Austell Pharmaceuticals (Pty) Ltd, 54/34/0447-9, TACROLIMUS 0,5 mg, 1 mg, 5 mg AUSTELL, Hard gelatin capsules

Proposed Patient Information Leaflet for Medicines for Human Use:

TACROLIMUS 0,5 mg, 1 mg, 5 mg AUSTELL

SCHEDULING STATUS: S4

TACROLIMUS 0,5 mg AUSTELL hard gelatin capsules

TACROLIMUS 1 mg AUSTELL hard gelatin capsules

TACROLIMUS 1 mg AUSTELL hard gelatin capsules

Tacrolimus

Contains Sugar:

Each 0,5 mg hard gelatin capsule contains 120,820 mg lactose monohydrate.

Each 1 mg hard gelatin capsule contains 120,320 mg lactose monohydrate.

Each 5 mg hard gelatin capsule contains 116,320 mg lactose monohydrate.

Read all of this leaflet carefully before you start taking TACROLIMUS AUSTELL

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- TACROLIMUS AUSTELL 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 is in this leaflet

1. What TACROLIMUS AUSTELL is and what it is used for

Each hard gelatin capsule contains the active ingredient tacrolimus.

Tacrolimus is an immunosuppressive medicine.

TACROLIMUS AUSTELL is used to control your body's immune response enabling your body to accept the transplanted organ. TACROLIMUS AUSTELL is often used in combination with other medicines that also suppress the immune system.

2. What you need to know before you take TACROLIMUS AUSTELL

Do not take TACROLIMUS AUSTELL:

- if you are hypersensitive (allergic) to tacrolimus or any other macrolide antibiotic (erythromycin, clarithromycin).
- if you are hypersensitive (allergic) to any of the other ingredients of TACROLIMUS AUSTELL (listed in section 6).
- If you are pregnant or breastfeeding.
- if you are taking oral contraceptives TACROLIMUS AUSTELL may alter the metabolism of oral contraceptives, other forms of contraception should be used.
- With live attenuated vaccines.
- With ciclosporin.
- With grapefruit juice.

Warnings and precautions

Special care should be taken with TACROLIMUS AUSTELL**:**

- You will need to take TACROLIMUS AUSTELL 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 AUSTELL 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 AUSTELL for you.
- Please avoid taking any herbal remedies, e.g. St. John's wort (*Hypericum perforatum*) or another herbal products as this may affect the effectiveness and the dose of TACROLIMUS AUSTELL 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 AUSTELL 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 AUSTELL 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 AUSTELL 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. See also Do not take TACROLIMUS AUSTELL.
- Patients treated with TACROLIMUS AUSTELL 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 TACROLIMUS AUSTELL

Always tell your health care provider if you are taking any other medicine. (This includes all complementary or traditional medicines.)

TACROLIMUS AUSTELL must not be taken with ciclosporin.

TACROLIMUS AUSTELL blood levels can be affected by other medicines you take, and blood levels of other medicines can be affected by taking TACROLIMUS AUSTELL which may require interruption, an increase or a decrease in TACROLIMUS AUSTELL 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. See also Do not take TACROLIMUS AUSTELL.
- 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 AUSTELL.

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 AUSTELL.

If you need to have any vaccinations, please inform your doctor beforehand. See also Do not take TACROLIMUS AUSTELL.

TACROLIMUS AUSTELL contains lactose

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

TACROLIMUS AUSTELL with food and drink

Take TACROLIMUS AUSTELL 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 TACROLIMUS AUSTELL, since it can affect its levels in your

blood.

Pregnancy and breastfeeding

You should not use TACROLIMUS AUSTELL 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 machines

TACROLIMUS AUSTELL may cause blurred vision, photophobia, eye disorders and headache, dizziness, seizures and tremor. If you are being treated with TACROLIMUS AUSTELL and you are affected by you should not drive a car or operate dangerous machines. This

effect may be made worse when you use TACROLIMUS AUSTELL with alcohol.

3. How to take TACROLIMUS AUSTELL

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

Always take TACROLIMUS AUSTELL exactly as your doctor or pharmacist has instructed you. Check with your doctor or pharmacist if you are not sure.

Method of administration

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. It is recommended that the oral daily dose be taken in two divided doses. 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.

Dose

Your doctor will determine your dose depending on your type of transplant and your weight.
TACROLIMUS AUSTELL is taken orally twice daily, usually in the morning and evening. You should generally take TACROLIMUS AUSTELL on an empty stomach or at least 1 hour before or 2 to 3 hours after the meal.

The hard gelatin capsules should be swallowed whole with a glass of water. Do not drink grapefruit juice while taking TACROLIMUS AUSTELL (see also Do not take TACROLIMUS AUSTELL). Do not swallow the desiccant contained in the foil wrapper.

Duration of administration

Your doctor will tell you how long your treatment with TACROLIMUS AUSTELL will last. If you have the impression that the effect of TACROLIMUS AUSTELL is too strong or too weak, tell your doctor or pharmacist.

