For the use of a Registered Medical Practitioner only

1. GENERIC NAME AND BRAND NAME
Tacrolimus Capsules I.P. 0.5mg
Rengraf™ 0.5

Tacrolimus Capsules I.P. 1mg
Rengraf™ 1

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:
Rengraf™ 0.5
Each hard gelatin capsule contains:
Tacrolimus I.P. 0.5 mg
Colours used in Capsule shell:
Tartrazine, Titanium Dioxide I.P.
Capsule Meets IP related substance Test B.

Rengraf™ 1
Each hard gelatin capsule contains:
Tacrolimus I.P. 1 mg
Colours used in Capsule shell:
Brilliant Blue FCF, Tartrazine, Titanium Dioxide I.P.
Capsule Meets IP related substance Test B.

3. DOSAGE FORM AND STRENGTH
Refer section 1 & 2

4. CLINICAL PARTICULARS
4.1 THERAPEUTIC INDICATIONINDICATION:
Indicated for:
1. Treatment of lupus nephritis (in a case where the effect of steroids is insufficient, or administration of steroids is difficult because of their adverse reactions).
2. Treatment for the prophylaxis of organ rejection in patients receiving allogeneic liver or kidney transplant.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION
Initial Oral Dosage Recommendations and Observed Whole Blood Trough Concentrations in Adults

Patient population	**Recommended Tacrolimus initial oral dosage (Daily dose should be administered as divided doses, every 12 hours**	**Observed Tacrolimus trough blood concentration**
Adult kidney transplant patient		
In combination with azathioprine	0.2 mg/kg/day	month 1-3: 7-20 ng/mL month 4-12: 5-15 ng/mL
In combination with MMF/IL-2 receptor antagonist [a]	0.1 mg/kg/day	month 1-12: 4-11 ng/mL

Adult liver transplant patients	0.10-0.15 mg/kg/day	month 1-12: 5-20 ng/mL
Adult heart transplant patients	0.075 mg/kg/day	month 1-3: 10-20 ng/mL month >4: 5-15 ng/mL
In a second smaller trial, the initial dose of tacrolimus was 0.15-0.2 mg/kg/day and observed tacrolimus concentrations were 6-16 ng/mL during month 1-3 and 5-12 ng/mL during month 4-12		

Initial Oral Dosage Recommendations and Observed Whole Blood Trough Concentrations in Children

Patient population	**Recommended Tacrolimus initial oral dosage (Daily dose should be administered as divided doses, every 12 hours**	**Observed tacrolimus trough blood concentration**
Pediatric liver transplant patients	0.15-0.20 mg/kg/day	Month 1-12: 5-20 ng/mL

4.3 CONTRAINDICATIONS

Known hypersensitivity to tacrolimus or to any excipients of product

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Lymphoma and Other Malignancies

Patients receiving tacrolimus are at increased risk of developing lymphomas and other malignancies, particularly of the skin. Posttransplant lymphoproliferative disorder (PTLD) has been reported in immunosuppressed organ transplant recipients. The risk of PTLD appears greatest in those individuals who are Epstein Barr Virus (EBV) seronegative, a population which includes many young children.

Serious infections: Increased risk of developing bacterial, viral, fungal, and protozoal infections, including opportunistic infections. Opportunistic infections, including polyoma virus infections.

Cytomegalovirus (CMV) Infections: Patients receiving immunosuppressants, are at increased risk of developing CMV viremia and CMV disease. For the patients who develop CMV viremia and/or CMV disease should reduce the amount of Tacrolimus.

New Onset Diabetes after Transplant: It has been reported to cause new onset of diabetes mellitus in patients of kidney, liver and heart transplant.

