

CERTICAN[®] DISPERSIBLE TABLET

Everolimus (0.1mg and 0.25mg)

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What Certican is used for

Certican contains active ingredient everolimus and belongs to a group of medicines known as immunosuppressants. Certican is used to help prevent your body from rejecting a transplanted kidney, heart or liver.

How Certican works

Certican must be used together with other immunosuppressant medicines, notably ciclosporin for kidney and heart transplantation or tacrolimus for liver transplantation, and corticosteroids.

Before you use Certican

Certican will only be prescribed for you by a doctor with experience in transplantation medicine. Follow your doctor's instructions carefully. They may differ from the general information contained in this leaflet.

When you must not use it

If you are allergic (hypersensitive) to everolimus, sirolimus or to any of the other components of Certican. The ingredients contained in each tablet are listed at the end of this leaflet. Tell your doctor if you suspect you may have had an allergic reaction to any of these ingredients in the past.

Pregnancy and breast-feeding

Certican must not be used during pregnancy unless indicated by your doctor. If you are pregnant or think that you may be, tell your doctor who will discuss with you the

potential risk of taking Certican 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. Certican may have an impact on male fertility.

Before you start to use it

Should you develop any of the following:

- swelling of the face, lips, throat or tongue, or sudden difficulty swallowing or breathing.
- persistent or worsening lung/breathing symptoms like cough, difficulty breathing, or wheezing.
- skin bruising without obvious cause
- pain, hernia, unusual warmth, swelling or oozing from the site of surgery
- sudden reduction in your urine output, especially if accompanied by pain where your transplanted kidney is located.

If this applies to you tell your doctor straight away.

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 center in case of fever, malaise or local symptoms such as cough, burning sensation when urinating which are severe or persistent over several days.

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.

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. Please inform your doctor of any other medicines you are receiving, especially if you are taking any medicines containing, rifampicin, rifabutin or ketoconazole, itraconazole, voriconazole, clarithromycin, telithromycin or ritonavir. It may be necessary to modify the dose of Certican.

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 physician.

Older people (patients aged 65 years and over)

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

Children and adolescents

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

If you need to avoid sugars

If you have been told by your doctor that you have an intolerance to certain sugars (glucose, galactose, lactose), talk to your doctor before taking Certican. Certican contains lactose.

Taking other medicines

Please inform your doctor if you are taking or have recently taken any other medicines, even those you have obtained without a prescription.

Some medicines may interfere with the action of Certican. In particular, you should inform your

doctor if you are taking one of the following medicines:

- Immunosuppressive medicines other than ciclosporin, tacrolimus or corticosteroids.
- Antibiotics or antifungal medicines used to treat infections, e.g. erythromycin, clarithromycin, telithromycin or fluconazole, ketoconazole, itraconazole, voriconazole.
- Medicines used to treat tuberculosis like rifampicin or rifabutin
- *Hypericum perforatum* (St. John's Wort) – a herbal product used to treat depression and other conditions.
- Anti convulsants such as phenytoin, carbamazepine, phenobarbital,
- Calcium channel blockers, such as verapamil, nifedipine, diltiazem, used to treat heart conditions or high blood pressure.
- Anti-HIV medicines such as efavirenz, nevirapine and protease inhibitors (such as nelfinavir, indinavir and amprenavir) used to treat AIDS.
- Midazolam, a medicine used to treat acute seizures, or used as a sedative before or during surgery or other medical procedure.
- Octreotide, a medicine used to treat acromegaly, a rare hormonal disorder that usually occurs in middle-aged adults.

How to use Certican

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 carefully and never alter the dose yourself. Do not exceed the recommended dosage. Certican is for oral use only.

How much to use

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 and corticosteroids.

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 and corticosteroids.

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.

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

When to use it

Certican may be taken with or without food but should either always be taken with food or always be taken without food. Do not take Certican with grapefruit or grapefruit juice. Ciclosporin or tacrolimus and corticosteroids should be taken at the same time as Certican.

How long to use Certican

Treatment will continue for as long as you need immunosuppression to prevent you from rejecting your transplanted organ.

If you forget to use 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.

If you used too much (overdose)

If you take more tablets than you have been told to take, or if someone else accidentally takes your medicine, immediately see your doctor or go to a hospital.

While you are using Certican

Things you must do

If you need to receive a vaccine, seek your doctor's advice first.

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.

Always comply with the follow-ups given to you as your doctor might need to do regular check ups on you.

Regular check-ups with blood and urine tests are essential for your doctor to assess the good function of your transplanted organ, to detect possible unwanted side effects and to adapt the dosages of your medicines to obtain the best treatment.

Blood tests allow the doctor to measure levels of your medicines (everolimus, ciclosporin, tacrolimus), to check your kidney activity and the levels of sugar and cholesterol in your blood. Measurement of proteins in a urine sample also helps the physician to assess kidney activity.

Things you must not do

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.

Things to be careful of

Driving and using machines

No specific studies of the effects of Certican on the ability to drive and use machines have been conducted. Do not drive or operate machineries until you know how Certican affects you.

Side effects

Like all medicines, Certican can have side effects, although not everybody gets them. However, since it is taken in combination with other medicines, the side effects cannot always be directly attributed with certainty to Certican itself.