If you take more TACROLIMUS AUSTELL than you should

You would have the symptoms including tremor, headache, nausea and vomiting, infections, urticaria, lethargy, increased blood urea nitrogen and elevated serum creatinine concentrations, and increase in alanine aminotransferase levels.

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

If you forget to take TACROLIMUS AUSTELL

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

Effects when treatment with TACROLIMUS AUSTELL is stopped:

Stopping your treatment with TACROLIMUS AUSTELL 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 TACROLIMUS AUSTELL, ask your doctor or pharmacist.

4. Possible side effects

TACROLIMUS AUSTELL can have side effects.

Not all side effects reported for TACROLIMUS AUSTELL are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking TACROLIMUS AUSTELL, please consult your health care provider for advice.

If any of the following happens, stop taking TACROLIMUS AUSTELL and tell your doctor immediately or go to the casualty department at your nearest hospital.

These are very serious side effects. If you have them, you may have had a serious reaction to TACROLIMUS AUSTELL. You may need urgent medical attention or hospitalisation.

These are all serious side effects. You may need urgent medical attention

Tell your doctor if you notice any of the following:

Austell Pharmaceuticals (Pty) Ltd, 54/34/0447-9, TACROLIMUS 0,5 mg, 1 mg, 5 mg AUSTELL, Hard gelatin capsules

Frequent side effects:

- opportunistic infections Viral, Bacterial, Fungal, Protozoal Infection. Generalised and localised infections can occur
- benign as well as malignant tumours have been reported
- anaemia, Leukopenia, Thrombocytopenia, Leukocytosis, Red blood cell analyses abnormal
- allergic and anaphylactoid reactions have been observed in patients receiving tacrolimus
- hyperglycaemic conditions, Diabetes mellitus, Hyperkalaemia Hypomagnesaemia, Hypophosphataemia, Hypokalaemia, Hypocalcaemia, Hyponatraemia, Fluid overload, Hyperuricaemia, Appetite decreased, Metabolic acidoses, Hyperlipidaemia, Hypercholesterolaemia, Hypertriglyceridaemia, Other electrolyte abnormalities
- Insomnia, Anxiety symptoms, Confusion and Disorientation, Depression, Depressed mood, Mood disorders and Disturbances, nightmare, hallucination, mental disorders
- Tremor, Headache, Seizures, Disturbances in consciousness, Paraesthesias and Dysaesthesias, Peripheral neuropathies, Dizziness, Writing impaired, nervous system disorders
- Blurred Vision, Photophobia, Eye disorders
- Tinnitus
- Ischaemic coronary artery disorders, Tachycardia
- Hypertension, Haemorrhage, Thrombembolic and ischaemic events, Peripheral vascular disorders, Vascular hypotensive disorders
- Dyspnoea, Parenchymal lung disorders, Pleural effusion, Pharyngitis, Cough, Nasal congestion and Inflammations
- Diarrhoea, Nausea, Gastrointestinal inflammatory conditions, Gastrointestinal ulceration and Perforation, Gastrointestinal Haemorrhages, Stomatitis and Ulceration, Ascites, Vomiting, Gastrointestinal and abdominal pains, Dyspeptic signs and Symptoms, Constipation, Flatulence, Bloating and Distension, Loose stools, Gastrointestinal signs and symptoms
- Cholestasis and Jaundice, Hepatocellular damage and Hepatitis, Cholangitis
- Pruritus, Rash, Alopecias, Acne, Sweating increased

- Arthralgia, Muscle spasms, Pain in extremity, Back pain
- Renal failure, Renal failure acute, Oliguria, Renal tubular necrosis, Nephropathy toxic, Urinary abnormalities, Bladder and urethral symptoms
- Asthenic conditions, Febrile disorders, Oedema, Pain and Discomfort, Body temperature perception disturbed
- Hepatic enzymes and Function abnormalities, Blood alkaline Phosphatase increased, Weight increased
- Primary graft dysfunction

Less frequent side effects:

- Coagulopathies, Abnormal Coagulation and Bleeding analyses, Pancytopenia, Neutropenia Thrombotic Thrombocytopenic Purpura, Hypoprothrombinaemia, Thrombotic microangiopathy
- Hirsutism
- Ventricular arrhythmias and Cardiac arrest, Heart failures, Cardiomyopathies, Ventricular hypertrophy, Supraventricular arrhythmias, Palpitations
- Dehydration, Hypoproteinaemia, Hyperphosphataemia, Hypoglycaemia
- Psychotic disorder
- Coma, Central nervous system haemorrhages and Cerebrovascular accidents, Paralysis and Paresis, Encephalopathy, Speech and language abnormalities, Amnesia, Hypertonia, Myasthenia
- Cataract, Blindness
- Hypoacusis, Deafness neurosensory, Hearing impaired
- Pericardial effusion, *Torsades de Pointes*
- Infarction, Venous thrombosis deep limb, Shock
- Respiratory failures, Respiratory tract disorders, Asthma, Acute respiratory distress syndrome
- Ileus paralytic, Acute and Chronic pancreatitis, Gastrooesophageal reflux disease, Impaired gastric emptying, Subileus, Pancreatic pseudocyst
- Hepatitic artery thrombosis, Venoocclusive liver disease, hepatic failure, Bile duct stenosis

