

 **NOVARTIS**

PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

The medicine is dispensed with a doctor's prescription only

COMTAN®

200 mg

Film-coated tablets

The active ingredient

Each tablet contains: Entacapone 200 mg

Inactive ingredients:

See section 6 "Further Information".

Read this package insert carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed for the treatment of your ailment. Do not pass it on to others. It may harm them even if it seems to you that their ailment is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?

Comtan is used to treat Parkinson's disease, in combination with levodopa/carbidopa or levodopa/benserazide.

Parkinson's disease is a disorder of the nervous system. It is caused by a lack of dopamine, a natural substance that is produced in the brain. Dopamine relays messages in the part of the brain that controls muscle movement. When too little dopamine is produced, problems with movement result.

Levodopa increases the level of dopamine in the brain. Comtan aids levodopa in relieving the symptoms of Parkinson's disease, such as shaking of the limbs, stiffness and slowness of movements, which make it difficult to perform daily activities.

Comtan has no effect on the symptoms of Parkinson's disease unless taken with levodopa.

You may receive additional medicines to treat your condition.

If you have any additional questions about how Comtan works and why Comtan has been prescribed for you, ask the doctor.

Therapeutic group:

catechol-O-methyl transferase inhibitor.

2. BEFORE USING THE MEDICINE

⚠ Do not use the medicine if:

you are hypersensitive (allergic) to the active ingredient, entacapone, or to any of the medicine's other ingredients.

you have a liver disease.

you have a tumor of the adrenal gland (pheochromocytoma; this may increase the risk of severe high blood pressure).

you are taking certain antidepressants (ask your doctor whether the antidepressant medication you are taking can be taken together with Comtan).

you have ever suffered from a rare reaction to antipsychotic medicines called neuroleptic malignant syndrome (NMS) (with

symptoms such as rigidity, agitation, extreme increase in body temperature, rapid heartbeat and extreme fluctuations in blood pressure).

you have ever suffered from a rare muscle disorder called rhabdomyolysis which was not caused by injury. you are pregnant or breastfeeding.

If you think you are allergic, consult the doctor.

If one or more of these applies to you, contact the doctor without taking Comtan.

Special warnings regarding use of the medicine:

Consult the doctor if any of the following situations apply to you:

If you have ever had a heart attack or any other disease of the heart.

If you are receiving dialysis for renal insufficiency, it may be necessary to leave a longer interval between doses of the medicine.

Comtan tablets contain a sugar called sucrose. If you have been told by your attending doctor that you have an inherited intolerance to sucrose, contact the doctor before taking Comtan.

If you experience symptoms such as sudden increase in body temperature, more rapid heartbeat, extremely high blood pressure or severe convulsions.

If you experience temporary paralysis or severe weakness of the muscles.

If you are taking a medicine which may cause dizziness (low blood pressure) when rising from a chair or bed.

If you experience prolonged diarrhea, consult your doctor as it may be a sign of inflammation of the colon.

If you experience prolonged diarrhea, your doctor may monitor your weight in order to prevent excessive weight loss.

Tell your doctor if you or your family or your caregiver notice that you are developing urges or cravings to behave in ways that are unusual for you or if 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 preoccupation with an increase in sexual thoughts or feelings. Your doctor may need to review your treatments.

If you experience increasing lack of appetite, weakness, exhaustion and weight loss within a relatively short period of time, contact your doctor. He/she may decide to conduct a general medical evaluation including liver function.

As Comtan tablets are taken together with levodopa medicines, you should also read the patient leaflet of these medicines.

It may be necessary to adjust the dosages of the other medicines for treatment of Parkinson's disease when you start taking Comtan. Follow the doctor's instructions.

Neuroleptic malignant syndrome (NMS) is a serious but rare reaction to certain medicines, and may occur especially when treatment with Comtan and other medicines for Parkinson's disease is stopped abruptly or when the dosage is suddenly reduced (for characteristics of NMS see section 4 "Side Effects"). Your doctor may recommend that treatment with Comtan and other medicines for Parkinson's disease be stopped gradually.

