

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

The medicine is dispensed with a doctor's prescription only

Certican® 0.25 mg Tablets

Each tablet contains:
Everolimus 0.25 mg

Certican® 0.5 mg Tablets

Each tablet contains:
Everolimus 0.5 mg

Certican® 0.75 mg Tablets

Each tablet contains:
Everolimus 0.75 mg

Inactive and allergenic ingredients in the preparation: See section 2 "Important information about some of the ingredients of the medicine" and section 6 "Further Information".

Read this leaflet 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?

Certican is used to prevent implant rejection in adult kidney, heart and liver transplant recipients. For kidney and heart transplant recipients, Certican must be taken together with ciclosporin in microemulsion and corticosteroids and for liver transplant recipients, Certican must be taken together with tacrolimus and corticosteroids.

Therapeutic Group: Certican belongs to a group of medicines called immunosuppressants.

2. BEFORE USING THE MEDICINE

Do not use the medicine:

If you are sensitive (allergic) to everolimus or any of the other ingredients of the medicine. See section 6 "Further Information".

If you are sensitive (allergic) to sirolimus.

Special warnings regarding use of the medicine: Before using Certican, tell your doctor if:

- Medicines that suppress the immune system, like Certican, reduce your body's ability to fight against infections. It is advisable to consult your doctor or transplant centre if you have a fever or generally feel unwell, or have symptoms such as coughing or a burning sensation when urinating that are severe or persistent over several days.

Consult your doctor or transplant centre right away if you feel confused, have problems speaking, memory loss, a headache, impaired vision or seizures, as these may be symptoms of a rare but severe condition called progressive multiple leukoencephalopathy (PML).

- You have had recent major surgery, or if you still have an unhealed wound following surgery, Certican may increase the risk of wound-healing problems.

- Medicines that suppress the immune system, like Certican, increase the risk of developing cancerous tumours, particularly of the skin and the lymphoid system. Therefore, you should limit your exposure to sunlight and UV light by wearing appropriate clothes and frequently applying sunscreens with a high protection factor.

- Your doctor will monitor your kidney function, the amounts of fats (lipids) and sugar in your blood as well as the amount of proteins in your urine.

- You have liver problems or have ever had a disease which may have affected your liver, please tell your doctor. The Certican dosage may have to be adjusted by the doctor.

- You experience respiratory symptoms (e.g., coughing, difficulty in breathing and wheezing), please inform your doctor. Your doctor will decide whether and how you need to continue treatment with Certican, and/or whether you need to receive other medicines to treat the condition.

- Certican may reduce sperm production in men, thereby reducing the ability to father children. The effect is generally reversible. Male patients wanting to father children should discuss their treatment with their doctor.

Drug interactions:

If you are taking, or have recently taken, other medicines, including non-prescription medicines and food supplements, tell the doctor or pharmacist. In particular, if you are taking:

- Immunosuppressive medicines other than ciclosporin in microemulsion, tacrolimus or corticosteroids.
- Antibiotics e.g., rifampicin, rifabutin, clarithromycin, erythromycin or telithromycin.

- Antiviral medicines e.g., ritonavir, efavirenz, nevirapine, nelfinavir, indinavir or amprenavir, used to treat HIV infection.
- Antifungals e.g., voriconazole, fluconazole, ketoconazole or itraconazole.

- Medicines used to treat epilepsy, e.g., phenytoin, phenobarbital or carbamazepine.
- Medicines used to treat high blood pressure or heart problems, e.g., verapamil, nicardipine or diltiazem.

- Dronedarone, a medicine used to regulate heart beat.
- Medicines used to lower blood cholesterol levels e.g., atorvastatin, pravastatin or fibrates.

- Medicines used to treat acute seizures or used as a sedative before or during surgery or other medical procedures, e.g., midazolam.
- Cannabidiol (uses amongst others include treatment of seizures).

- Octreotide, a medicine used to treat acromegaly, a rare hormonal disorder that usually occurs in middle-aged adults.
- Imatinib, a medicine used to inhibit the growth of abnormal cells.

- Hypericum perforatum* (St. John's wort) – a herbal medicine used to treat depression.
- If you need to have a vaccination, talk to your doctor first.

Use of Certican and food

The presence of food can affect the absorption of Certican in your body. In order to keep constant Certican levels in your body, take Certican in the same way. You should either always take it with food, or always take it on an empty stomach. Do not take Certican with grapefruit or grapefruit juice. Grapefruit affects Certican's activity in the body.

