

Package leaflet: Information for the user

Certican 0.1 mg dispersible tablets Certican 0.25 mg dispersible tablets

Everolimus

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

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

1. What Certican is and what it is used for

The active substance of Certican is everolimus.

Everolimus belongs to a group of medicines called immunosuppressants. It is used in adults to prevent the body's immune system from rejecting a transplanted kidney, heart or liver.

Certican is used together with other medicines, such as ciclosporin for kidney and heart transplantation, tacrolimus for liver transplantation, and corticosteroids.

2. What you need to know before you take Certican

Do not take Certican

- if you are allergic (hypersensitive) to everolimus or any of the other ingredients of this medicine (listed in section 6).
- if you are allergic (hypersensitive) to sirolimus.

If any of the above applies to you, tell your doctor and do not take Certican.

Warnings and precautions

Talk to your doctor before taking Certican:

- 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 local 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 very serious condition called progressive multiple leukoencephalopathy (PML).

- If 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 cancers, particularly of the skin and the lymphoid system. Therefore, you should limit your exposure to sunlight and UV light by wearing appropriate protective clothing and frequently applying a sunscreen 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.
- If you have liver problems or have ever had a disease which may have affected your liver, please tell your doctor. Your doctor may need to modify the dose of Certican you are taking.
- If you experience respiratory symptoms (e.g. coughing, difficulty in breathing and wheezing), please inform your doctor. Your doctor may decide whether and how you need to continue Certican, and/or whether you need to receive other medicines to resolve this 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 physician.

Older people (65 years and over)

There is limited experience with the administration of Certican in elderly people.

Children and adolescents (younger than 18 years of age)

Certican is not recommended for use in children and adolescents with a transplanted kidney because there is not enough experience in the use of Certican in this age group. Certican should not be used in children and adolescents with a transplanted liver.

Other medicines and Certican

Tell your doctor or pharmacist if you are taking or have recently taken or might take any other medicines, including medicines obtained without a prescription.

Certain medicines may affect the way in which Certican works in the body. It is very important that you tell your doctor if you are taking any of the following medicines:

- immunosuppressive medicines other than ciclosporin, tacrolimus or corticosteroids.
- antibiotics, such as rifampicin, rifabutin, clarithromycin, erythromycin or telithromycin.
- antiviral medicines, such as ritonavir, efavirenz, nevirapine, nelfinavir, indinavir or amprenavir, which are used to treat HIV infection.
- medicines used to treat fungal infections, such as voriconazole, fluconazole, ketoconazole or itraconazole.
- medicines used to treat epilepsy, such as phenytoin, phenobarbital or carbamazepine.
- medicines used to treat high blood pressure or heart problems, such as verapamil, nicardipine or diltiazem.
- dronedarone, a medicine used to help regulate your heart beat.
- medicines used to lower blood cholesterol, such as atorvastatin, pravastatin or fibrates.
- medicines used to treat acute seizures, or used as a sedative before or during surgery or other medical procedures, such as midazolam.
- 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.
- St. John's wort (*Hypericum perforatum*), a herbal medicine used to treat depression.
- If you need to have a vaccination, talk to your doctor first.

Certican with food and drink

The presence of food can affect how much Certican is absorbed. In order to keep constant levels in your body, you should always take Certican in the same way. You should either always take it with food, or always on an empty stomach.

Do not take Certican with grapefruit juice or grapefruit. They affect how Certican works in the body.

Pregnancy breast-feeding and fertility

If you are pregnant, do not take Certican unless your doctor thinks it is absolutely necessary. If you are a woman and you could get pregnant, you should use an effective method of contraception during treatment with Certican and for 8 weeks after stopping treatment.

If you think you may be pregnant, ask your doctor or pharmacist for advice before taking Certican.

You should not breast-feed while taking Certican. It is not known whether Certican passes into breast milk.

Certican may have an impact on male fertility.

Driving and using machines

No studies on the effects on the ability to drive and use machines have been performed.

