

CONSUMER INFORMATION

Pr **STALEVO*** (levodopa, carbidopa and entacapone)

This leaflet is part III of a three-part "Product Monograph" published when STALEVO* was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about STALEVO*. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

STALEVO* is used to treat people with Parkinson's disease in whom the effect of each levodopa dose becomes shorter and who subsequently experience fluctuations in the symptoms of Parkinson's disease (end-of-dose "wearing-off").

What it does:

STALEVO* contains three active substances in one film-coated tablet. Each tablet contains levodopa, used to treat Parkinson's disease. The two other active substances: carbidopa and entacapone help improve the antiparkinson effects of levodopa.

Symptoms of Parkinson's disease are thought to be caused by a decrease in the amount of dopamine in certain areas of the brain. Levodopa is given to increase the levels of dopamine in the brain. Part of the dose of levodopa is broken down in the body to an inactive substance, before it reaches the brain. Entacapone and carbidopa help to prevent this breakdown and ensure that enough levodopa gets to the brain, where it will be converted to dopamine.

STALEVO* helps in relieving the symptoms of Parkinson's disease, such as shaking of the limbs and stiffness and slowness of movement.

When it should not be used:

You should NOT take STALEVO* if:

- You have a history of allergic reactions to levodopa, carbidopa or entacapone or any other components of the STALEVO* tablet (see "What the important nonmedicinal ingredients are").
- You have liver impairment.
- You have narrow angle glaucoma.
- You have untreated heart, kidney, lung, blood or hormonal disease.
- You have pheochromocytoma (a tumor of the adrenal gland), because it may increase the risk of severe hypertensive reactions.
- You are taking or have been treated during the last two weeks with certain antidepressants (both MAO-A and MAO-B inhibitors simultaneously, or non-selective MAO inhibitors).

- You have a history of Neuroleptic Malignant Syndrome (NMS) (rare reaction to medicines used to treat severe mental disorders).
- You have a history of rhabdomyolysis (rare form of muscle disorder), which was not caused by an injury.
- You have been told you should not take sympathomimetic drugs such as isoproterenol, amphetamines, epinephrine or cough and cold medications containing drugs related to epinephrine.

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

What the medicinal ingredient is:

The active substances of STALEVO* are levodopa, carbidopa and entacapone.

What the nonmedicinal ingredients are:

The nonmedicinal ingredients are croscarmellose sodium, glycerol 85%, hypromellose, magnesium stearate, maize starch, mannitol, polysorbate 80, povidone, red iron oxide (E 172), sucrose, titanium dioxide (E 171), yellow iron oxide (E 172) (note: yellow iron oxide is not used in 75/18.75/200 mg and 125/31.25/200 mg tablets) (see WARNINGS AND PRECAUTIONS).

What dosage forms it comes in:

STALEVO* is available in five different dosage strengths: 50/12.5/200 mg, 75/18.75/200 mg, 100/25/200 mg, 125/31.25/200 mg and 150/37.5/200 mg film-coated tablets.

WARNINGS AND PRECAUTIONS

Some people feel sleepy, drowsy, or, rarely, may suddenly fall asleep without warning (i.e. without feeling sleepy or drowsy) when taking STALEVO*. During treatment with STALEVO* take special care when you drive or operate a machine. If you experience excessive drowsiness or a sudden sleep onset episode, refrain from driving and operating machines, and contact your physician.

Studies of people with Parkinson's disease show that they may be at an increased risk of developing melanoma, a form of skin cancer, when compared to people without Parkinson's disease. It is not known if this problem is associated with Parkinson's disease or the drugs used to treat Parkinson's disease. Therefore, your doctor should perform periodic skin examinations.

In a study of patients with early stage Parkinson's disease, who were treated with levodopa/carbidopa or STALEVO* (levodopa/carbidopa/entacapone) for an average of about 3 years, prostate cancer was reported more frequently in the group of patients that received STALEVO*. It is not known if treatment with STALEVO* affects the risk of having prostate cancer. Therefore, it is important for men to have their regular prostate examinations during treatment with STALEVO*. STALEVO*

should not be used for the treatment of early stage Parkinson's disease.

