APPROVED
By Marlienka at 3:01 pm, Nov 15, 2021

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

STALEVO® 50/12,5 film-coated tablets

STALEVO® 100/25 film-coated tablets

STALEVO® 150/37,5 film-coated tablets

Levodopa/carbidopa/entacapone

Read all of this leaflet carefully before taking STALEVO

- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor or your pharmacist.
- STALEVO has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What STALEVO is and what it is used for.
2. What you need to know before you take STALEVO**.**
3. How to take STALEVO**.**
4. Possible side effects.
5. How to store STALEVO**.**
6. Contents of the pack and other information.

1. What STALEVO is and what it is used for

What STALEVO is:

STALEVO contains three active substances in one film-coated tablet. Each tablet contains levodopa, used to treat Parkinson's disease. Levodopa works by increasing the level of dopamine in the brain.

The two other active substances: carbidopa and entacapone improve the effects of levodopa in treating Parkinson's disease.

What STALEVO is used for:

STALEVO is used to treat patients with Parkinson's disease who have end-of-dose motor fluctuations.

2. What you need to know before you take STALEVO

Do not take STALEVO:

- If you are allergic (hypersensitive) to levodopa, carbidopa or entacapone or any of the other ingredients in STALEVO.
- If you are pregnant or breastfeeding.
- If you have a severe liver impairment.
- If you have narrow-angle glaucoma (an eye disorder).
- If you have suspicious undiagnosed skin lesions or history of melanoma (darkening of skin as a result of a tumour)
- If you have a tumour of the adrenal gland (known as pheochromocytoma; this may increase the risk of severe high blood pressure).
- If you are taking certain medicines to treat depression or some antibiotics (selective MAO-A plus MAO-B inhibitors, or non- selective MAO-inhibitors such as phenelzine, tranylcypromine and linezolid).

- If you have ever had neuroleptic malignant syndrome (NMS; this is a reaction to medicines used to treat severe mental disorders).
- If you have ever had non-traumatic rhabdomyolysis (a muscle disorder).

If any of these applies to you, talk to your doctor before taking STALEVO.

Warnings and precautions

Take special care with STALEVO:

- If you have ever had a heart attack, asthma or any other diseases of the heart, blood vessels or lungs.
- If you have a liver problem.
- If you have a severe renal problem.
- If you have ever had kidney, liver or hormone-related diseases.
- If you have ever had stomach ulcers.
- If you have ever had convulsions.
- If you have ever suffered from any form of severe mental disorder.
- If you feel depressed, have suicidal thoughts, or notice unusual changes in your behaviour.
- If you have chronic wide-angle glaucoma. Your dose may need to be adjusted and the pressure in your eyes may need to be monitored.
- If you are taking other medicines that can cause low blood pressure. You should be aware that STALEVO may make these reactions worse.
- If uncontrolled movements begin or get worse after you start taking STALEVO, your doctor may need to change the dose of your antiparkinson medications.
- Tell your doctor if you or your family/caregiver notices you are developing urges or cravings to behave in ways that are unusual for you or you cannot resist the impulse, drive or

temptation to carry out certain activities that could harm yourself or others. These behaviours are called impulse control disorders and can include addictive gambling, excessive eating or spending, an abnormally high sex drive or a preoccupation with an increase in sexual thoughts or feelings. Your doctor may need to review your treatments.

Children/ and adolescents

Do not give STALEVO to children under 18 years of age as it is unlikely to be safe.

Other medicines and STALEVO

Always tell your healthcare provider if you are taking any other medicine (this includes complementary or traditional medicines).

Tell your doctor if you are taking any of the following medicines:
STALEVO may increase the effects and side effects of certain antidepressants and some other medicines.
These include MAO-A inhibitors (e.g. moclobemide), tricyclic antidepressants (e.g. amitryptiline) and noradrenaline reuptake inhibitors (e.g. desipramine, maprotiline and venlafaxine), as well as paroxetine, rimiterole, isoprenaline, adrenaline, noradrenaline, dopamine, dobutamine, alpha-methyldopa and apomorphine.
Watch out for additional effects if you take these medicines while being treated with STALEVO.

The effects of STALEVO may be weakened by certain medicines. It includes medicines:

- used to treat mental disorders (dopamine antagonists),
- used to treat nausea and vomiting (dopamine antagonists),
- used to prevent convulsions (phenytoin),

- used to relax the muscles (papaverine).

STALEVO may make it harder for you to digest iron. Therefore, do not take STALEVO and iron supplements at the same time. After taking one of them, wait at least 2 to 3 hours before taking the other.

STALEVO with food and drink and alcohol

STALEVO may be taken with or without food.

For some patients, STALEVO may not be well absorbed if it is taken with, or shortly after eating protein-rich food (such as meats, fish, dairy products, seeds and nuts). Consult your doctor if you think this applies to you.

