

**EMCURE**

**Vingraf 0.5** [*Tacrolimus Capsule USP 0.5 mg*], Module-1

### **1.6.3 Patient information Leaflet**

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## **Package leaflet: Information for the patient**

### **Vingraf 0.5 mg hard capsules**

(tacrolimus)

**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, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their symptoms 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 Vingraf is and what it is used for
2. What you need to know before you take Vingraf
3. How to take Vingraf
4. Possible side effects
5. How to store Vingraf
6. Contents of the pack and other information

#### **1. What Vingraf is and what it is used for**

Vingraf belongs to a group of medicines called immunosuppressants. Following your organ transplant (e.g. liver, kidney, heart), your body's immune system will try to reject the new organ. Tacrolimus is used to control your body's immune response enabling your body to accept the transplanted organ. Tacrolimus is often used in combination with other medicines that also suppress the immune system.

You may also be given tacrolimus for an ongoing rejection of your transplanted liver, kidney, heart or other organ or if any previous treatment you were taking was unable to control this immune response after your transplantation.

#### **2. What you need to know before you take Vingraf**

##### **Do not take Vingraf:**

- if you are allergic (hypersensitive) to tacrolimus or any of the other ingredients of this medicine (listed in section 6).
- if you are allergic (hypersensitive) to any antibiotic belonging to the subgroup of macrolide antibiotics (e.g. erythromycin, clarithromycin, josamycin).

#### **Warnings and precautions**

##### **Talk to your doctor or pharmacist before taking Vingraf**

- You will need to take tacrolimus every day as long as you need immunosuppression to prevent rejection of your transplanted organ. You should keep in regular contact with your doctor.

- Whilst you are taking tacrolimus your doctor may want to carry out a number of tests (including blood, urine, heart function, visual and neurological tests) from time to time. This is quite normal and will help your doctor to decide on the most appropriate dose of tacrolimus for you.
- Please avoid taking any herbal remedies, e.g. St. John's wort (*Hypericum perforatum*) or any other herbal products as this may affect the effectiveness and the dose of tacrolimus that you need to receive. If in doubt, please consult your doctor prior to taking any herbal products or remedies.
- If you have liver problems or have had a disease which may have affected your liver, please tell your doctor as this may affect the dose of tacrolimus that you receive.
- If you feel strong abdominal pain accompanied or not with other symptoms, such as chills, fever, nausea or vomiting.
- If you have diarrhoea for more than one day, please tell your doctor, because it might be necessary to adapt the dose of tacrolimus that you receive.
- If you have an alteration of the electrical activity of your heart called "QT prolongation".
- Limit your exposure to sunlight and UV light whilst taking tacrolimus by wearing appropriate protective clothing and using a sunscreen with a high sun protection factor. This is because of the potential risk of malignant skin changes with immunosuppressive therapy.
- If you need to have any vaccinations, please inform your doctor beforehand. Your doctor will advise you on the best course of action.
- Patients treated with tacrolimus have been reported to have an increased risk of developing lymphoproliferative disorders (see section 4). Ask your doctor for specific advice on these disorders.

Tell your doctor immediately if during treatment you suffer from:  
problems with your vision such as blurred vision, changes in colour vision, difficulty in seeing detail or if your field of vision becomes restricted.

### **Other medicines and Vingraf**

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

Tacrolimus must not be taken with ciclosporin.

Tacrolimus blood levels can be affected by other medicines you take, and blood levels of other medicines can be affected by taking tacrolimus which may require interruption, an increase or a decrease in tacrolimus dose. In particular, you should tell your doctor if you are taking or have recently taken medicines with active substances like:

- antifungal medicines and antibiotics, particularly so-called macrolide antibiotics, used to treat infections e.g. ketoconazole, fluconazole, itraconazole, voriconazole, clotrimazole, and isavuconazole, erythromycin, clarithromycin, josamycin, and rifampicin
- letermovir, used to prevent illness caused by CMV (human cytomegalovirus)
- HIV protease inhibitors (e.g. ritonavir, nelfinavir, saquinavir), the booster medicine cobicistat, and combination tablets, used to treat HIV infection
- HCV protease inhibitors (e.g. telaprevir, boceprevir, and the combination ombitasvir/paritaprevir/ritonavir with or without dasabuvir), used to treat hepatitis C infection
- nilotinib and imatinib (used to treat certain cancers)
- mycophenolic acid, used to suppress the immune system to prevent transplant rejection

