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EPAR summary for the public

Stalevo

Levodopa/carbidopa/entacapone

This is a summary of the European public assessment report (EPAR) for Stalevo. 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 Stalevo.

What is Stalevo?

Stalevo 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 Stalevo used for?

Stalevo 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. Stalevo 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. Stalevo is used when these fluctuations cannot be treated with the standard combination alone.

The medicine can only be obtained with a prescription

How is Stalevo used?

Each Stalevo tablet contains one complete dose of levodopa, in seven strengths, with corresponding amounts of carbidopa and entacapone to improve its effectiveness. The strength of Stalevo 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 Stalevo, and on how the dose is adjusted during treatment.

The maximum daily dose of Stalevo is 10 tablets, except for the tablets containing 200 mg levodopa and 50 mg carbidopa, for which the maximum daily dose is seven tablets. Stalevo tablets should be taken whole, with or without food. They should be used with caution in patients with mild to moderate problems with their liver or severe problems with their kidneys. They should not be used in patients with severe liver problems.

How does Stalevo work?

In patients with Parkinson's disease, the cells in the brain that produce the neurotransmitter dopamine 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 Stalevo 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 being 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 Stalevo been studied?

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

The company carried out 'bioequivalence' studies to show that taking Stalevo produces the same levels of levodopa, carbidopa and entacapone in the blood as taking separate tablets containing entacapone and the combination of levodopa and carbidopa.

What benefit has Stalevo shown during the studies?

The studies showed that Stalevo is bioequivalent to the separate tablets.

What is the risk associated with Stalevo?

The most common side effects with Stalevo (seen in more than 1 patient in 10) are dyskinesia (uncontrollable movements), aggravated Parkinsonism (worsening of Parkinson's disease), nausea (feeling sick) and harmless urine discoloration. For the full list of all side effects reported with Stalevo, see the package leaflet.

Stalevo should not be used in people who may be hypersensitive (allergic) to levodopa, carbidopa, entacapone or any of the other ingredients. Stalevo must not be used in patients with:

severe liver disease;

narrow-angle glaucoma (increased pressure within the eye);

phaeochromocytoma (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).

Stalevo 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 Stalevo been approved?

The CHMP decided that Stalevo's benefits are greater than its risks for the treatment of patients with Parkinson's disease and end-of-dose motor fluctuations not stabilised on levodopa/dopa decarboxylase inhibitor treatment. The Committee recommended that Stalevo be given marketing authorisation.

Other information about Stalevo

The European Commission granted a marketing authorisation valid throughout the European Union for Stalevo to on 17 October 2008.

The full EPAR for Stalevo can be found on the Agency's website: ema.europa.eu/Find_medicine/Human_medicines/European_Public_Assessment_Reports. For more information about treatment with Stalevo, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 07-2011.