Pregnancy, breast-feeding and fertility
If you are pregnant, do not take Certican unless your doctor thinks it is necessary. If you are able to become pregnant, you should use an effective method of contraception during treatment with Certican and for 8 additional weeks after stopping treatment. If you think you are pregnant, consult with a doctor or pharmacist before taking Certican.

Do not breast-feed during the course of treatment with Certican. It is not known whether Certican passes into breast milk. Certican may have an impact on male fertility.

Elderly population (65 years of age and up)

There is limited experience with administering Certican to elderly patients over the age of 65.

Children and adolescents (under 18 years of age)

This medicine is not intended for children and adolescents under 18 years of age.

Driving and using machines

No studies of the effects of Certican on the ability to drive and use dangerous machines have been conducted.

Important information about some of the ingredients of the medicine

Certican tablets contain lactose. If you have been told by your doctor that you have an intolerance to certain sugars, contact the doctor before taking this product. See also section 6 "Further Information".

3. HOW SHOULD YOU USE THE MEDICINE?

Always use according to the doctor's instructions. Your doctor will decide exactly which dose of Certican you should take and when it should be taken. Follow your doctor's or pharmacist's instructions.

Check with the doctor or pharmacist if you are uncertain.

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

Kidney and heart transplantations: The general recommended dosage is 0.75 mg Certican twice daily, taken in the morning and in the evening, together with ciclosporin in microemulsion. The first dose of Certican will be given as soon as possible after transplantation.

Liver transplantation: The general recommended dosage is 1 mg Certican twice daily, taken in the morning and in the evening, together with tacrolimus. The first dose of Certican will be given approximately four weeks after transplantation.

Do not exceed the recommended dose.

Directions for use:
Intended for oral use only. Swallow the tablets whole with a glass of water. Do not crush the tablets.

Duration of treatment:
Treatment will continue for as long as you need immunosuppression, to prevent you from rejecting your transplanted organ.

Tests and follow-up:
Your doctor will adjust the dose you are taking in accordance with your blood Certican levels and your response to treatment. Your doctor will regularly perform blood tests to measure the levels of everolimus and ciclosporin in your blood.

Your doctor will also monitor your kidney function, blood lipid and blood sugar levels and the amount of proteins in your urine.

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

If you forgot to take this medicine at the required time, take it as soon as you remember and then take the next dose at the usual time. Ask your doctor for advice. Do not take a double dose to compensate for a forgotten dose. Adhere to the treatment as recommended by the doctor.

Even if there is an improvement in your condition, do not stop taking this medicine without consulting the doctor.

If you stop taking Certican, this may increase the chance of rejection of your transplanted organ. Therefore, do not stop taking Certican without instructions from the doctor.

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 a doctor or pharmacist.

4. SIDE EFFECTS

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

Because you take Certican together with other medicines, it is not always clear whether the side effects are caused by Certican.

The following side effects need immediate medical attention:

- Infections**
- Inflammation of the lungs**
- Allergic reactions**
- Fever and bruising under the skin that may appear as red dots, with or without unexplained tiredness, confusion, yellowing of the skin or eyes, reduced urine output (thrombotic microangiopathy, haemolytic uraemic syndrome).**

Stop taking Certican and report to the doctor immediately in the following cases:

- Persistent or worsening lung/breathing symptoms such as coughing, difficulty breathing, or wheezing.

- Fever, generally feeling unwell, chest or abdominal pain, chills, burning sensation when urinating.
- Swelling of face, lips, tongue or throat.
- Difficulty swallowing.
- Spontaneous bruising or bleeding for no obvious reason.
- Rash.
- Pain, unusual warmth, swelling or oozing from the site of surgery.

Other reported side effects include:

Very common side effects (may affect more than 1 in 10 patients):

Infections (viral, bacterial and fungal infections); lower respiratory tract infections, such as lung infections (pneumonia); upper respiratory tract infections, such as inflammation of the pharynx, and common cold; urinary tract infections; anaemia (reduced red blood cell count); high level of fats (lipids, cholesterol and triglycerides) in the blood; low levels of white blood cells, that increase the risk of infection; reduced blood platelet count, which can lead to bleeding and/or bruising underneath the skin; fluid collection in the sac around the heart, which if severe, can decrease the heart's ability to pump blood; fluid collection on the lungs and in the chest cavity, which, if severe, could make you breathless; onset of diabetes (high level of sugar in the blood); reduced level of potassium in the blood; anxiety; problems falling asleep (insomnia); headache; high blood pressure; venous thrombosis (blockage of a major vein by a blood clot); coughing; breathlessness; diarrhoea; nausea; vomiting; abdominal pain; general pain; fever; accumulation of fluid in the tissues; abnormal wound healing.