- medicines for stomach ulcer and acid reflux (e.g. omeprazole, lansoprazole or cimetidine)
- antiemetics, used to treat nausea and vomiting (e.g. metoclopramide)
- magnesium-aluminium-hydroxide (antacid), used to treat heartburn
- hormone treatments with ethinylestradiol (e.g. the oral contraceptive pill) or danazol
- medicines for high blood pressure or heart problems such as nifedipine, nicardipine, diltiazem and verapamil
- anti-arrhythmic medicines (amiodarone) used to control arrhythmia (uneven beating of the heart)
- medicines known as “statins” used to treat elevated cholesterol and triglycerides
- the anti-epileptic medicines phenytoin or phenobarbital
- the corticosteroids prednisolone and methylprednisolone
- the anti-depressant nefazodone
- Herbal preparations containing St. John’s Wort (*Hypericum perforatum*) or extracts of *Schisandra sphenanthera*.

Tell your doctor if you are taking or need to take ibuprofen, amphotericin B, or antivirals (e.g. aciclovir). These may worsen kidney or nervous system problems when taken together with tacrolimus.

Your doctor also needs to know if you are taking potassium supplements or potassium-sparing diuretics (e.g., amiloride, triamterene, or spironolactone), certain pain killers (so-called NSAIDs, e.g. ibuprofen), anticoagulants, or oral medication for diabetic treatment, while you take tacrolimus.

If you need to have any vaccinations, please inform your doctor beforehand.

### **Vingraf with food and drink**

You should generally take tacrolimus on an empty stomach or at least 1 hour before or 2 to 3 hours after a meal. Grapefruit and grapefruit juice should be avoided while taking tacrolimus.

### **Pregnancy and breast-feeding**

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine. Tacrolimus is excreted into breast milk. Therefore, you should not breast-feed whilst receiving tacrolimus.

### **Driving and using machines**

Do not drive or use any tools or machines if you feel dizzy or sleepy, or have problems seeing clearly after taking tacrolimus. These effects are more frequently observed if tacrolimus is taken in conjunction with alcohol use.

### **Vingraf contains lactose, sodium and lecithin (soya)**

Vingraf contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

This medicine contains less than 1 mmol sodium (23 mg) per capsule, that is to say essentially ‘sodium-free’.

The printing ink used on Vingraf capsules 0.5 mg and 1 mg contains soya lecithin. If you are allergic to peanut or soya, talk to your doctor to determine whether you should use this medicine.

### **3. How to take Vingraf**

Always take Vingraf exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

Make sure that you receive the same tacrolimus medicine every time you collect your prescription, unless your transplant specialist has agreed to change to a different tacrolimus medicine. This medicine should be taken twice a day. If the appearance of this medicine is not the same as usual, or if dosage instructions have changed, speak to your doctor or pharmacist as soon as possible to make sure that you have the right medicine.

The starting dose to prevent the rejection of your transplanted organ will be determined by your doctor calculated according to your body weight. Initial doses just after transplantation will generally be in the range of

0.075 – 0.30 mg per kg body weight per day

depending on the transplanted organ.

Your dose depends on your general condition and on which other immunosuppressive medication you are taking. Regular blood tests by your doctor will be required to define the correct dose and to adjust the dose from time to time. Your doctor will usually reduce your tacrolimus dose once your condition has stabilised. Your doctor will tell you exactly how many capsules to take and how often.

Tacrolimus is taken orally twice daily, usually in the morning and evening. You should generally take tacrolimus on an empty stomach or at least 1 hour before or 2 to 3 hours after the meal. The capsules should be swallowed whole with a glass of water. Take the capsules immediately following removal from the blister. Avoid grapefruit and grapefruit juice while taking tacrolimus. Do not swallow the desiccant contained in the foil wrapper.

#### **If you take more Vingraf than you should**

If you have accidentally taken too much Vingraf see your doctor or contact your nearest hospital emergency department immediately.