- Do not take STALEVO and iron supplements at the same time.
- After taking one of them, wait at least 2 to 3 hours before taking the other.

Pregnancy and breastfeeding and fertility

If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before taking STALEVO.

- You should not take STALEVO if you are pregnant.
- You should not breastfeed your baby if you are taking STALEVO.

Driving and using machinery

It is not always possible to predict to what extent STALEVO may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which STALEVO affects them.

- STALEVO may lower your blood pressure, which may make you feel light-headed or dizzy. Therefore, be particularly careful when you drive or when you operate any tools or machines.
- If you feel very drowsy, or if you sometimes find yourself suddenly falling asleep, you must not drive or do anything else that requires you to be alert (operate tools or machines).

STALEVO contains mannitol and sucrose

STALEVO contains mannitol and sucrose which may have an effect on the control of your blood sugar if you have diabetes mellitus.

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking STALEVO.

3. How to take STALEVO

Do not share medicines prescribed for you with any other person.

Always take STALEVO exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

The usual dose is:

- Each STALEVO tablet contains one complete dose of levodopa, carbidopa and entacapone.
- Each time you take STALEVO, take only one tablet.
- The tablet is not intended to be split or broken into smaller pieces.
- Your doctor will tell you exactly how many tablets of STALEVO to take each day.
- Depending on how you respond to treatment, your doctor may suggest a higher or lower dose.
- Do not take more than 10 tablets a day.

- Your doctor will tell you how long your treatment with STALEVO will last.
- Do not stop taking treatment early because this may cause your symptoms to return.
- If you have the impression that the effect of STALEVO is too strong or too weak, tell your doctor or pharmacist.

If any of the above applies to you, contact your doctor**.**

- If you find yourself suddenly falling asleep, or if you feel very drowsy *(see also the section 'Driving and using machinery')*.
- If your muscles get very rigid or jerk violently, or if you suffer from tremors, agitation, confusion, fever, rapid pulse, or wide fluctuations in your blood pressure.
- If you experience diarrhoea, a follow-up of weight is recommended in order to prevent potential excessive weight loss.
- If you experience progressive anorexia, asthenia (weakness, exhaustion) and weight decrease within a relatively short period of time, contact your doctor. He/she may decide to conduct a general medical evaluation including liver function.

If any of these occurs, tell your doctor immediately.

If you are going to have a surgery with a general anaesthesia, inform the doctor that you are taking STALEVO.

Older people:

If you are over 65, you can take STALEVO without dose adjustment.

Children and adolescents:

The safe use of STALEVO has not been established in children and adolescents less than 18 years of age and can therefore not be recommended.

When and how to take STALEVO:

- Strictly follow your doctor's instructions on when and how to use STALEVO, other levodopa medications and other antiparkinson medicines.
- Check with your doctor or pharmacist if you are unsure about these instructions or the text printed on the packaging.

If you take more STALEVO than you should:

If you have accidentally taken too many STALEVO tablets, talk to your doctor or pharmacist immediately. You may require medical attention.

In the event of overdosage, consult your doctor or pharmacist. If neither is available, rush the patient to the nearest hospital or poison control centre.

If you forget to take STALEVO:

If there is more than an hour until your next dose: take one tablet now, and the next tablet at the normal time.

If there is less than an hour until your next dose: take a tablet now, wait an hour, then take another tablet. After that go back to your normal schedule.

Do not take a double dose to make up for forgotten doses. Always leave at least an hour between STALEVO tablets, to avoid possible side effects.

If you are unsure about what to do, consult your doctor.

If you stop taking STALEVO

Do not stop taking STALEVO unless your doctor tells you to. In such case, your doctor may need to re-adjust the dosage of your other anti-Parkinson medications, especially levodopa, to give sufficient control of your symptoms. Abrupt discontinuation of both STALEVO and other antiparkinsonian medication may result in unwanted side effects, such as severe muscular stiffness, high fever and altered consciousness.

4. Possible side effects

STALEVO can have side effects.

Not all side effects reported for STALEVO are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking STALEVO, please consult your healthcare professional for advice.

If any of the following happens, stop taking STALEVO and tell your doctor immediately or go to the casualty department at your nearest hospital:

- Swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing;
- rash or itching;
- fainting;
- muscles get very rigid or jerk violently;
- tremors;
- agitation;
- confusion;

- fever;
- rapid pulse, or wide fluctuations in your blood pressure.

These can be symptoms of neuroleptic malignant syndrome (NMS, a rare severe reaction to medicines used to treat disorders of the central nervous system) or rhabdomyolysis (a rare severe muscle disorder).

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to STALEVO. You may need urgent medical attention or hospitalisation.