Common side effects (may affect between 1-10 in 100 patients):

Blood poisoning; wound infection; cancerous and benign tumours; skin cancer; kidney damage with low blood platelet and low red blood cell counts, with or without a rash; breakdown of red blood cells; pain in the mouth or throat; acne; clotting in the blood vessels of the kidney, which may result in graft loss mostly within the first 30 days after kidney transplantation; defect in blood clotting; low levels of red blood cells and platelets; fast heart beat; nose bleeds; reduced number of blood cells (symptoms may include weakness, bruising and frequent infections); cysts containing lymph fluid; hives (urticaria) and other allergic reactions, such as swelling of the face or throat (angioedema), rash; inflammation of the pancreas; mouth sores; joint pain; muscle pain; protein in the urine; kidney disorders; impotence; hernia at the site of surgery; abnormal liver test results; menstrual disorders (including absent or heavy periods).

Uncommon side effects (may affect between 1-10 in 1,000 patients):

Cancerous tumour of the lymph tissue (lymphoma); low levels of testosterone; inflammation of the lungs; inflammation of the liver; jaundice; ovarian cysts.

Other side effects:

Other side effects have occurred in a small number of people, but their exact frequency is unknown: Abnormal accumulation of protein in the lungs (symptoms may include persistent dry cough, fatigue and difficulty breathing); inflammation of blood vessels; swelling, feeling of heaviness or tightness, pain, limited mobility of body parts (this could occur anywhere in the body and is a potential sign of an abnormal build-up of fluid in soft tissue due to a blockage in the lymphatic system, also known as lymphoedema); severe rash with skin swelling; low iron levels in the blood.

If you have any questions regarding any of the side effects mentioned above, refer to your doctor.

There may also be side effects of which you are not aware, such as abnormal results of laboratory tests, including tests of kidney function. Therefore, your doctor will perform blood tests to monitor any changes during your treatment with Certican.

If a side effect occurs, if one of the side effects worsens or if you suffer from a side effect not mentioned in the leaflet, consult with the doctor.

Side effects can be reported to the Ministry of Health by clicking on the link: "Reporting side effects from drug treatment", which can be found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link: <https://sideeffects.health.gov.il>

5. HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine, and any other medicine, should be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (exp. date) appearing on the package. The expiry date refers to the last day of that month.
- Do not store above 30°C. Protect from light and moisture.
- Store in the original package.
- Do not use this medicine if the package is damaged or if it shows signs of tampering.

- Do not throw away medicines via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer in use. These measures will help protect the environment.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:

Lactose anhydrous; Crospovidone; Hypromellose; Lactose monohydrate; Magnesium stearate; Butylated hydroxytoluene.

Estimated amount of lactose per Certican 0.25 mg tablet is 53 mg.

Estimated amount of lactose per Certican 0.5 mg tablet is 79 mg.

Estimated amount of lactose per Certican 0.75 mg tablet is 118 mg.

What the medicine looks like and the contents of the package:

Certican is marketed in the form of tablets. Certican 0.25 mg, 0.5 mg and 0.75 mg tablets are white to yellowish, round, flat with bevelled edges. Engraved on the tablets:

Certican 0.25 mg: On one side "NVR" and on the other side "C"
Certican 0.5 mg: On one side "NVR" and on the other side "CH"
Certican 0.75 mg: On one side "NVR" and on the other side "CL"

The Certican 0.25 mg, 0.5 mg and 0.75 mg product is supplied in packs containing 60 tablets.

Registration Holder and Importer and its address: Novartis Israel Ltd., P.O.B 7126, Tel Aviv.

Registration numbers of the medicine in the National Drug Registry of the Ministry of Health:

Certican 0.25 mg tablets: 132 60 31066
Certican 0.5 mg tablets: 132 58 31064
Certican 0.75 mg tablets: 132 59 31065

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