Comtan taken concomitantly with levodopa may cause drowsiness and may sometimes cause you to suddenly fall asleep. If this happens, do not drive or use tools or machines (read section "Driving and using machines").

⚠ Older patients (over 65 year of age)

Comtan can be used by patients over the age of 65.

⚠ Children and adolescents

This medicine is not intended for children and adolescents under 18 years of age, since experience with this population is limited.

⚠ Pregnancy and breast-feeding

Do not use Comtan if you are pregnant or breast-feeding.

If you become pregnant during treatment stop taking the medicine immediately and consult your doctor. Ask your doctor or pharmacist for advice before taking any medicine.

⚠ Driving and using machines

Use of Comtan together with levodopa may cause a drop in blood pressure, and as a result may make you feel dizzy. Caution is therefore required especially when you drive or when you operate tools or machinery.

In addition, Comtan taken with levodopa may make you feel very drowsy or sometimes cause you to suddenly fall asleep. Do not drive or operate machinery if you experience these side effects.

⚠ Taking other medicines

If you are taking or have recently taken other medicines, including non-prescription medicines and nutritional supplements or herbal remedies, tell the doctor or pharmacist.

Comtan may increase the effect of other medicines.

It is especially important to tell the doctor or pharmacist if you are taking:

- antidepressants such as desipramine, maprotiline, venlafaxine, paroxetine
- warfarin used to thin the blood
- iron supplements. Comtan may make it harder to digest iron. Therefore, do not take Comtan and iron supplements at the same time. After taking one of them, wait at least 2 to 3 hours before taking the other
- as well as any of the following: rimiterol, isoprenaline, adrenaline, noradrenaline, dopamine, dobutamine, alpha-methyldopa, apomorphine

⚠ Important information about some of Comtan's ingredients

The tablet contains sucrose.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use according to the doctor's instructions. Check with the doctor or pharmacist if you are not sure.

Dosage

The dosage and treatment regimen will be determined by the doctor only. The usual dosage is generally:

Comtan is taken together with medicines containing levodopa (either levodopa/carbidopa or levodopa/benserazide preparations). You may also be prescribed other medicines to treat Parkinson's disease at the same time.

The usual dose of Comtan is one 200 mg tablet with each levodopa dose. The maximum recommended dosage is 10 tablets per day, i.e., 2,000 mg of Comtan.

If you are receiving dialysis for renal insufficiency, the doctor may tell you to increase the time between doses.

The doctor will tell you exactly how many Comtan tablets to take.

The doctor may suggest a higher or lower dosage, according to your response to the treatment.

If you feel that the effect of the medicine is too strong or too weak, refer to the doctor or pharmacist.

Do not exceed the recommended dose.

How to take the medicine

Take Comtan at the same time you take a dose of levodopa.

Swallow the tablet with a full glass of water. Comtan can be taken with or without food.

Do not chew!

Duration of treatment

Continue to take Comtan for the duration of time recommended by the doctor.

Taking more Comtan than required

If you have accidentally taken an overdose or if a child has accidentally swallowed the medicine, immediately refer to the doctor or proceed to a hospital emergency room and bring the package of the medicine with you.

Medical attention may be required.

If you forget to take Comtan

If you forget to take a Comtan tablet with the levodopa dose, you should continue the treatment by taking the next Comtan tablet with the next levodopa tablet.

Do not take a double dose of Comtan to make up for the one that you missed.

Adhere to the treatment as recommended by the doctor.

Stopping treatment

Even if there is an improvement in your health, do not stop taking the medicine without consulting the doctor or pharmacist.

In case of stoppage of treatment, the doctor may need to readjust the dosage of the other medicines for treating Parkinson's disease. Suddenly stopping Comtan and other medicines for treatment of Parkinson's disease may result in unwanted side effects, such as severe muscle stiffness, high fever and altered consciousness.

Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them.

If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Comtan may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not experience any of them.