BEFORE you use STALEVO* talk to your doctor or pharmacist if:

- You have ever had a heart attack, asthma or any other diseases of the heart, blood vessels or lungs.
- You have or ever had a liver problem, such as liver disease or abnormal liver function tests.
- You have or ever had a severe kidney problem.
- You have or ever had hormone-related diseases.
- You have ever had inflammatory bowel disease.
- You have problems urinating, or have been told you have an enlarged prostate, prostate cancer, or elevated levels of Prostate Specific Antigen (PSA).
- You have ever had stomach ulcers.
- You have ever had convulsions.
- You have ever suffered from any form of severe mental disorder.
- You feel depressed, have suicidal thoughts, or notice unusual changes in your behavior.
- You have chronic wide-angle glaucoma. Your dose may need to be adjusted and the pressure in your eyes may need to be monitored.
- You are taking other medicines that can cause low blood pressure. You should be aware that STALEVO* may make these reactions worse.
- Uncontrolled movements begin or get worse after you start taking STALEVO*, your doctor may need to change the dose of your antiparkinson medications.
- You have been told by your doctor that you have a hereditary intolerance to some sugars, contact your doctor before taking this medicinal product.
- You are taking any iron supplements or multivitamins containing iron.
- 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 behaviors 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.

If any of the following occurs, tell your doctor immediately:

- If you find yourself suddenly falling asleep, or if you feel very drowsy (see precaution in box above).
- 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 (signs of Neuroleptic Malignant Syndrome, NMS).
- If you experience diarrhea, your doctor may follow-up on your weight in order to prevent potential excessive weight loss.
- If you experience increasing loss of appetite, weakness, exhaustion and weight loss within a relatively short period of time after starting treatment with entacapone, contact your

doctor. He/she may decide to do a general medical evaluation, including blood tests to check liver function.

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

If you feel the need to stop using STALEVO*, please consult your doctor first. Abruptly stopping treatment or rapidly decreasing the dose can lead to serious side effects in some patients. It may be necessary to reduce the dose of STALEVO* gradually, and make changes in your other antiparkinson medication, in order to prevent side effects and keep your Parkinson's symptoms from getting worse (see PROPER USE OF THIS MEDICATION - Stopping STALEVO* treatment).

Driving and using machines

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 (see precaution in box above).

Older people

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

Pregnant women

If you are pregnant or think you may be pregnant, do not take STALEVO* before consulting your doctor. STALEVO* is not to be used during pregnancy unless clearly necessary. Your doctor will discuss with you the potential risk of taking STALEVO* during pregnancy.

Breast-feeding mothers

If you are breast-feeding, tell your doctor. You should not breast-feed while under treatment with STALEVO*.

Children and adolescents

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

INTERACTIONS WITH THIS MEDICATION

Tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including any to lower your blood-pressure, non-prescription medicines or herbal products. 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. amitriptyline) and noradrenaline re-uptake inhibitors (e.g. desipramine, maprotiline and venlafaxine), as well as paroxetine, rimiterole, isoprenaline, adrenaline, noradrenaline, dopamine, dobutamine, alpha-methyl dopa 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 (certain antipsychotics, such as chlorpromazine, haloperidol and risperidone),
- used to treat nausea and vomiting (certain antiemetics, such as prochlorperazine and promethazine),
- used to prevent convulsions (such as phenytoin),
- used to relax the muscles (such as papaverine).

Tell your doctor if you are taking these medicines, or if you notice that STALEVO* does not work as well when you take them.

Iron supplements or multivitamins containing iron may reduce the amount of levodopa and/or carbidopa available to the body, and may make STALEVO* less effective. STALEVO* may also make it harder for you to digest iron. Therefore, do not take STALEVO* and iron supplements or multivitamins containing iron at the same time. After taking one of them, wait at least 2 to 3 hours before taking the other.

