PART III: CONSUMER INFORMATION

[Pr]COMTAN*
(entacapone)

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

ABOUT THIS MEDICATION

What the medication is used for:

COMTAN* tablets contain entacapone and are used together with levodopa/carbidopa or levodopa/benserazide 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:

In Parkinson's disease the amount of dopamine is decreased in certain areas of the brain and oral levodopa is given to compensate for this decrease. Levodopa is converted to dopamine in the brain, but part of the dose of levodopa is broken down in the body to an inactive substance before it reaches the brain. COMTAN* helps to prevent this breakdown of levodopa, and increases the amount of levodopa that gets to the brain. When taken together with levodopa, COMTAN* aids levodopa in relieving the symptoms of Parkinson's disease, such as shaking of the limbs and stiffness and slowness of movement. COMTAN* has no effect on relieving the symptoms of Parkinson's disease unless taken with levodopa.

When it should not be used:

You should NOT take COMTAN* if:

- You have a history of allergic reactions to entacapone or any other components of the COMTAN* tablet (see "What the important nonmedicinal ingredients are").
- You have liver disease.
- You are taking or have been treated in the last two weeks with certain antidepressants (both MAO-A and MAO-B inhibitors simultaneously, or non-selective MAO-inhibitors). If you are taking antidepressants and need further information, please ask your doctor or your pharmacist whether your antidepressant medication can be taken together with COMTAN*.
- You have a history of Neuroleptic Malignant Syndrome (NMS) (rare serious reaction to certain medicines used to treat severe mental disorders).
- You have ever suffered from rhabdomyolysis (rare form of muscle disorder) which was not caused by an injury.
- 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 have been told you should not take sympathomimetic drugs such as isoproterenol, amphetamines, epinephrine or cough and cold medications containing drugs related to epinephrine.
- You have narrow angle glaucoma.
- You are pregnant (see below).
- You are breast-feeding (see below).
- You are under 18 years of age.

If you think you may be allergic, ask your doctor for advice.

If any of these apply to you, tell your doctor before taking COMTAN*.

What the medicinal ingredient is:

The active substance of COMTAN* is entacapone.

What the nonmedicinal ingredients are:

COMTAN* tablet contains the following non-medicinal ingredients: Core: croscarmellose sodium, hydrogenated vegetable oil, magnesium stearate, mannitol, microcrystalline cellulose. Coating: glycerol 85%, hydroxypropylmethyl cellulose, polysorbate 80, red iron oxide, sucrose, titanium dioxide, yellow iron oxide.

What dosage forms it comes in:

COMTAN* is available in 200 mg tablets. COMTAN* tablets are brownish-orange, unscored, oval-shaped film-coated tablets embossed with "COMTAN" on one side.

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 COMTAN* in combination with levodopa and other drugs used to treat Parkinson's disease. 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 entacapone in combination with levodopa/carbidopa for an average of about 3 years, prostate cancer was reported more frequently in the group of patients that received entacapone. It is not known if treatment with entacapone affects the risk of having prostate cancer. Therefore, it is important for men to have their regular prostate examinations during treatment with entacapone.

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

- You have any other illnesses.
- You have ever had a heart attack or any other diseases of the heart, blood vessels or lungs.
- You have liver disease or have ever had abnormal liver function tests.
- You have severe kidney disease.
- 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 any allergies to medicines, food, dyes, or preservatives.

COMTAN* tablets contain a sugar called sucrose. Therefore, if you have been told by your doctor that you have an inherited intolerance to sucrose or fructose, you should not take COMTAN*.

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.

As COMTAN* tablets will be taken together with levodopa medicines, please also read the package leaflets of the levodopa medicines carefully.

The dose of other medicines to treat Parkinson's disease may need to be adjusted when you start taking COMTAN*. Follow the instructions that your doctor has given you.

Neuroleptic Malignant Syndrome (NMS) is a serious but rare reaction to certain medicines, and may occur especially when COMTAN* and other medicines to treat Parkinson's disease are suddenly stopped or the dose is suddenly reduced. For the symptoms of NMS see the section "Side effects and what to do about them". Your doctor may advise you to slowly discontinue the treatment with COMTAN* and other medicines to treat Parkinson's disease.

Driving and using machines

COMTAN* taken together with levodopa may lower your blood pressure, which may make you feel light-headed or dizzy. You should not drive a car or operate machinery until you are reasonably certain that COMTAN* does not affect your ability to carry out these activities (see precaution in box above).

Pregnancy and breast-feeding

COMTAN* is not to be used if you are pregnant. It is therefore important to tell your doctor immediately if you think you may have become pregnant, or are planning to become pregnant.

