

FIXGRAF ^{Capsules}

(Tacrolimus)

فکس گراف کپسولز
(ٹیکرولیمس)

Composition:

Fixgraf 1mg

Each capsule contains:

Tacrolimus (as Monohydrate)1mg
(USP Specs.)

BOX WARNING – MALIGNANCIES AND SERIOUS INFECTIONS

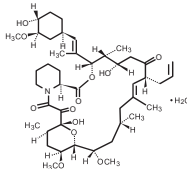
- Increased risk of development of lymphoma and other malignancies, particularly of the skin, due to immunosuppression.
- Increased susceptibility to bacterial, viral, fungal, and protozoal infections, including opportunistic infections.
- Only physicians experienced in immunosuppressive therapy and management of organ transplant patients should prescribe Fixgraf. Patients receiving the drug should be managed in facilities equipped and staffed with adequate laboratory and supportive medical resources. The physician responsible for maintenance therapy should have complete information requisite for the follow-up of the patient.

DESCRIPTION

Fixgraf is available for oral administration as capsules (tacrolimus capsules) containing the equivalent of 1 mg or 5 mg of anhydrous tacrolimus. Tacrolimus inhibits T-lymphocyte activation, although the exact mechanism of action is not known. Experimental evidence suggests that tacrolimus binds to an intracellular protein, FKBP-12. A complex of tacrolimus-FKBP-12, calcium, calmodulin, and calcineurin is then formed and the phosphatase activity of calcineurin inhibited. This effect may prevent the dephosphorylation and translocation of nuclear factor of activated T-cells (NF-AT), a nuclear component thought to initiate gene transcription for the formation of lymphokines (such as interleukin-2, gamma interferon). The net result is the inhibition of T-lymphocyte activation (i.e., immunosuppression).

Tacrolimus prolongs the survival of the host and transplanted graft in animal transplant models of liver, kidney, heart, bone marrow, small bowel and pancreas, lung and trachea, skin, cornea, and limb.

In animals, tacrolimus has been demonstrated to suppress some humoral immunity and, to a greater extent, cell-mediated reactions such as allograft rejection, delayed type hypersensitivity, collagen-induced arthritis, experimental allergic encephalomyelitis, and graft versus host disease.



INDICATIONS AND USAGE

Fixgraf 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. Fixgraf is used to control your body's immune response enabling your body to accept the transplanted organ.

Fixgraf is often used in combination with other medicines that also suppress the immune system.

You may also be given Fixgraf 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.

DOSAGE AND ADMINISTRATION

Always take Fixgraf 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 Fixgraf dose once your condition has stabilised. Your doctor will tell you exactly how many capsules to take and how often.

Fixgraf is taken orally twice daily, usually in the morning and evening. You should generally take Fixgraf 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 Fixgraf. Do not swallow the desiccant contained in the foil wrapper.

• You will need to take Fixgraf 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 Fixgraf 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 Fixgraf 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 Fixgraf that you need to receive. 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 Fixgraf 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 Fixgraf 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 Fixgraf 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 Fixgraf have been reported to have an increased risk of developing lymphoproliferative disorders.

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.

ADVERSE REACTIONS

The following adverse reaction may occur:

- Lymphoma and Other Malignancies
- Serious Infections
- Polyoma Virus Infections
- CMV Infections
- New Onset Diabetes After Transplant
- Nephrotoxicity
- Neurotoxicity
- Hyperkalemia
- Hypertension
- Anaphylaxis with Fixgraf Injection
- Myocardial Hypertrophy
- Pure Red Cell Aplasia

DRUGINTERACTIONS

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.

Fixgraf must not be taken with cyclosporine.

Fixgraf blood levels can be affected by other medicines you take, and blood levels of other medicines can be affected by taking Fixgraf which may require interruption, an increase or a decrease in Fixgraf 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

USE IN SPECIFIC POPULATIONS

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.

Fixgraf is excreted into breast milk. Therefore you should not breast-feed whilst receiving Fixgraf.

OVERDOSAGE

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

STORAGE:

Protect from heat light & moisture

All medicines should be kept out of the reach of children.

Store below 30°C.



Manufactured by:
GENOME PHARMACEUTICALS (PVT.) LTD.
Plot # 16/1, Phase IV, Industrial Estate Hattar-Pakistan.

Marketed by
AMP
ALLIANZE MED PHARMA

خود راک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایت: روشنی، نمی اور گرمی سے محفوظ رکھیں۔

تمام ادویات بچوں کی پہنچ سے دور رکھیں۔

دوا کو 30°C سے کم درجہ حرارت پر رکھیں۔