PATIENT INFORMATION LEAFLET

SCHEDULING STATUS:

South Africa: S4

Namibia: NS2

Botswana: Schedule 2

PROPRIETARY NAME, STRENGTH AND PHARMACEUTICAL FORM

PROGRAF 0,5 mg capsules

PROGRAF 1 mg capsules

PROGRAF 5 mg capsules

Read all of this leaflet carefully before you start taking PROGRAF.

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- PROGRAF 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 PROGRAF CONTAINS:

Prograf 0,5 mg (Capsules); Prograf 1 mg (Capsules); Prograf 5 mg (Capsules):

Active Ingredient: Each capsule contains 0,5 mg; 1 mg and 5 mg tacrolimus, respectively.

Excipients:

Capsule contents: hypromellose, croscarmellose sodium, lactose monohydrate, magnesium stearate.

Contains sugar: lactose

Prograf 0,5 mg:

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:

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:

Capsule shell: titanium dioxide (E 171), red iron oxide (E 172), gelatine

Printing ink of capsule shell: shellac, titanium dioxide (E 171), propylene glycol

WHAT PROGRAF IS USED FOR :

Prograf belongs to a group of medicines called immunosuppressants. Prograf is used to control your body's immune response enabling your body to accept the transplanted organ. Prograf is often used in combination with other medicines that also suppress the immune system.

BEFORE YOU TAKE PROGRAF:

Do not take PROGRAF:

- If you are allergic (hypersensitive) to tacrolimus or to any antibiotic belonging to the subgroup of macrolide antibiotics (e.g. erythromycin, clarithromycin, josamycin).
- If you are allergic (hypersensitive) to any of the other ingredients of PROGRAF.
- If you are pregnant and breastfeeding.
- As PROGRAF may alter the metabolism of oral contraceptives, other forms of contraception should be used.
- With live attenuated vaccines.
- With ciclosporin.
- With grapefruit juice.

Take special care:

- Do not switch between different types of tacrolimus formulations.
- If you are taking any medicines mentioned below under " Taking other medicines with PROGRAF".
- If you have or have had liver problems.
- If you have diarrhoea for more than one day.
- If you feel 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 tuberculosis.
- Patients treated with PROGRAF have been reported to have an abnormality of some cells in the blood that is associated with a virus that is commonly known as Epstein-Barr Virus (EBV).
- PROGRAF should not be administered together with ciclosporin.
- Patients switched to PROGRAF rescue therapy should not receive concomitantly anti-lymphocyte treatment.
- Patients treated with PROGRAF have been reported to develop posterior reversible encephalopathy syndrome (PRES). If patients taking PROGRAF present with symptoms indicating PRES such as headache, altered mental status, seizures, and visual disturbances, a radiological procedure (e.g. MRI) should be performed. If PRES is diagnosed, adequate blood pressure control and immediate discontinuation of PROGRAF is advised. Most patients completely recover after appropriate measures are taken.
- In view of potential risk of cancers or non-cancerous growths, patients who spend extended periods in the sun, or are otherwise exposed to ultraviolet light, should apply a high protection sun-cream.
- The use of PROGRAF is not recommended in children and adolescents under 18 years.

Taking PROGRAF with food and drink:

Take PROGRAF on an empty stomach one hour before a meal or 2 to 3 hours after a meal. Do not use grapefruit (also as juice) while on treatment with PROGRAF, since it can affect its levels in your blood.

Pregnancy and Breastfeeding:

You should not use PROGRAF when you are pregnant or breastfeeding your baby.
If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before taking this medicine.

Driving and using machinery:

PROGRAF may cause visual and nervous system disturbances. If you are being treated with PROGRAF and you are affected by you should not drive a car or operate dangerous machines. This effect may be made worse when you use PROGRAF with alcohol.

Important information about some of the ingredients of 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.
The printing ink used on Prograf 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 Prograf.

Taking other medicines with PROGRAF:

Always tell your healthcare professional if you are taking any other medicine.
(This includes complementary or traditional medicines.)
It is not recommended that Prograf is taken with ciclosporin (another medicine used for the prevention of transplant organ rejection).

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 like:

- antifungal medicines and antibiotics, particularly so-called macrolide antibiotics, used to treat infections e.g. ketoconazole, fluconazole, itraconazole, voriconazole, clotrimazole, erythromycin, clarithromycin, josamycin, rifampicin and anti-epileptic medicine.
- HIV protease inhibitors (e.g ritonavir, nelfinavir, saquinavir), used to treat HIV infection
- HCV protease inhibitors (e.g. telaprevir, boceprevir), used to treat hepatitis C infection
- medicines for stomach ulcer and acid reflux (e.g. omeprazole, lansoprazole or cimetidine)
- antiemetics, used to treat nausea and vomiting (e.g. metoclopramide)
- antacid magnesium-aluminium-hydroxide, used to treat heartburn
- the contraceptive pill or other hormone treatments with ethinylestradiol, hormone treatments with danazol
- medicines used to treat high blood pressure or heart problems (e.g. nifedipine, nicardipine, diltiazem and verapamil)
- antidysrhythmic drugs (amiodarone) used to control arrhythmia (uneven beating of the heart)
- medicines known as “statins” used to treat elevated cholesterol and triglycerides
- phenytoin or phenobarbitone, used to treat epilepsy
- the corticosteroids prednisolone and methylprednisolone (cortisone), belonging to the class of corticosteroids used to treat inflammations or suppress the immune system (e.g. in transplant rejection)
- nefazodone, used to treat depression

Tell your doctor if you are taking or need to take ibuprofen (used to treat fever, inflammation and pain), amphotericin B (used to treat bacterial infections) or antivirals (used to treat viral infections 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 certain diuretics used for heart failure, hypertension and kidney disease, (e.g. amiloride, triamterene, or spironolactone), non-steroidal anti-inflammatory drugs (NSAIDs, e.g. ibuprofen) used for fever, inflammation and pain, anticoagulants (blood thinners), or oral medicines for diabetes, while you take Prograf.