Certican contains

Certican dispersible tablets contain lactose. If you do not tolerate certain sugars (glucose, galactose, lactose), you should talk to your doctor before taking Certican.

3. How to take Certican

Your doctor will decide exactly what dose of Certican you should take and when you should take it.

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

How much to take

- The usual starting dose is 1.5 mg/day in kidney and heart transplantation and 2.0 mg/day in liver transplantation.
- This is usually divided into two doses, one in the morning and one in the evening.

How to take Certican

Certican should only be taken by mouth.

You should take the first dose of this medicine as early as possible after kidney and heart transplantation and approximately four weeks after liver transplantation.

You should take the tablets together with ciclosporin for microemulsion in kidney and heart transplantation, and with tacrolimus in liver transplantation.

Do not switch from Certican dispersible tablets to Certican tablets without first telling your doctor.

- Place the Certican dispersible tablets in approximately 25 ml of water in a plastic cup.
- The largest amount of Certican that may be dispersed in 25 ml of water is 1.5 mg.
- Wait for 2 minutes to allow the tablets to disintegrate and then carefully swirl the cup before you drink the liquid.
- Straight afterwards, rinse the cup with another 25 ml of water and drink the water completely.

Monitoring during your treatment with Certican

Your doctor may adjust your dose depending on how much Certican there is in your blood and depending on how well you respond to the treatment. Your doctor will perform regular blood tests to measure the amount of everolimus and ciclosporin in your blood. Your doctor will also carefully monitor your kidney function, blood lipids and blood sugar, as well as the amount of proteins in your urine.

If you take more Certican than you should

If you take more of this medicine than you should, talk to your doctor immediately.

If you forget to take Certican

If you have forgotten to take your dose of Certican, 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 make up for a forgotten tablet.

If you stop taking Certican

Do not stop taking the tablets unless your doctor tells you to. You will need to take this medicine for as long as you need to have immunosuppressants to prevent the rejection of your transplanted kidney, heart or liver. If you stop taking Certican, you will have a greater risk of your body rejecting the transplanted organ.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

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

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).

Should you develop any of the following:

- 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

you should stop taking Certican and **tell your doctor straight away**.

Other reported side effects include:**Very common** (*may affect more than 1 in 10 patients*)

- infections (viral, bacterial and fungal infections),
- lower respiratory tract infections, such as lung infections, including pneumonia
- upper respiratory tract infections, such as inflammation of the pharynx, and common cold,
- urinary tract infections,
- anaemia (reduced red blood cell count),

- low levels of white blood cells, leading to a higher risk of infection, reduced blood platelet count, which can lead to bleeding and/or bruising underneath the skin,
- high level of fats (lipids, cholesterol and triglycerides) in the blood,
- onset of diabetes (high level of sugar in the blood),
- reduced level of potassium in the blood,
- anxiety,
- problems falling asleep (insomnia),
- headache,
- fluid collection in the sac around the heart, which if severe, can decrease the heart's ability to pump blood,
- high blood pressure,
- venous thrombosis (blockage of a major vein by a blood clot),
- fluid collection on the lungs and in the chest cavity, which if severe, could make you breathless,
- coughing,
- breathlessness,
- diarrhoea,
- feeling sick (nausea),
- being sick (vomiting),
- stomach (abdominal) pain,
- general pain,
- fever,
- accumulation of fluid in the tissues,
- abnormal wound healing.

Common (*may affect up to 1 in 10 patients*)

- blood poisoning,
- wound infection,
- cancers and benign tumours,
- skin cancer,
- kidney damage with low blood platelets and low red blood cell counts, with or without a rash (thrombocytopenic purpura/haemolytic uraemic syndrome),
- breakdown of red blood cells,
- low levels of red blood cells and platelets,
- fast heart beat,
- nose bleeds,
- reduced numbers of blood cells (symptoms may include weakness, bruising and frequent infections),
- clotting in the blood vessels of the kidney, which may result in graft loss mostly within the first 30 days after kidney transplantation,
- bleeding disorders,
- cyst containing lymph fluid,
- pain in the mouth or throat,
- inflammation of the pancreas,
- mouth sores,
- acne,
- hives (urticaria) and other allergic symptoms, such as swelling of the face or throat (angiooedema),
- rash,
- 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 (*may affect up to 1 in 100 patients*):

- cancer of the lymph tissue (lymphoma/post-transplant lymphoproliferative disorder),
- 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.

