



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/289448/2013
EMA/H/C/002441

EPAR summary for the public

Levodopa/Carbidopa/Entacapone Orion

levodopa/carbidopa/entacapone

This is a summary of the European public assessment report (EPAR) for Levodopa/Carbidopa/Entacapone Orion. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Levodopa/Carbidopa/Entacapone Orion.

What is Levodopa/Carbidopa/Entacapone Orion?

Levodopa/Carbidopa/Entacapone Orion is a medicine that contains three active substances: levodopa, carbidopa and entacapone. It is available as a range of tablets in seven strengths, containing 50 to 200 mg levodopa and 12.5 to 50 mg carbidopa. All of the tablets contain 200 mg entacapone.

What is Levodopa/Carbidopa/Entacapone Orion used for?

Levodopa/Carbidopa/Entacapone Orion is used to treat adults with Parkinson's disease. Parkinson's disease is a progressive brain disorder that causes shaking, slow movement and muscle stiffness. Levodopa/Carbidopa/Entacapone Orion is used in patients who are being treated with a combination of levodopa and an inhibitor of dopa decarboxylase (two standard treatments for Parkinson's disease) but are having 'fluctuations' towards the end of the period between two doses of their medication. Fluctuations happen when the effects of the medication wear off and symptoms re-emerge. They are linked with a reduction in the effect of levodopa, when the patient experiences sudden switches between being 'on' and able to move, and being 'off' and having difficulty moving about. Levodopa/Carbidopa/Entacapone Orion is used when these fluctuations cannot be treated with the standard combination alone.



The medicine can only be obtained with a prescription.

How is Levodopa/Carbidopa/Entacapone Orion used?

Each Levodopa/Carbidopa/Entacapone Orion tablet contains one complete dose of levodopa, in seven strengths, with corresponding amounts of carbidopa and entacapone to improve its effectiveness. The strength of Levodopa/Carbidopa/Entacapone Orion that the patient should use is based on the amount of levodopa they need to control their symptoms. See the summary of product characteristics (also part of the EPAR) for full instructions on how patients should be switched to Levodopa/Carbidopa/Entacapone Orion, and on how the dose is adjusted during treatment.

The maximum daily dose of Levodopa/Carbidopa/Entacapone Orion is 10 tablets, except for the tablets containing 175 mg levodopa and 43.75 mg carbidopa, for which the maximum daily dose is eight tablets, and those containing 200 mg levodopa and 50 mg carbidopa, for which it is seven tablets. Levodopa/Carbidopa/Entacapone Orion tablets should be taken whole, with or without food. They should be used with caution in patients with mild to moderately reduced liver function or severely reduced kidney function. They should not be used in patients with severe liver problems.

How does Levodopa/Carbidopa/Entacapone Orion work?

In patients with Parkinson's disease, the cells in the brain that produce dopamine (a substance used to transmit signals between nerve cells that help to control muscle movement) begin to die and the amount of dopamine in the brain decreases. The patients then lose their ability to control their movements reliably. All of the active substances in Levodopa/Carbidopa/Entacapone Orion work to restore the levels of dopamine in the parts of the brain that control movement and co-ordination.

Levodopa is converted into dopamine in the brain. Both carbidopa and entacapone block some of the enzymes that are involved in the breakdown of levodopa in the body: carbidopa blocks the enzyme dopa decarboxylase, and entacapone blocks the enzyme catechol-O-methyl transferase (COMT). As a result, levodopa remains active for longer. This helps to improve the symptoms of Parkinson's disease, such as stiffness and slowness of movement. Entacapone has been authorised in the European Union (EU) as Comtess/Comtan since 1998. The use of combinations of levodopa and carbidopa is well established, having been in use since the mid-1970s. Having all three substances in the same tablet can lower the number of tablets the patients have to take and help them stick to treatment.

How has Levodopa/Carbidopa/Entacapone Orion been studied?

The company used some of the data from Comtess/Comtan to support the use of Levodopa/Carbidopa/Entacapone Orion and presented data from the published literature for levodopa and carbidopa.

The company carried out 'bioequivalence' studies to show that taking Levodopa/Carbidopa/Entacapone Orion produces the same levels of levodopa, carbidopa and entecapone in the blood as taking separate tablets containing entecapone and the combination of levodopa and carbidopa.

What benefit has Levodopa/Carbidopa/Entacapone Orion shown during the studies?

The studies showed that Levodopa/Carbidopa/Entacapone Orion is bioequivalent to the separate tablets.

What is the risk associated with Levodopa/Carbidopa/Entacapone Orion?

The most common side effects with Levodopa/Carbidopa/Entacapone Orion (seen in more than 1 patient in 10) are dyskinesia (uncontrollable movements), muscle pain, diarrhoea and nausea (feeling sick) and harmless urine discoloration. Serious side effects which have been reported much less often include gastrointestinal haemorrhage (bleeding in the gut) and angioedema (swelling under the skin of face or limbs). For the full list of all side effects reported with Levodopa/Carbidopa/Entacapone Orion, see the package leaflet.

Levodopa/Carbidopa/Entacapone Orion must not be used in people who are hypersensitive (allergic) to levodopa, carbidopa, entacapone or any of the other ingredients. Levodopa/Carbidopa/Entacapone Orion must not be used in patients with:

- severely reduced liver function;
- narrow-angle glaucoma (increased pressure within the eye);
- pheochromocytoma (a tumour of the adrenal gland);
- a history of neuroleptic malignant syndrome (a dangerous nervous system disorder usually caused by antipsychotic medicines) or rhabdomyolysis (breakdown of muscle fibres).

Levodopa/Carbidopa/Entacapone Orion must not be used together with other medicines that belong to the group 'monoamine oxidase inhibitors' (a type of antidepressant). See the summary of product characteristics (also part of the EPAR) for full details.

Why has Levodopa/Carbidopa/Entacapone Orion been approved?

The CHMP decided that Levodopa/Carbidopa/Entacapone Orion's benefits are greater than its risks and recommended that it be given marketing authorisation.

Other information about Levodopa/Carbidopa/Entacapone Orion

The European Commission granted a marketing authorisation valid throughout the European Union for Levodopa/Carbidopa/Entacapone Orion on 24 August 2011. This authorisation was based on the authorisation granted to Stalevo in 2003 ('informed consent').

The full EPAR for Levodopa/Carbidopa/Entacapone Orion can be found on the Agency's website: [ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports](http://ema.europa.eu/Find%20medicine/Human%20medicines/European%20Public%20Assessment%20Reports). For more information about treatment with Levodopa/Carbidopa/Entacapone Orion, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 05-2013.