If you need to have any vaccinations, please tell your doctor before.

HOW TO TAKE PROGRAF:

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

Always take PROGRAF exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

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.

Prograf 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. Avoid grapefruit and grapefruit juice while taking Prograf. Do not swallow the desiccant contained in the foil wrapper.

Your doctor will tell you how long your treatment with PROGRAF will last. Do not stop treatment early because you may have a rejection of your transplanted organ.

If you have the impression that the effect of PROGRAF is too strong or too weak, tell your doctor or pharmacist.

Your dose depends on your general condition and on which other immunosuppressive medication you are taking.

Following the initiation of your treatment with PROGRAF, frequent blood tests will be taken by your doctor to determine the correct dose and adjust the dose if needed. Your doctor will usually reduce your PROGRAF dose once your condition has stabilised. Your doctor will tell you exactly how many capsules to take.

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

If you take more PROGRAF than you should:

If you have taken too much PROGRAF, your doctor will amend your next dose.

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 / missed a dose of PROGRAF:

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

Effects when treatment with PROGRAF is stopped:

Stopping your treatment with PROGRAF 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 PROGRAF, ask your doctor or pharmacist.

POSSIBLE SIDE-EFFECTS:

PROGRAF can have side effects.

Not all side effects reported for PROGRAF are included in this leaflet. Should your general health worsen while taking PROGRAF, please consult your doctor, pharmacist or other health care professional for advice.

PROGRAF reduces your body's own defence mechanism to stop you rejecting your transplanted organ. Cancerous and noncancerous tumours have been reported following PROGRAF treatment as a result of immunosuppression.

Severe effects have been reported, including allergic and anaphylactic reactions.

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 been reported.

Your body will not be as good as usual at fighting infections. So if you are taking PROGRAF you may therefore get more infections than usual such as infections of the skin, mouth, stomach and intestines, lungs, urinary tract, and tuberculosis.

Possible side effects are listed according to the following categories:

Frequent side effects:

- Increased blood sugar, diabetes mellitus, increased potassium in the blood (which manifests as nausea, tiredness, muscle weakness, tingling sensation)
- Increased blood pressure
- Abnormal liver function tests
- Kidney problems
- 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 (muscle weakness, confusion, decreased reflexes), fluid overload, increased uric acid or lipids in the blood, decreased appetite, increased acidity of the blood, other changes in the blood salts
- 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 (throat), cough, flu-like symptoms
- Stomach problems such as 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
- Bile duct disorders, 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 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
- Insufficient function of your transplanted organ
- Anxiety symptoms, confusion and disorientation, depression, mood changes, nightmare, hallucination, mental disorders
- Diarrhoea, nausea
- Trembling, headache
- Difficulty in sleeping

Less frequent side effects:

- Coma, bleeding in the brain, stroke, paralysis, brain disorder, speech and language abnormalities, memory problems
- Changes in blood clotting, reduction in the number of all types of blood cells
- Dehydration, inability to urinate
- Abnormal blood test results: reduced protein or sugar, increased phosphate, increase of the enzyme lactate dehydrogenase

- Clouding of the eye 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, QT prolonged
- 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
- Inflammation of the skin, burning sensation in the sunlight
- Joint disorders
- Painful menstruation and abnormal menstrual bleeding
- Multiple organ failure, flu-like illness, increased sensitivity to heat and cold, feeling of pressure on your chest, jittery or abnormal feeling, weight loss
- 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
- Muscular weakness
- Abnormal heart scan
- Liver failure
- Painful urination with blood in the urine

- Increase of fat tissue

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

STORING AND DISPOSING OF PROGRAF:

Store all medicines out of reach of children.

Store at or below 30 °C.

Protect from light.

Do not use PROGRAF after the expiry date which is stated on the carton after “Exp”. The expiry date refers to the last day of that month.

Store in the original package in order to protect from moisture.

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.

PRESENTATION OF PROGRAF:

Prograf 0,5mg/ Prograf 1 mg/ Prograf 5 mg:

Ten capsules per blister sheet.

Three, five or ten blister sheets with one desiccant sachet in one aluminium wrapper.

IDENTIFICATION OF PROGRAF:

Prograf 0,5 mg:

Hard gelatin capsules, red imprinted with “0.5 mg” on capsule cap and “[f]607” on capsule body. Capsule cap and capsule body light yellow and capsule content a white powder.

Prograf 1 mg:

Hard gelatin capsules, red imprinted with “1 mg” on capsule cap and “[f]617” on capsule body. Capsule cap and capsule body opaque white and capsule content a white powder.

Prograf 5 mg:

Hard gelatin capsules, white imprinted with “5 mg” on capsule cap and “[f]657” on capsule body. Capsule cap and capsule body opaque greyish-red and capsule content a white powder.

REGISTRATION NUMBERS

	South Africa:	**Namibia:**	**Botswana:**
Prograf 0,5 mg (Capsules):	A39/34/0647	10/34/0465	
Prograf 1 mg (Capsules):	32/34/0559	04/34/1668	BOT0701038
Prograf 5 mg (Capsules):	32/34/0560	04/34/1670	BOT0801181

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE REGISTRATION CERTIFICATE

Astellas Pharma (Pty) Ltd, 7 Mirage Road, Bedfordview, 2007, South Africa

DATE OF PUBLICATION:

Date of registration: 14 Aug 2009

Date of most recently revised patient information leaflet: 24 April 2020