

CERTICAN® 0,25 mg / 0, 75 mg

TABLETS

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PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

CERTICAN® 0.25 mg (tablets)

Everolimus, 0.25 mg

CERTICAN® 0.75 mg (tablets)

Everolimus 0.75 mg

Read all of this leaflet carefully before you start taking CERTICAN

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- CERTICAN has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

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

What CERTICAN is:

The active substance of CERTICAN is everolimus.

CERTICAN belongs to a group of medicines known as immunosuppressants, the function of which is to control your body's immune system and to prevent organ rejection after you have received a kidney, heart or liver transplant.

What CERTICAN is used for:

CERTICAN is used to prevent your body from rejecting the transplanted organ. CERTICAN is used together with medicines called ciclosporin for kidney and heart transplantation or tacrolimus for liver transplantation and corticosteroids.

2. What you need to know before you take CERTICAN

CERTICAN will only be prescribed for you by a doctor with experience in transplantation medicine. Follow your doctor's instructions carefully.

CERTICAN and older people (patients aged 65 years and over):

There is limited experience with the administration of CERTICAN in elderly patients.

CERTICAN in children and adolescents:

There is limited experience with the administration of CERTICAN in children and adolescents.

Do not take CERTICAN:

- if you are hypersensitive (allergic) to everolimus, sirolimus or to any of the other components of CERTICAN;
- if you are pregnant, breastfeeding or a woman of childbearing potential not using effective contraception;
- If you plan to receive a vaccine. You should not receive certain types of vaccines (called live attenuated vaccines).

Warnings and precautions

Take special care with CERTICAN:

- Medicines which suppress the immune system like CERTICAN reduce your body's ability to fight against infection. It is advisable to consult your doctor or transplant centre in case of fever, malaise (general feeling of fatigue and bodily unease) or local symptoms such as cough, burning sensations when urinating which are severe or persistent over several days.
- If you have any problems with your liver or have previously had a disease which may have affected your liver, please inform your doctor as it may be necessary to modify the dose of CERTICAN you receive.
- Many medicines can interact with CERTICAN (see section Other medicines and CERTICAN)

- If you need to receive a vaccine, seek your doctor's advice first (see section Do not take CERTICAN).
- 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 the condition.
- CERTICAN may reduce the quality of sperm in men reducing their ability to father children. The effect is generally reversible. Male patients wanting to father children should discuss their treatment with their doctor.

Special warning:

- Medicines which suppress the immune system like CERTICAN increase the risk of developing cancers, particularly of the skin and 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.
- 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 multifocal 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.
- 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 have angioedema (the rapid edema, or swelling, of the area beneath the skin or mucosa)

Children/ and adolescents

Do not give CERTICAN to children under the age of 18 years as it is unlikely to be safe.

Other medicines and CERTICAN

Always tell your healthcare provider if you are taking any other medicine (this includes complementary or traditional medicines).

Tell your doctor if you are taking any of the following medicines:

- immunosuppressive medicines other than ciclosporin, tacrolimus or corticosteroids;

- antibiotics or antifungal medicines used to treat infections, e.g., rifampicin, erythromycin, or fluconazole; ketoconazole or itraconazole;
- St. John's Wort (*hypericum perforatum*) - a herbal product used to treat depression and other conditions;
- anti-convulsants used for epilepsy such as phenytoin, carbamazepine, phenobarbitone;
- calcium channel blockers, such as verapamil, nifedipine, diltiazem, used to treat heart conditions or high blood pressure;
- protease inhibitors (a type of drug that is used to treat or prevent infection by viruses,) such as nelfinavir, indinavir or zidovudine which are used to treat HIV infections;
- midazolam, a medicine used to treat acute seizures, or used as a sedative before or during surgery or other medical procedures;
- medicines used to lower blood cholesterol, such as atorvastatin, pravastatin or fibrates;
- octreotide, a medicine used to treat acromegaly, a rare hormonal disorder that usually occurs in middle-aged adults.

CERTICAN with food and drink and alcohol

- Take CERTICAN consistently, either with or without food.
- Do not take CERTICAN with grapefruit or grapefruit juice since this can interfere with certain enzymes in the body that influence CERTICAN's effects (see section 2 How to take CERTICAN).

