

Store in a cool and dry place.
Protect from light.
Keep out of the reach of children.
Dosage as directed by the physician.
To be dispensed on the prescription of a registered medical practitioner only.

ہدایات:
دوا کو ٹھنڈی اور خشک جگہ پر روشنی سے بچا کر رکھیں۔
بچوں کی پہنچ سے دور رکھیں۔
ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
صرف رجسٹرڈ ڈاکٹر کے نسخے پر ہی فروخت کریں۔

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