#### **If you forget to take Vingraf**

Do not take a double dose to make up for forgotten individual doses. If you have forgotten to take your Vingraf capsules, wait until it is time for the next dose, and then continue as before.

#### **If you stop taking Vingraf**

Stopping your treatment with Vingraf may increase the risk of rejection of your transplanted organ. Do not stop your treatment unless your doctor tells you to do so.

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.

Tacrolimus reduces your body's own defence mechanism to stop you rejecting your transplanted organ. Consequently, your body will not be as good as usual at fighting infections. So if you are taking tacrolimus you may therefore catch more infections than

usual such as infections of the skin, mouth, stomach and intestines, lungs and urinary tract.

Severe side effects may occur, including the ones listed below. Tell your doctor immediately if you have or suspect you may have any of the following serious side effects:

- Opportunistic infections (bacterial, fungal, viral and protozoal): prolonged diarrhea, fever and sore throat.
- Benign and malignant tumours have been reported following treatment as a result of immunosuppression.
- Thrombotic Thrombocytopenic Purpura (or TTP) a condition characterised by fever and bruising under the skin that may appear as red pinpoint dots, with or without unexplained extreme tiredness, confusion, yellowing of the skin or eyes (jaundice), with symptoms of acute renal failure (low or no urine output).
- Cases of pure red cell aplasia (a very severe reduction in red blood cell counts), haemolytic anaemia (decreased number of red blood cells due to abnormal breakdown accompanied with tiredness) and febrile neutropenia (a decrease in the type of white blood cells which fight infection, accompanied by fever) have been reported. It is not known exactly how often these side effects occur. You may have no symptoms or depending on the severity of the condition, you may feel: fatigue, apathy, abnormal paleness of the skin (pallor), shortness of breath, dizziness, headache, chest pain and coldness in hands and feet.
- Cases of agranulocytosis (a severely lowered number of white blood cells accompanied with ulcers in the mouth, fever and infection(s)). You may have no symptoms or you may feel sudden fever, rigors and sore throat.
- Allergic and anaphylactic reactions with the following symptoms: a sudden itchy rash (hives), swelling of hands, feet, ankle, face, lips, mouth or throat (which may cause difficulty in swallowing or breathing) and you may feel you are going to faint.
- Posterior Reversible Encephalopathy Syndrome (PRES): headache, altered mental status, seizures, and visual disturbances.
- Torsades de Pointes: change in the heart frequency that can be accompanied or not of symptoms, such as chest pain (angina), faint, vertigo or nausea, palpitations (feeling the heartbeat) and difficulty breathing.
- Gastrointestinal perforation: strong abdominal pain accompanied or not with other symptoms, such as chills, fever, nausea or vomiting.
- Stevens-Johnson syndrome: unexplained widespread skin pain, facial swelling, serious illness with blistering of skin, mouth, eyes and genitals, hives, tongue swelling, red or purple skin rash that spreads, skin shedding.
- Toxic epidermal necrolysis: erosion and blistering of skin or mucous membranes, red swollen skin that can detach in large parts of the body.
- Haemolytic uraemic syndrome, a condition with the following symptoms: low or no urine output (acute renal failure), extreme tiredness, yellowing of the skin or eyes (jaundice) and abnormal bruising or bleeding and signs of infection.
- Insufficient function of your transplanted organ

**Very common side effects (may affect more than 1 in 10 people)**

- Increased blood sugar, diabetes mellitus, increased potassium in the blood

- Difficulty in sleeping
- Trembling, headache
- Increased blood pressure
- Diarrhoea, nausea
- Kidney problems