PROPER USE OF THIS MEDICATION

Always take STALEVO* exactly as your doctor has instructed you to. You should check with your doctor or pharmacist if you are unsure.

Usual dose:

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 8 tablets a day.

Talk to your doctor or pharmacist if you think the effect of STALEVO* is too strong or too weak, or if you detect possible side effects.

When and how to take STALEVO*

Strictly follow your doctor's instructions on when and how to use STALEVO*, and any other antiparkinson drugs. Check with your doctor or pharmacist if you are unsure about these instructions or the instructions printed on the packaging.

STALEVO* may be taken with or without food.

Taking STALEVO* with food and drink

For some patients, taking STALEVO* with, or shortly after eating protein-rich food (such as meats, fish, dairy products, seeds and

nuts), may reduce the amount of levodopa available to the body, and STALEVO* may be less effective. Tell your doctor if you are on a high protein diet.

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.

Stopping STALEVO* treatment

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 antiparkinson 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.

Overdose:

If you have taken more medication than what has been prescribed, contact either a hospital emergency department, the nearest Poison Control Centre or your doctor immediately. You may require medical attention even if there are no symptoms.

Missed Dose:

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.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

As with all medicines, patients treated with STALEVO* may experience side effects, although not everybody gets them. If you experience any of these side effects, talk to your doctor as soon as you can. Many of the side effects can be relieved by adjusting the dose.

If any of the side effects get serious, tell your doctor, nurse or pharmacist.

Entacapone enhances the effectiveness and effects of levodopa. If you were not previously taking entacapone tablets with your levodopa/carbidopa tablets, switching to STALEVO* may cause an increase in certain side effects of levodopa, such as uncontrolled movements, feeling sick (nausea), being sick (vomiting) or hallucinations.

Very common (affecting more than 1 user in 10)

- Uncontrolled movements (dyskinesia);
- Feeling sick (nausea);
- Harmless reddish-brown discoloration of the urine;
- Diarrhea;
- Muscle and/or joint pain.

Common (affecting 1 to 10 users in 100)

- Heart or artery disease events other than a heart attack (e.g. chest pain, swelling or blue coloration of the extremities, shortness of breath on exertion, angina, disease of the heart valves or other conditions identified by your physician), irregular heart rate or rhythm;
- Light-headedness or fainting due to low blood pressure; high blood pressure;
- Worsening of Parkinson’s symptoms;
- Dizziness; drowsiness; tingling or numbness;
- Vomiting; abdominal pain and discomfort; heartburn; dry mouth; constipation;
- 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; rashes;
- Muscle cramps; involuntary muscle contractions; swelling of legs;
- Blurred vision;
- Anemia, decreased appetite; decreased weight;
- Headache;
- Urinary tract infection.

Uncommon (affecting 1 to 10 users in 1,000)

- Heart attack (chest pain often associated with left shoulder or jaw pain, feeling of constriction around chest and sweating);
- Bleeding in the gut;
- Abnormal liver function tests;
- Psychotic symptoms; feeling agitated;
- Inflammation of the colon (colitis) which may lead to diarrhea and weight loss;
- Skin, nail, hair and sweat discolorations;
- Inflammation of the veins in the legs;
- Changes in the blood cell count which may result in bleeding;
- Swallowing difficulties;
- Inability to urinate;
- Generally feeling unwell.

Rare or very rare effects

- Convulsions.

STALEVO* may lower your blood pressure and cause a decrease in your blood pressure when standing up rapidly after sitting or lying down, with or without symptoms such as dizziness, nausea,

syncope (fainting) and sweating. Decreases in blood pressure may occur more frequently during the start of treatment with STALEVO*. Therefore, you should avoid standing rapidly after sitting or lying down, especially after prolonged periods. You should also be careful if you are taking other medicinal products that may decrease blood pressure.

Severe diarrhea while taking STALEVO* can cause significant loss of weight for some individuals. In some cases diarrhea and weight loss have been caused by inflammation of the colon, which has occurred during treatment with entacapone. Therefore, it is important to tell your doctor if you have diarrhea so that the cause of your symptoms can be determined. Your weight should also be closely monitored. Your treatment may need to be adjusted to avoid diarrhea and excessive weight loss.