- Dermatitis, Photosensitivity, Toxic epidermal necrolysis (Lyell's syndrome), Stevens Johnson syndrome
- Joint disorders, Mobility decreased
- Anuria, Haemolytic uraemic syndrome, Nephropathy, Cystitis haemorrhagic Dysmenorrhoea and Uterine bleeding
- Multi-organ failure, Influenza like illness, Temperature intolerance, Chest pressure sensation, Feeling jittery, Feeling abnormal, Thirst, Fall, Chest tightness, Ulcer, Fat tissue increased
- Amylase increased, ECG investigations abnormal, Heart rate and Pulse investigations abnormal, Weight decreased, Blood lactate Dehydrogenase increased, Echocardiogram abnormal, Electrocardiogram QT prolonged

Side effects with frequency unknown:

- Pure red cell aplasia, Agranulocytosis, Haemolytic anaemia
- Optic neuropathy

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

Reporting of side effects

If you get side effects, talk to your doctor or pharmacist or nurse. You can also report side effects to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of TACROLIMUS AUSTELL**.**

5. How to store TACROLIMUS AUSTELL

Store all medicines out of reach of children.

Store at or below 25 °C.

Do not remove blisters from carton until required for use.

Store in original packaging.

Austell Pharmaceuticals (Pty) Ltd, 54/34/0447-9, TACROLIMUS 0,5 mg, 1 mg, 5 mg AUSTELL, Hard gelatin capsules

There are no special storage instructions for TACROLIMUS AUSTELL.

Do not use after the expiry date stated on the carton.

Return all unused medicine to your pharmacist.

6. Contents of the pack and other information

What TACROLIMUS AUSTELL contains

The active substance is ~~t~~acrolimus.

TACROLIMUS 0,5 mg AUSTELL: Each hard gelatin capsule contains 0,5 mg tacrolimus.

TACROLIMUS 1 mg AUSTELL: Each hard gelatin capsule contains 1 mg tacrolimus.

TACROLIMUS 5 mg AUSTELL: Each hard gelatin capsule contains 5 mg tacrolimus.

Contains sugar (lactose monohydrate):

Each 0,5 mg hard gelatin capsule contains 120,820 mg lactose monohydrate.

Each 1 mg hard gelatin capsule contains 120,320 mg lactose monohydrate.

Each 5 mg hard gelatin capsule contains 116,320 mg lactose monohydrate.

The other ingredients are:

For capsule content: Hypromellose 6 cps, lactose anhydrous, croscarmellose and sodium magnesium stearate.

For Capsule shell: Iron oxide yellow (TACROLIMUS AUSTELL 0,5)n, Iron oxide red TACROLIMUS AUSTELL 5) and titanium dioxide.

What TACROLIMUS AUSTELL looks like and contents of the pack

TACROLIMUS 0,5 mg AUSTELL:

Light yellow hard gelatin capsules, size “4” imprinted with “TCR” on cap & “ABZ 0.5” on body containing white to off white granular powder.

Austell Pharmaceuticals (Pty) Ltd, 54/34/0447-9, TACROLIMUS 0,5 mg, 1 mg, 5 mg AUSTELL, Hard gelatin capsules

TACROLIMUS 1 mg AUSTELL:

White hard gelatin capsules, size “4” imprinted with “TCR” on cap & “ABZ 1” on body containing white to off white granular powder.

TACROLIMUS 5 mg AUSTELL:

Pink hard gelatin capsules, size “4” imprinted with “TCR” on cap & “ABZ 5” on body containing white to off white granular powder.

TACROLIMUS AUSTELL is packed in Alu/Alu blisters and packed into cardboard cartons in pack sizes of 30’s or 50’s.

Not all pack sizes may be marketed.

Holder of Certificate of Registration

Austell Pharmaceuticals (Pty) Ltd

1 Sherborne Road

Parktown

JOHANNESBURG

2193

South Africa

Tel: 0860287835

This leaflet was last revised in

Austell Pharmaceuticals (Pty) Ltd, 54/34/0447-9, TACROLIMUS 0,5 mg, 1 mg, 5 mg AUSTELL, Hard gelatin capsules

Registration Application number

TACROLIMUS 0,5 mg AUSTELL: 54/34/0447.444.

TACROLIMUS 1 mg AUSTELL: 54/34/0448.445.

TACROLIMUS 5 mg AUSTELL: 54/34/0449.446.

Access to the corresponding Professional Information

Professional Information for this medicine is available on the following URL: https://austell.co.za/product-info/

Austell Pharmaceuticals (Pty) Ltd

Tel: +27 11 611 1400 or +27 860 287 835