Some side effects could be serious

- 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, cough 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.

If you experience any of these, tell your doctor straight away.

Some side effects are very common

These side effects may affect more than 1 in every 10 patients.

- Infections (viral, bacterial and fungal infections)
- Lower respiratory tract infection such as lung infections and pneumonia
- upper respiratory tract infection, such as inflammation of the pharynx and common cold
- urinary tract infections
- anemia (reduced red blood cell count)
- reduced blood platelet count which can lead to bleeding and/or bruising underneath the skin
- high levels of some fats (lipids, cholesterol and triglycerides) in the blood
- reduced level of potassium in the blood
- reduced level of white blood cells (increasing risk of infection)
- problem to fall asleep (insomnia)
- anxiety
- headache
- fluid collection in the sac around the heart, which if severe, can decrease the heart's ability to pump blood
- venous thrombosis (blockage of a major vein by a blood clot)
- fluid collection on the lungs/chest cavity, which if severe, could make you breathless.
- Cough
- Breathlessness
- Diarrhoea
- Nausea
- vomiting
- onset of diabetes (high level sugar in the blood)
- high blood pressure
- abdominal pain
- general pain
- oedema (accumulation of fluid in the tissues)
- fever

If you have concerns on any of these effects, tell your doctor.

Some side effects are common

These side effects may affect between 1 and 10 in every 100 patients.

- Sepsis (the body's overwhelming and life-threatening response to infection which can lead to death)
- wound infection
- cancers and benign tumours
- Skin cancer
- fast heart beat
- nose bleeds
- joint and muscle pain
- pain in the oral cavity like the throat
- acne
- kidney graft thrombosis (sudden blockage of the blood vessels supplying the transplanted kidney which may result in graft loss)
- 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
- kidney disorders
- erectile dysfunction
- hernia at the site of surgery
- abnormal liver tests results
- rash

If you have concerns on any of these effects, tell your doctor.

Some side effects are uncommon

These side effects may affect between 1 and 10 in every 1,000 patients.

- cancer of the lymph tissue (lymphoma/post-transplant lympho-proliferative disorder)
- Interstitial lung disease (ILD), is a group of lung diseases
- liver disease with feeling generally unwell
- jaundice (yellowing of the skin and eyes with darkened urine)

- decrease in number of spermatozoids in sperm (decreases likelihood of men being able to father children).

If you have concerns on any of these effects, tell your doctor.

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 in breathing)
- inflammation of blood vessels. (localized rash on skin)
- severe rash with skin swelling

If you have concerns on any of these effects, tell your doctor. Additionally, there may be side effects that you are not aware of, such as abnormal results of laboratory tests, including tests of liver function. During your treatment with Certican your doctor will therefore perform blood tests to monitor any changes. If you notice any side effects not mentioned in this leaflet or are concerned about those listed, please inform your doctor.

You may report any side effects or adverse drug reactions directly to the National Centre for Adverse Drug Reaction Monitoring by calling Tel: 03-78835550, or visiting the website portal.bpfk.gov.my (Consumers → Reporting).

Storage and disposal of Certican

- Storage
 - Store Certican in the original package in order to protect from light and moisture.
 - 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 above 30°C
 - Keep Certican out of the reach and sight of children.
- Disposal
 - Any unused product or waste material should be disposed of

in accordance with local requirements.

Product Description

What it looks like

Certican 0.1mg Dispersible Tablets are white to yellowish, marbled, round, flat with a bevelled edge, engraved with “I” on one side and “NVR” on the other.

Certican 0.25mg Dispersible Tablets are white to yellowish, marbled, round, flat with a bevelled edge, engraved with “JO” on one side and “NVR” on the other.

Certican dispersible tablets are supplied in packs containing 50/60/100/250 tablets.

Not all pack sizes may be marketed.

Certican is also available as tablets.

Ingredients

- Active ingredient
Your medicine is called Certican and comes in the form of dispersible tablets. Each dispersible tablet contains the active substance everolimus (0.1 mg, 0.25 mg respectively).
- Inactive ingredients
The other ingredients are butylated hydroxytoluene (E 321), magnesium stearate, lactose monohydrate (9 mg, 2 mg respectively), hypromellose, crospovidone, lactose anhydrous (72 mg, 179 mg respectively) and colloidal anhydrous silica.

MAL Number

Certican 0.1mg Dispersible Tablet: MAL20071693AR

Certican 0.25mg Dispersible Tablet: MAL20071694AR

Information for the health care professional

Instructions for 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 sec while shaking gently. After dispersion

deliver directly into the mouth. Rinse the syringe with 5 mL water and administer into the mouth. Further drink 10 to 100 mL of water, or diluted syrup.

Administration via nasogastric tube. Place the Certican dispersible tablets in a small plastic medicine beaker which contain 10 mL water and wait 90 sec while swirling gently. Put the dispersion into a syringe and inject slowly (within 40 sec) 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 nasogastric tube should be clamped for a minimum of 30 minutes after Certican administration. If ciclosporin is also administered via nasogastric tube it should be administered before Certican. The two drugs should not be mixed.

Manufacturer

Novartis Pharma Stein AG, Schaffhauserstrasse, CH-4332, Stein, Switzerland

Product Registration Holder

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