These side effects are generally mild to moderate in severity. During the first few days or weeks of therapy, you may experience side effects such as nausea, vomiting, hallucinations (seeing, hearing, smelling or feeling things that are not really there), unusual or uncontrolled movements of the body. To reduce these effects, your doctor may need to change the levodopa dosage in the first few days or weeks after starting treatment with Comtan.

The frequencies of the side effects are defined as:

Very common - affecting more than 1 patient in 10, common - affecting 1 to 10 patients in 100, uncommon - affecting 1 to 10

patients in 1,000, rare - affecting 1 to 10 patients in 10,000, very rare - affecting less than 1 patient in 10,000, frequency unknown - cannot be estimated from the available data.

If you experience any of the following side effects, inform the doctor immediately:

Very common side effects:

- uncontrollable movements with difficulty in performing voluntary movements (dyskinesias)
- nausea
- reddish-brown discoloration of urine (not harmful)

Common side effects:

- excessive movements of the body (hyperkinesias)
- prolonged muscle cramps (dystonia)
- hallucinations (seeing, hearing, feeling or smelling things that are not really there), confusion
- heart or artery disease events (e.g., chest pain)
- worsening of symptoms of Parkinson's disease
- vomiting, diarrhea, abdominal pain, constipation, dry mouth
- dizziness, tiredness, increased sweating, falling
- sleeplessness, nightmares

Uncommon side effects:

- heart attack

Rare side effects:

- rashes
- abnormal results in liver function test

Very rare side effects:

- inflammation of the colon (colitis) which may lead to diarrhea and weight loss
- agitation
- decreased appetite, weight loss
- hives

Side effects of unknown frequency:

- inflammation of the liver (hepatitis) with yellowing of the skin or the white part of the eyes
- discoloration of the skin, hair, beard and nails

Side effects requiring special attention:

Comtan may have other important side effects:

- a rare severe muscle disorder (rhabdomyolysis) which causes pain, tenderness and weakness of the muscles and may lead to kidney problems
- Taking Comtan with levodopa may rarely make you feel very drowsy during the day, and cause you to suddenly fall asleep
- Neuroleptic malignant syndrome (NMS) is a severe but rare reaction to medicines used to treat disorders of the nervous system. It is characterized by stiffness, muscle twitching, shaking, agitation, confusion, coma, high body temperature, increased heart rate, and unstable blood pressure
- headache, fever, leg cramps, vertigo (sensation of spinning or whirling motion), tremor, low blood pressure

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 that are of significant concern to you or to others, for example, an increased sexual drive

- uncontrollable 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)

Contact the doctor if you experience any of these behaviors; the doctor will advise you regarding the way to manage the symptoms or reduce them.

Comtan at higher doses:

At doses of 1,400 to 2,000 mg per day, the following side effects are more common:

- uncontrollable movements
- nausea
- abdominal pain

If any of the side effects worsen, or if you experience a side effect not mentioned in this leaflet, consult the doctor or pharmacist.

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine, and all other medicines, must be stored in a safe place out of the reach and sight of children and/or infants, to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by a doctor.

Do not use after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.

Do not use if the package is damaged or if there are signs of tampering.

Store in the original container.

Do not store above 30°C. After first opening the bottle, the medicine may be used for up to 12 months. Pay particular attention to close the bottle immediately after each use.

6. FURTHER INFORMATION

In addition to the active ingredient the medicine also contains: Microcrystalline cellulose, mannitol, croscarmellose sodium, hydrogenated vegetable oil, hypromellose cellulose 6CPs, poly sorbate 80, glycerol 85%, sucrose, magnesium stearate, yellow iron oxide, red iron oxide, titanium dioxide.

Each tablet contains 1.82 mg sucrose and approximately 5.6 mg sodium.

What the medicine looks like and the contents of the package

A brownish orange oval tablet with COMTAN engraved on one side.

Dispensed in a bottle containing 30 tablets.

Registration holder and address: Novartis Israel Ltd., 36 Shacham St., Petach-Tikva.

Manufacturer and address: Orion Corporation, Espoo, Finland for Novartis Pharma AG, Basel, Switzerland.

This leaflet was checked and approved by the Ministry of Health in February 2014.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 1140729631