PROGRAF®

Tacrolimus (0.5mg, 1mg, 5mg)

What is in this leaflet

What *Prograf* is used for

Prograf is used to control your body's immune response enabling your body to accept the transplanted liver or kidney.
Prograf is often used in combination with other medicines that also suppress the immune system.
You may also be given Prograf for an ongoing rejection of your transplanted liver or kidney, or if any previous treatment you were taking was unable to control this immune response after your transplantation.

How *Prograf* works

Prograf contains an active ingredient called tacrolimus. It belongs to a group of medicines called immunosuppressants. Prograf reduces your body's own defence mechanism to stop you rejecting your transplanted organ

Before you use *Prograf*

- *When you must not use it*

-If you are allergic (hypersensitive) to tacrolimus or any of the other ingredients of Prograf
- If you are allergic (hypersensitive) to macrolide antibiotics (e.g. *erythromycin, clarithromycin, josamycin).*

Pregnancy and lactation

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

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

- *Before you start to use it*

Talk to your doctor or pharmacist before taking Prograf

- 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 Prograf that you receive.
- If you have strong abdominal pain accompanied or not with other symptoms, such as chills, fever, nausea or vomiting.
- If you have an alteration of the electrical activity of your heart called QT prolongation.
- If you have diarrhoea for more than one day, please tell your doctor, because it might be necessary to adapt the dose of Prograf that you receive.

- *Taking other medicines*

Tell your doctor if you are taking any other medicines, including any that you buy without a prescription from a pharmacy, supermarket or health food shop.

Prograf must not be taken with ciclosporin.
Prograf blood levels can be affected by other medicines you take, and blood levels of other medicines can be affected by taking Prograf which may require interruption, an increase or a decrease in Prograf 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, used to treat infections e.g. ketoconazole, fluconazole, itraconazole, voriconazole, clotrimazole, erythromycin, clarithromycin, josamycin, and rifampicin
- HCV protease inhibitors (e.g. telaprevir, boceprevir), used to treat hepatitis C infection
- antiemetics, used to treat nausea and vomiting (e.g. metoclopramide)
- magnesium-aluminium-hydroxide (antacid), used to treat heartburn
- HIV protease inhibitors (e.g. ritonavir), used to treat HIV infection
- omeprazole, used for treating stomach ulcers
- 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
- the anti-epileptic medicines phenytoin or phenobarbital
- the corticosteroids (e.g.prednisolone and methylprednisolone)
- the anti-depressant nefazodone
- St. John's Wort (Hypericum perforatum)

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 Prograf.
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 Prograf.

Food and drink

Grapefruit and grapefruit juice should be avoided while using Prograf.

How to use *Prograf*

- *How much to use*

Follow all directions given to you by your doctor and pharmacist carefully.
They may differ from the information contained in this leaflet. If you do not understand the instructions on the label, ask your doctor or pharmacist for help.
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.

Initial oral doses just after transplantation will generally be in the range of 0.1 – 0.3 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 Prograf dose once your condition has stabilised. Your doctor will tell you exactly how many capsules to take and how often.
Prograf capsule is taken orally twice daily, usually in the morning and evening. You should generally take Prograf 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.

- *When to use it*
Use as directed by your doctor or pharmacist.

- *How long to use it*
Continue taking *Prograf* for as long as your doctor recommends.

If you forget to use it
Consult your doctor or pharmacist on what you should do if you forget to use it.
Take the missed dose as soon as you remember. If it is almost time for your next dose, wait until then to take the medicine and skip the missed dose. Do not take a double dose to make up for the missed dose.

- *If you use too much (overdose)*
Contact your doctor immediately or go to the Emergency Department of your nearest hospital, if you think you or anyone else may have taken too much of this medicine. Do this even if there are no signs of discomfort or poisoning. You may need urgent medical attention.

Taking too many tablets may cause tremor, headache, nausea and vomiting, infections, hives, lethargy, increase in blood levels of urea and creatinine (urea and creatinine are waste products of the body), and increase in alanine aminotransferase levels which is related to liver damage.

While you are using it
- *Things you must do*
- Tell all the doctors, dentists and pharmacists treating you that you are taking Prograf.