Other

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.

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

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM[§]				
Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and seek immediate emergency treatment
		Only if severe	In all cases	
Very common	Uncontrolled movements (dyskinesia)		√	
	Feeling sick (nausea)		√	
	Diarrhea		√	
Common	Mental changes, including problems with memory or thinking; anxiety and depression (possibly with thoughts of suicide)		√	
	Hallucinations		√	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM[§]

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and seek immediate emergency treatment
		Only if severe	In all cases	
	Decrease in blood pressure when standing up rapidly, after sitting or lying down, with or without symptoms such as dizziness, nausea, fainting and sweating.		√	
	Heart or artery disease events other than a heart attack (symptoms may include chest pain, swelling or blue coloration of the extremities, shortness of breath on exertion, angina, disease of the heart valves)			√
	Chest pain, shortness of breath		√	
Uncommon	Irregular heart beat		√	
	Psychotic symptoms; feeling agitated		√	
	Bleeding gut and ulcers (symptoms may include abdominal pain, nausea, vomiting blood, blood in stools)		√	
	Infections, bleeding		√	
	Inflammation of the colon (symptoms of severe diarrhea with significant weight loss)		√	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM[§]

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and seek immediate emergency treatment
		Only if severe	In all cases	
	Heart attack (chest pain often associated with left shoulder or jaw pain, feeling of constriction around chest and sweating)			√
	Inability to control impulse to perform an action that could be harmful, such as: strong impulse to gamble excessively, altered or increased sexual interest and behavior of significant concern to you or to others, uncontrollable excessive shopping or spending, binge eating or compulsive eating.		√	
Very rarely	Convulsions			√
	Muscle rigidity, muscle twitching, tremors, agitation, confusion, altered consciousness, fever, rapid pulse, or wide fluctuations in blood pressure			√
	Excessive sleepiness, drowsiness, suddenly falling asleep		√	
	Hepatitis (yellow skin and eyes, nausea, loss of appetite, dark-colored urine)			√

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM[§]

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and seek immediate emergency treatment
		Only if severe	In all cases	
	Serious skin reactions (rash, red skin, blistering of the lips, eyes or mouth, skin peeling)			√
Frequency not established	Allergic reactions/Angioedema. Symptoms may include redness, itching, rash, or swelling of your skin; hives (nettle rash), swelling around eyes or lips; swelling of hands, feet, face, tongue or throat; any trouble with breathing or swallowing not present before using this medicine			√

This is not a complete list of side effects. For any unexpected effects while taking STALEVO, contact your doctor or pharmacist.*

HOW TO STORE IT

- Store STALEVO* at room temperature (15-30°C).
- 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 out of the reach and sight of children.

REPORTING SUSPECTED SIDE EFFECTS

To monitor drug safety, Health Canada through the Canada Vigilance Program collects information on serious and unexpected side effects of drugs. If you suspect you have had a serious or unexpected reaction to this drug you may notify Canada Vigilance:

By toll-free telephone: 866-234-2345

By toll-free fax: 866-678-6789

Online: www.healthcanada.gc.ca/medeffect

By email: CanadaVigilance@hc-sc.gc.ca

By regular mail:

Canada Vigilance National Office

Marketed Health Products Safety and Effectiveness Information Bureau
 Marketed Health Products Directorate
 Health Products and Food Branch
 Health Canada
 Tunney's Pasture, AL 0701E
 Ottawa ON K1A 0K9

NOTE: Should you require information related to the management of the side effect, please contact your health care provider before notifying Canada Vigilance. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

Please consult your doctor or pharmacist with any questions or concerns you may have regarding your individual condition.

This document plus the full product monograph, prepared for health professionals can be found at:

<http://www.novartis.ca>

or by contacting the sponsor, Novartis Pharmaceuticals Canada Inc., at:

1-800-363-8883

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