COMTAN* is not to be used if you are breast-feeding. Tell your doctor if you are breast-feeding, so that other treatment options can be tried.

Ask your doctor or pharmacist for advice before taking any medicine.

INTERACTIONS WITH THIS MEDICATION

Tell your doctor if you are taking or have recently taken any medicines, including medicines obtained without a prescription or herbal medicines. It may be necessary to change the dose, take other precautions, or perhaps stop one of the medicines. This applies to both prescription and non-prescription medicines.

In particular, tell you doctor if you are taking any of the following:

- antidepressants such as MAO inhibitors, desipramine, maprotiline, venlafaxine and paroxetine;
- warfarin used to thin the blood;
- iron supplements or multivitamins containing iron. Similar to levodopa, COMTAN* may impair the absorption of iron from the gastrointestinal tract. Therefore, COMTAN* and iron-containing medicinal products should be taken at least 2 to 3 hours apart;
- other medicines that can cause low blood pressure;
- as well as any of the following: rimiterol, isoprenaline, adrenaline, noradrenaline, dopamine, dobutamine, alpha-methyldopa, and apomorphine.

PROPER USE OF THIS MEDICATION

Follow your doctor's instructions carefully. Do not exceed the recommended dosage.

If you have any concerns about the schedule for taking your medication, talk to your doctor or pharmacist to help you sort it out.

Usual dose:

COMTAN* should always be used in combination with medicines containing levodopa (either levodopa/carbidopa preparations or levodopa/benserazide preparations). You may also use other medicines to treat Parkinson's disease at the same time, as advised by your doctor.

To obtain the maximum benefit from your antiparkinsonian therapy always take all medicines, including COMTAN*, exactly as prescribed by your doctor.

The usual dose of COMTAN* is one 200 mg tablet with each levodopa dose. The maximum recommended dose is 200 mg eight times a day, which is a total of 1600 mg of entacapone per day.

Your doctor will tell you exactly how many tablets of COMTAN* to take.

Depending on how you respond to the treatment, your doctor may suggest a higher or lower dose.

When and how to take COMTAN*

COMTAN* can be taken with or without food. Do not break or crush the tablets.

What to expect when you start taking COMTAN*?

Soon after beginning and during treatment with COMTAN*, you may experience an increase in uncontrolled movements (dyskinesia), nausea and abdominal pain. These effects may also be more common with higher doses (1400 to 1600 mg per day) than with lower doses. This is because COMTAN* increases the availability of levodopa and enhances both its effectiveness and side effects. Therefore, if, for example, you notice a disturbing increase in involuntary movements (dyskinesias) after starting treatment with COMTAN*, you should contact your doctor for possible adjustment of your levodopa dosage to decrease the severity and frequency of these effects.

If you stop taking COMTAN*

DO NOT stop taking COMTAN* unless your doctor tells you to. When stopping, your doctor may need to re-adjust the dosage of your other medicines to treat Parkinson's disease. Suddenly stopping COMTAN* and other medicines to treat Parkinson's disease 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 you have forgotten to take the COMTAN* tablet with your levodopa dose, you should continue the treatment by taking the next COMTAN* tablet with your next levodopa dose. If you are unsure about what to do, consult your doctor.

Do not take a double dose of COMTAN* to make up for the one that you missed. If you have missed several doses, please inform your doctor immediately and follow the advice given to you.

Do not change the dose of COMTAN* unless instructed by your doctor.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

As with all medicines, patients treated with COMTAN* may experience side effects, although not everybody gets them. These side effects are most likely to occur when you begin treatment with COMTAN* and are usually mild to moderate and rarely necessitate discontinuation of the treatment.

If you experience any of the side effects listed below, tell your doctor immediately.

Very common side effects *(affect more than 1 patient in 10)*

- Uncontrollable movements with difficulty in performing voluntary movements (dyskinesias);
- feeling sick (nausea);
- harmless reddish-brown discoloration of urine. COMTAN* may also cause darkening of sweat and saliva.

Common side effects *(affect 1 to 10 patients in 100)*

- Excessive movements of the body (hyperkinesias);
- headache;
- fever;
- tremor;
- prolonged muscle cramps (dystonia), leg cramps;
- hallucinations (seeing/hearing/feeling/smelling things that are not really there), confusion;
- 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);
- worsening of symptoms of Parkinson's disease;
- being sick (vomiting), diarrhea, abdominal pain, constipation, dry mouth;
- decrease in blood pressure when standing up rapidly after sitting or lying down, with or without symptoms such as dizziness or light headedness, increased sweating, falling, fainting;
- dizziness, tiredness, increased sweating, falling;
- vertigo (sensation of spinning or whirling motion);
- sleeplessness, nightmares.