Pregnancy and breastfeeding and fertility

- If you are pregnant or breastfeeding your baby while taking CERTICAN, please consult your doctor, pharmacist or health care professional for advice.
- CERTICAN must not be used during pregnancy.
- You should use an effective contraceptive method during treatment with CERTICAN and for 8 weeks after treatment has stopped. If you are unsure or think you may have become pregnant, ask your doctor for advice before taking CERTICAN.
- It is not known if CERTICAN passes into breast milk. Breast-feeding should be discontinued by patients taking CERTICAN.

Driving and using machinery

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

It is not always possible to predict to what extent CERTICAN may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which CERTICAN affects them.

CERTICAN contains lactose

CERTICAN contains lactose which may have an effect on the control of your blood sugar if you have diabetes mellitus. If you have an intolerance or have rare hereditary conditions to some sugars (galactose, glucose, lactose), talk to your doctor before taking CERTICAN.

3. How to take CERTICAN

Do not share medicines prescribed for you with any other person.

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

- Do not exceed the recommended dosage.
- CERTICAN is for oral use only.
- Always take CERTICAN exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure. Your doctor will decide exactly which dose of CERTICAN should be taken by you and when this should be taken.
- Follow your doctor's instructions and never alter the dose yourself.

The usual dose is:

Kidney and heart transplantations

- The general recommended daily dose is 0,75 mg CERTICAN twice daily, taken in the morning and in the evening, together with ciclosporin for microemulsion.
- The first dose of Certican will be given as soon as possible after transplantation.

Liver transplantation

- The general recommended daily dose 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.
- Your dose may be adjusted depending on the level of CERTICAN in your blood and on clinical signs.
- Your doctor will need to perform regular blood tests to measure CERTICAN levels.
Swallow the tablets whole with a glass of water.

- Do not crush CERTICAN tablets before use.
- Do not take CERTICAN with grapefruit or grapefruit juice.
- CERTICAN may be taken with or without food but should either always be taken with food or always be taken without food.
- Treatment will continue for as long as you need immunosuppression to prevent you from rejecting your transplanted organ.
- Your doctor will tell you how long your treatment with CERTICAN will last.
- If you have the impression that the effect of CERTICAN is too strong or too weak, tell your doctor or pharmacist.

If you take more CERTICAN than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

If you forget to take a dose of CERTICAN

If you forget to take CERTICAN, take it as soon as you remember, then continue to take it at the usual times. Ask your doctor for advice.

Do not take a double dose to make up for forgotten individual doses.

If you stop taking CERTICAN

Stopping your treatment with CERTICAN may increase the chance of rejection of your transplanted organ. Do not stop taking your medicine unless your doctor tells you to.

4. Possible side effects

CERTICAN can have side effects.

However, since it is taken in combination with other medicines, the side effects cannot always be directly attributed with certainty to CERTICAN itself.

Not all side effects reported for CERTICAN are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking CERTICAN, please consult your healthcare professional for advice.

If any of the following happens, stop taking CERTICAN and tell your doctor immediately or go to the casualty department at your nearest hospital:

- **Swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing;**
- **rash or itching;**
- **fainting.**

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to CERTICAN. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- **Inflammation of the lungs:** Tell your doctor straight away if you experience persistent or worsening lung/breathing symptoms like cough, difficulty breathing, or wheezing. This might indicate that you have lung inflammation which can be life-threatening. Your doctor might need to discontinue your treatment with CERTICAN or add another medicine to help with this side effect.
- **Infection:** CERTICAN can increase your risk of getting infections (e.g., chest infections, urinary infections, general viral or fungal infections). These infections can be serious and even life-threatening. Tell your doctor straight away if you have increased temperature or shivering or other signs of an infection as you might need urgent treatment.
- **Angioedema:** CERTICAN can cause angioedema which typically appears as sudden swelling of your face, lips, tongue or throat. Tell your doctor straight away as this can lead to difficulties of swallowing and breathing which may be life-threatening.
- **Thrombotic microangiopathy** is a post-transplant disorder which can occur with CERTICAN. It causes a sudden reduction in the number of platelets in your blood. Platelets help stop bleeding. You should tell your doctor straight away if you notice spontaneous bruising or bleed for no obvious reason.
- **Kidney graft thrombosis** is the sudden blockage of the blood vessels supplying a transplanted kidney. Typically it occurs within the first month after transplantation. Tell your doctor straight away if you have an important drop in your urine production, especially if accompanied by pain where your transplanted kidney is located.