- Tell your doctor immediately if you become pregnant while taking this medication.

- Attend all the appointments given to you as your doctor may carry out a number of tests from time to time. This is important and will help your doctor to decide on the most appropriate dose of Prograf for you.

- Limit your exposure to sunlight and UV light whilst taking Prograf 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.

- *Things you must not do*
- Do not stop taking the medicine unless advised by your doctor. Stopping your treatment with Prograf may increase the risk of rejection of your transplanted organ.

- Do not take any new medicines without consulting your doctor.

- Do not give Prograf to anyone else, even if they have the same symptoms or condition as you.

- *Things to be careful of*
Driving and using machines
This medicine may affect your ability to drive or use machines. If the tablets make you feel sick, dizzy or tired, or give you a headache, do not drive or use machines and contact your doctor immediately.

Tacrolimus may cause visual and neurological disturbances. This effect may be enhanced if Prograf is administered in association with alcohol.

Side effects
Like all medicines, Prograf can cause side effects, although not everybody gets them.
Visit your doctor or pharmacist immediately if you experience any side effects after taking this medicine.

Prograf 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 Prograf you may therefore catch more infections than usual such as infections of the skin, mouth, stomach and intestines, lungs and urinary tract.

Severe effects have been reported, including allergic and anaphylactic reactions. Benign and malignant tumours have been reported following Prograf treatment as a result of immunosuppression.

Possible side effects are listed below in descending order by frequency of occurrence:

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):
- Reduction in blood cell counts (platelets, red or white blood cells), increase in white blood cell counts, changes in red blood cell counts
- 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, bleedings 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 or back, muscle cramps
- 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
- Insufficient function of your transplanted organ

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
- Opacity of the lens
- 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 1,000 people):
- Small bleedings 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
- Serious illness with blistering of skin, mouth, eyes and genitals, 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

Cases of pure red cell aplasia (a very severe reduction in red blood cell counts), agranulocytosis (a severely lowered number of white blood cells) and haemolytic anaemia (decreased number of red blood cells due to abnormal breakdown) have also been reported.

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 *Prograf*

- *Storage*

  Keep out of the reach and sight of children.

  Prograf Capsules 0.5mg: Store below 25°C in a dry place.

  Prograf Capsules 1mg and 5mg

  Store below 30°C in a dry place.

  After opening of the aluminium wrapper, the capsules are stable for 12 months.

- *Disposal*

  Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

Product Description

- *What it looks like*

  Prograf Capsules 0.5mg, 1mg and 5mg

  Ten capsules per blister sheet.

- *Ingredients*

  Active ingredient

  Prograf Capsule 0.5mg contains 0.5mg of tacrolimus

  Prograf Capsule 1mg contains 1mg of tacrolimus

  Prograf Capsule 5mg contains 5mg of tacrolimus.

  Inactive ingredients

  Prograf 0.5 mg hard capsules:
  - Capsule content: Hypromellose, croscarmellose sodium, lactose

monohydrate, magnesium stearate.
- Capsule shell: Titanium dioxide (E 171), yellow iron oxide (E 172), gelatine.
- Printing ink of capsule shell: Shellac, lecithin (soya), hydroxypropyl cellulose, simeticone, red iron oxide (E 172).

Prograf 1 mg hard capsules:
- Capsule content: Hypromellose, croscarmellose sodium, lactose monohydrate, magnesium stearate.
- Capsule shell: Titanium dioxide (E 171), gelatine.
- Printing ink of capsule shell: Shellac, lecithin (soya), hydroxypropyl cellulose, simeticone, red iron oxide (E 172).

Prograf 5 mg hard capsules:
- Capsule content: Hypromellose, croscarmellose sodium, lactose monohydrate, magnesium stearate.
- Capsule shell: Titanium dioxide (E 171), red iron oxide (E 172), gelatine.
- Printing ink of capsule shell: Shellac, lecithin (soya), simeticone, titanium dioxide (E 171).

- *MAL number:*
- Prograf Capsule 0.5mg MAL20031738A
- Prograf Capsule 1mg MAL19990220A
- Prograf Capsule 5mg MAL19990221A

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