**Common side effects (may affect up to 1 in 10 people)**

- Reduced magnesium, phosphate, potassium, calcium or sodium in the blood, fluid overload, increased uric acid or lipids in the blood, decreased appetite, increased acidity of the blood, other changes in the blood salts
- Anxiety symptoms, confusion and disorientation, depression, mood changes, nightmare, hallucination, mental disorders
- Fits, disturbances in consciousness, tingling and numbness (sometimes painful) in the hands and feet, dizziness, impaired writing ability, nervous system disorders
- Blurred vision, increased sensitivity to light, eye disorders
- Ringing sound in your ears
- Reduced blood flow in the heart vessels, faster heartbeat
- Bleeding, partial or complete blocking of blood vessels, reduced blood pressure
- Shortness in breath, changes in the lung tissue, collection of liquid around the lung, inflammation of the pharynx, cough, flu-like symptoms
- Inflammations or ulcers causing abdominal pain or diarrhoea, bleeds in the stomach, inflammations or ulcers in the mouth, collection of fluid in the belly, vomiting, abdominal pains, indigestion, constipation, flatulence, bloating, loose stools, stomach problems
- Changes in liver enzymes and function, yellowing of the skin due to liver problems, liver tissue damage and inflammation of the liver
- Itching, rash, hair loss, acne, increased sweating
- Pain in joints, limbs, back and feet, muscle spasms
- Insufficient function of the kidneys, reduced production of urine, impaired or painful urination
- General weakness, fever, collection of fluid in your body, pain and discomfort, increase of the enzyme alkaline phosphatase in your blood, weight gain, feeling of temperature disturbed

**Uncommon side effects (may affect up to 1 in 100 people)**

- Changes in blood clotting, reduction in all blood cell counts
- Dehydration, reduced protein or sugar in the blood, increased phosphate in the blood
- Coma, bleeding in the brain, stroke, paralysis, brain disorder, speech and language abnormalities, memory problems
- Blurring of the vision due to abnormality in the lens of the eye
- Impaired hearing
- Irregular heartbeat, stop of heartbeat, reduced performance of your heart, disorder of the heart muscle, enlargement of the heart muscle, stronger heartbeat, abnormal ECG, heart rate and pulse abnormal
- Blood clot in a vein of a limb, shock
- Difficulties in breathing, respiratory tract disorders, asthma
- Obstruction of the gut, increased blood level of the enzyme amylase, reflux of stomach content in your throat, delayed emptying of the stomach
- Dermatitis, burning sensation in the sunlight
- Joint disorders

- Inability to urinate, painful menstruation and abnormal menstrual bleeding
- Failure of some organs, influenza like illness, increased sensitivity to heat and cold, feeling of pressure on your chest, jittery or abnormal feeling, increase of the enzyme lactate dehydrogenase in your blood, weight loss

**Rare side effects (may affect up to 1 in 1000 people)**

- Small bleeds in your skin due to blood clots
- Increased muscle stiffness
- Blindness
- Deafness
- Collection of fluid around the heart
- Acute breathlessness
- Cyst formation in your pancreas
- Problems with blood flow in the liver
- Increased hairiness
- Thirst, fall, feeling of tightness in your chest, decreased mobility, ulcer

**Very rare side effects (may affect up to 1 in 10,000 people):**

- Muscular weakness
- Echocardiogram abnormal
- Liver failure, narrowing of the bile vessel
- Painful urination with blood in the urine
- Increase of fat tissue

**Not known (frequency cannot be estimated from the available data):**

Abnormality of the optic nerve (optic neuropathy)

**5. How to store Vingraf**

Keep this medicine out of the sight and reach of children.

Take the hard capsules immediately following removal from the blister

Do not use this medicine after the expiry date which is stated on the box and on the label after the letters EXP. The expiry date refers to the last day of that month.

Store in a dry place, below 30°C. Protect from light.

**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 to protect the environment.

**6. Contents of the pack and other information**

**What Vingraf contains**

Vingraf 0.5 mg hard capsules

The **active** substance is tacrolimus. Each capsule contains 0.5 mg of tacrolimus.

The other ingredients are Hypromellose BP, Croscarmellose Sodium USP/NF, Ethanol BP/USP, Lactose Monohydrate BP, Magnesium Stearate BP and EHG Capsule size “4”.



**What Vingraf looks like and contents of the pack****Vingraf 0.5 mg hard capsules**

Capsule, Size '4' Hard gelatine capsule with Light yellow coloured cap & body, imprinted in black ink with " VGF 0.5" on cap & body filled with white to off white powder.

**Pack**

10 Capsules are packed in Alu - Alu Blister. Six (6 x 10) such blister is packed in a carton along with a leaflet.

**Marketing Authorisation Holder and Manufacturer****Marketing Authorisation Holder**

Emcure Pharmaceuticals Limited

**Manufacturer**

Emcure Pharmaceuticals Limited, Jammu, India

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