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

The following side effects have been reported frequently:

- infections;
- upper or lower respiratory tract infection;
- diarrhoea;

- nausea;
- vomiting;
- general pain;
- pain in the ear, nose or throat;
- acne;
- slowed wound healing;
- venous thrombosis (blockage of a major vein by a blood clot);
- kidney graft thrombosis (sudden blockage of the blood vessels supplying the transplanted kidney which may result in graft loss);
- defect in blood clotting;
- reduced blood platelet count which can lead to bleeding and/or bruising underneath the skin;
- anaemia (reduced red blood cell count);
- simultaneous reduction of white and red blood cells and of platelets (symptoms may include weakness, bruising and frequent infections);
- cyst containing lymph fluid;
- swelling of the face, lips, mouth, tongue or throat often associated with rash and itching;
- inflammation of the pancreas (symptoms may include severe upper stomach pain, vomiting and loss of appetite);
- mouth sores;
- protein in the urine;
- impotence;
- high levels of some fats (lipids, cholesterol and triglycerides) in the blood;
- reduced level of white blood cells (increasing risk of infection);
- 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/chest cavity, which if severe, could make you breathless;
- onset of diabetes (high level sugar in the blood);
- high blood pressure;
- abdominal pain;
- oedema (accumulation of fluid in the tissues);
- hernia at the site of surgery;
- urinary tract infections;
- wound infection;
- rash;
- muscle pain;

- kidney disorders.

The following side effects have been reported less frequently:

- haemolysis (destruction of red blood cells);
- inflammation of the lungs (symptoms may include coughing, difficulty in breathing and wheezing);
- liver disease with feeling generally unwell;
- jaundice (yellowing of the skin and eyes with darkened urine);
- decrease in number of spermatozooids in sperm (decreases likelihood of men being able to father children);
- skin cancer;
- reduced level of potassium in the blood;
- problem to fall asleep (insomnia);
- anxiety;
- headache;
- cough;
- breathlessness;
- fever;
- blood poisoning;
- cancers and benign tumours;
- cancer of the lymph tissue (lymphoma/post-transplant lympho-proliferative disorder);
- fast heart beat;
- nose bleeds;
- joint pain;
- kidney disorders;
- abnormal liver tests results.

The following side effects have been reported but the frequency is unknown:

- abnormal accumulation of protein in the lungs (symptoms may include persistent dry cough, fatigue and difficulty in breathing);
- inflammation of blood vessels (localised rash on skin);
- ovarian cysts.

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

Reporting of side effects

If you get side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects to SAHPRA via the "6.04 Adverse Drug Reaction

Reporting Form”, found online under SAHPRA’s publications: <https://www.sahpra.org.za/>. By reporting side effects, you can help provide more information on the safety of CERTICAN.

5. How to store CERTICAN

- Store at or below 30 °C.
- Protect from light and moisture.
- Store in original package.
- Do not use Certican after the expiry date stated on the box.
- Do not use any Certican pack that is damaged or shows signs of tampering.
- Do not store in bathrooms.
- Return all unused medicine to your pharmacist.
- Do not dispose of unused medicine in drains or sewerage systems (e.g., toilets).
- Store all medicines out of reach of children.

6. Contents of the pack and other information

What CERTICAN contains:

The active substance is:

Each tablet contains 0,25 /0,75 mg everolimus

The other ingredients are:

Butylated hydroxytoluene (E321), crospovidone, hypromellose, lactose anhydrous, lactose monohydrate, magnesium stearate.

What CERTICAN looks like and contents of the pack

What CERTICAN looks like:

Tablets are white to yellowish, marbled, round, flat with bevelled edge.

0.25 mg: engraved with “C” on one side and “NVR” on the other

0.75 mg: engraved with “CL” on one side and “NVR” on the other

Contents of the pack:

Packs containing 50/60/100/250 tablets.

Packed in a clear transparent thermoformed Aluminium /Aluminium blister.

The blister packs are packed in cardboard carton.

Not all pack sizes may be marketed.

Holder of Certificate of Registration and Manufacturer

NOVARTIS SOUTH AFRICA (Pty) Ltd
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2090

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Access to the corresponding Professional Information

Can be obtained on the SAHPRA website