If you have concerns regarding any of these effects, **tell 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. This means that your doctor will perform blood tests to monitor any changes to your kidneys during your treatment with Certican.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via [the national reporting system](#) listed in [Appendix V](#). By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Certican

- Keep Certican out of the sight and reach of children.
- Do not use Certican after the expiry date which is stated on the carton after EXP. The expiry date refers to the last day of that month.
- Store the blister packs in the original carton in order to protect from light and moisture.
- Do not use any Certican pack that is damaged or shows signs of tampering.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Content of the pack and other information

What Certican contains

- The active substance is everolimus. Each dispersible tablet contains 0.1 mg or 0.25 mg everolimus.
- The other ingredients are:
 - Certican 0.1 mg dispersible tablets: butylhydroxytoluene (E321), magnesium stearate, lactose monohydrate (1 mg), hypromellose, crospovidone, colloidal anhydrous silica and anhydrous lactose (72 mg).
 - Certican 0.25 mg dispersible tablets: butylhydroxytoluene (E321), magnesium stearate, lactose monohydrate (2 mg), hypromellose, crospovidone, colloidal anhydrous silica and anhydrous lactose (179 mg).

What Certican looks like and contents of the pack

- Certican 0.1 mg dispersible tablets are white to yellowish, marbled, round, flat tablets of 7 mm, engraved “I” on one side and “NVR” on the other.
- Certican 0.25 mg dispersible tablets are white to yellowish, marbled, round, flat tablets of 9 mm, engraved “JO” on one side and “NVR” on the other.

Certican dispersible tablets are supplied in packs containing 50, 60, 100 or 250 dispersible tablets. Not all pack sizes may be marketed. Certican is also available in the form of tablets.

Marketing Authorisation Holder and Manufacturer

To be completed nationally

This medicinal product is authorised in the Member States of the EEA under the following name:

Certican: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxemburg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, United Kingdom

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THE FOLLOWING INFORMATION IS FOR HEALTH CARE PROFESSIONALS ONLY

Information about the use and handling of the dispersible tablets

Administration in a 10 mL oral syringe. Place the Certican dispersible tablets into a syringe. The maximum amount of Certican that can be dispersed in a 10 mL syringe is 1,25 mg. Add water to the 5 mL mark. Wait 90 seconds while shaking the syringe gently. After dispersion, deliver directly into the mouth. Rinse the syringe with 5 mL water and administer into the mouth. Further, drink 10-100 mL water or diluted syrup.

Administration in a plastic cup. Place the Certican dispersible tablets into a plastic cup which contain about 25 mL water. The maximum amount of Certican that can be dispersed in a 25 mL plastic cup is 1,5 mg. Wait about 2 minutes so the tablets will disperse. Shake gently before drinking the dispersion. Flush the cup with another 25 mL portion immediate after administration and drink all of this fluid.

Administration via nasogastric tube. Place the Certican dispersible tablets in a small plastic medicine beaker which contain 10 mL water. Wait 90 seconds while swirling the medicine beaker gently. Put the dispersion into a syringe and inject slowly (within 40 seconds) into the nasogastric tube. Rinse the beaker (and the syringe) 3 times with 5 mL water and inject into the tube. Finally flush the tube with 10 mL water. The tube should be clamped for a minimum of 30 minutes after Certican administration.

If ciclosporin microemulsion is also administered via nasogastric tube it should also be administered before Certican. The two drugs should not be mixed.