Uncommon (*affects 1 to 10 patients in 1,000*)

- Heart attack (chest pain often associated with left shoulder or jaw pain, feeling of constriction around chest and sweating).

Rare side effects *(affect 1 to 10 patients in 10,000)*

- Abnormal results in liver function tests.

Very rare side effects *(affect less than 1 patient in 10,000)*

- Inflammation of the colon (colitis) which may cause severe diarrhea or weight loss;
- agitation;
- decreased appetite, weight loss;
- hives;
- discoloration of the skin, hair, beard and nails;
- Excessive daytime sleepiness and sleep onset episodes;
- Neuroleptic Malignant Syndrome (NMS), which can cause symptoms of stiffness, muscle twitching, shaking, agitation, confusion, coma, high body temperature, increased heart rate, and unstable blood pressure;
- inflammation of the liver (hepatitis), which can cause increasing loss of appetite, weakness, exhaustion, weight loss in a relatively short period of time, yellowing of your skin, hair, nail, or the white of your eyes, dark colored urine;
- serious skin reactions (rash that might be severe, red skin, blistering of the lips, eyes or mouth, peeling skin).
- severe muscle disorder (rhabdomyolysis) which causes pain, tenderness and weakness of the muscles and may lead to kidney

problems;
- allergic reactions (symptoms may include redness, itching, rash, swelling of your skin, hives, swelling around the eyes, lips; swelling of hands, feet, face, tongue or throat; any trouble breathing or swallowing not present before using this medicine).

Together with levodopa, COMTAN* may lower your blood pressure and cause postural (orthostatic) hypotension (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. Hypotension may occur more frequently during the start of treatment with COMTAN*. 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 which may cause dizziness or light-headedness (low blood pressure) when rising from a chair or bed.

Severe diarrhea while taking COMTAN* can cause significant loss of weight for some individuals. In some cases diarrhea and weight loss have been caused by inflammation of the colon that occurred during treatment with COMTAN*. 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.

If you experience increasing loss of appetite, weakness, exhaustion and weight loss in 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.

Abnormal results of blood tests, such as decrease in red blood cells, have been observed in people taking COMTAN*.

COMTAN* may also cause other adverse events. If you have any questions or concerns about these effects you should talk to 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 right away		Stop taking drug and seek immediate emergency medical attention
		Only if severe	In all cases	
Common	Hallucinations (seeing/hearing/feeling/smelling things that are not really there)		√	
	Diarrhea		√	
	Decrease in blood pressure when standing up rapidly after sitting or lying down, with or without symptoms such as dizziness or light headedness, increased sweating, falling, fainting		√	
	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)			√
Uncommon	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 rare	Excessive daytime sleepiness, drowsiness, suddenly falling asleep		√	
	Neuroleptic Malignant Syndrome (NMS) (stiffness, muscle twitching, shaking, agitation, confusion, coma, high body			√

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

Symptom / effect		Talk with your doctor or pharmacist right away		Stop taking drug and seek immediate emergency medical attention
		Only if severe	In all cases	
	temperature, increased heart rate, and unstable blood pressure)			
	Inflammation of the liver (hepatitis) which can cause increasing loss of appetite, weakness, exhaustion, weight loss in a relatively short period of time, yellowing of your skin, hair, nail, or the white of the eyes, dark colored urine			√
	Serious skin reactions (rash that might be severe, red skin, blistering of the lips, eyes or mouth, peeling skin)			√
	Rhabdomyolysis (pain, tenderness weakness of the muscles)			√
	Allergic reactions (symptoms may include redness, itching, rash, swelling of your skin, hives, swelling around the eyes, lips; swelling of hands, feet, face, tongue or throat; any trouble breathing or swallowing not present before using this medicine)			√

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

HOW TO STORE IT

- Store your COMTAN* tablets at room temperature (15-30ºC).
- Do not take COMTAN* past the expiry date shown on the bottle.
- 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

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

I. Report online at www.healthcanada.gc.ca/medeffect
II. Call toll-free at 1-866-234-2345
III. Complete a Canada Vigilance Reporting Form and:
- Fax toll-free to 1-866-678-6789, or
- Mail to: Canada Vigilance Program
Health Canada
Postal Locator 0701E
Ottawa, Ontario
K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. 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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Novartis Pharmaceuticals Canada Inc.
385 Bouchard Blvd.
Dorval, Quebec
H9S 1A9