Tell your doctor if you notice any of the following:

The following side effects have been reported frequently:

- uncontrolled movements (dyskinesias), worsening of Parkinson's symptoms
- feeling sick (nausea)
- harmless reddish-brown discolouration of urine
- light-headedness or fainting due to low blood pressure, high blood pressure
- heart or artery disease events other than a heart attack (e.g. chest pain), irregular heart rate or rhythm
- dizziness, drowsiness
- vomiting, abdominal pain and discomfort, heartburn, dry mouth, constipation, diarrhoea
- inability to sleep, hallucinations, confusion, abnormal dreams, including nightmares
- mental changes – including problems with memory or thinking, anxiety and depression (possibly with thoughts of suicide)
- tiredness, chest pain
- more frequent falling; impaired walking, loss of both strength and energy
- shortness of breath

- increased sweating
- muscle cramps and pain; involuntary muscle contraction, swelling of legs
- blurred vision
- anaemia, decreased appetite, decrease weight
- headache, joint pain
- urinary tract infection

The following side effects have been reported less frequently:

- heart attack
- bleeding in the gut
- abnormal liver function tests
- psychotic symptoms, feeling agitated
- changes in the blood cell count (which may result in bleeding)
- swallowing difficulties
- inability to urinate
- generally feeling unwell
- convulsions
- inflammation of the colon (colitis)
- skin, hair, nail and sweat discolourations

The following side effects have been reported but the frequency is unknown:

The exact frequencies of these side effects are not known but are based upon reports received since the product has been on the market:

- hepatitis (inflammation of the liver);

- itching;
- excessive daytime somnolence; sudden sleep onset episodes.

You may experience the following side effects:

- Inability to resist the impulse to perform an action that could be harmful, which may include:
  - Strong impulse to gamble excessively despite serious personal or family consequences,
  - Altered or increased sexual interest and behavior of significant concern to you or others, for example an increased sexual drive,
  - Uncontrolled excessive shopping or spending,
  - Binge eating (eating large amounts of food in a short time period) or compulsive eating (eating more food than normal and more than is needed to satisfy your hunger).

Tell your doctor if you experience any of these behaviors, your doctor will discuss ways of managing or reducing symptoms.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects to SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/. By reporting side effects, you can help provide more information on the safety of STALEVO.

5. How to store STALEVO

- Store at or below 25 °C.
- Keep the container well-closed and store in a dry place protected from light.
- Do not use after the expiry date printed on the pack.
- Do not use if the pack is damaged or shows signs of tampering.
- Keep all medicines out of the reach and sight of children.
- Return all unused medicine to your pharmacist.
- Do not dispose of unused medicine in drains or sewerage systems.
- Store in the original package / container.
- Do not store in a bathroom

6. Contents of the pack and other information

WHAT STALEVO CONTAINS

The active ingredients in STALEVO are:

Levodopa, carbidopa and entacapone.

STALEVO 50/12,5 film-coated tablets contain:

50 mg levodopa, 12,5 mg carbidopa and 200 mg entacapone.

STALEVO 100/25 film-coated tablets contain:

100 mg levodopa, 25 mg carbidopa and 200 mg entacapone.

STALEVO 150/37,5 film-coated tablets contain:

150 mg levodopa, 37,5 mg carbidopa and 200 mg entacapone.

The other ingredients are:

Croscarmellose sodium, magnesium stearate, maize starch, mannitol, povidone K30.

The film-coating contains:

Glycerol 85 %, hypromellose, magnesium stearate, polysorbate 80, red iron oxide (E172), sucrose, titanium dioxide (E171), yellow iron oxide (E172)

Contains sugar: Mannitol and sucrose

What STALEVO looks like and contents of the pack

STALEVO® 50/12.5 Film-coated tablets:

Film-coated tablet, brownish- or greyish-red, round, biconvex tablets marked with “LCE 50” on one side. Diameter 11 mm.

STALEVO® 100/25 Film-coated tablets:

Film-coated tablet, brownish- or greyish-red, oval, tablets marked with “LCE 100” on one side. Diameter 7,6 x 16,3 mm.

STALEVO® 150/37,5 Film-coated tablets:

Film-coated tablet, brownish- or greyish-red, elongated-ellipse shaped tablets marked with “LCE 150” on one side. Diameter 9,3 x 14,31 mm.

100 tablets packed into white HDPE plastic containers with tamper evident PP plastic closures. Heat sealable aluminium foil inner seals.

Holder of Certificate of Registration

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STALEVO® 50/12,5 film-coated tablets: 38/5.4.1/0067

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Access to the corresponding Professional Information

An electronic copy of the Professional Information (PI) is available on the Equity website (http://www.equitypharma.co.za) or http://www.sahpra.org.za