Nephrotoxicity: Dosage of Tacrolimus need to be monitored in the patients with impaired renal function and should be reduced when needed. Acute or chronic nephrotoxicity is observed when high dose of Tacrolimus is used. Chronic nephrotoxicity is associated with increased serum creatinine so patient with persistent increase in serum creatinine level should be considered and those who are unresponsive to dosage adjustments consideration should be given to changing to another immunosuppressive therapy. Care should be taken when administering tacrolimus with drugs that may be associated with renal dysfunction. These include, but are not limited to, protease inhibitors (e.g., ritonavir, indinavir), aminoglycosides, ganciclovir, amphotericin B, cisplatin, and nucleotide reverse transcriptase inhibitors (e.g., tenofovir). Similarly, when administering calcium channel blockers (e.g., diltiazem,

verapamil), CYP3A4 inhibitors such as antifungal drugs (e.g., ketoconazole), and macrolide antibiotics (e.g., clarithromycin, erythromycin, troleandomycin) which will result in elevated Tacrolimus whole blood concentrations due to inhibition of Tacrolimus metabolism.
Neurotoxicity: When Tacrolimus is used in high dose it cause spectrum of neurotoxicities which include coma, delirium and posterior reversible encephalopathy syndrome (PRES). Symptoms of PRES include seizures, visual disturbances headache, altered mental status, and hypertension. Immediate reduction of Tacrolimus is advised if PRES is suspected or diagnosed and should maintain the blood pressure. Less severe neurotoxicity includes paraesthesia, headache, tremors, and other changes in motor function, sensory function and mental status.

Pediatrics: Seizures have reported in adult and pediatric patients receiving Tacrolimus.

Hyperkalemia: With the use of Tacrolimus, hyperkalemia has been reported**.** Prior to use of other agents associated with hyperkalemia (e.g., ACE inhibitors, angiotensin receptor blockers potassium-sparing diuretics) careful consideration should be taken during Tacrolimus therapy.

Hypertension: Common adverse effect of Tacrolimus therapy is hypertension and antihypertensive therapy may be required. With any of the common antihypertensive agents, control of blood pressure can be accomplished, though careful consideration should be given prior to use of antihypertensive agents associated with hyperkalemia (e.g., potassium-sparing diuretics, ACE inhibitors, angiotensin receptor blockers). Tacrolimus blood concentration can increase with use of calcium-channel blocking agent so dosage of Tacrolimus should be reduced.

Use with CYP3A4 Inhibitors and Inducers: When strong CYP3A4-inhibitors (e.g., ritonavir, ketoconazole, itraconazole, voriconazole, clarithromycin telaprevir, boceprevir,) and strong inducers (e.g., rifampin, rifabutin) co-administering with tacrolimus, dose regime of Tacrolimus should be adjusted with subsequent frequent monitoring of tacrolimus blood concentration and associated adverse reaction.
Use with Sirolimus: In kidney transplant patients the safety and efficacy of tacrolimus with sirolimus has not been established.
Myocardial Hypertrophy: In infants, children, and adults, Myocardial hypertrophy has been reported with high tacrolimus trough concentrations and is manifested by echocardiographically demonstrated concentric elevation in left ventricular posterior wall and interventricular septum thickness. Dose should be reduced or discontinued if myocardial hypertrophy is diagnosed. While receiving tacrolimus therapy if patients who develop clinical manifestations of ventricular dysfunction or renal failure, echocardiographic evaluation should be considered.

Immunizations: During the treatment with tacrolimus avoid the use of live vaccines examples oral polio, BCG, yellow fever, varicella, intranasal influenza, measles, mumps, rubella, and TY21a typhoid vaccines.

Pure red blood cell aplasia: Patients treated with tacrolimus pure red blood cell aplasia (PRCA) has been reported. All patients reported risk factors for PRCA such as parvovirus B19 infection, underlying disease, or concomitant medications associated with PRCA. Tacrolimus dose should be discontinued when patient is diagnosed with PRCA.

Gastrointestinal Perforation: In patients treated with tacrolimus gastrointestinal perforation has been reported. All reported cases were considered to be accompanied by infection or

complication of transplant surgery or, diverticulum, or malignant neoplasm. Appropriate medical or surgical management should be instituted promptly if gastrointestinal perforation may be serious or life-threatening.

QT Prolongation: Tacrolimus may prolong QT/QTc interval and may cause Torsade de Pointes. Tacrolimus should to be avoided in patient with congenital long QT syndrome. During treatment with tacrolimus, patients with congestive heart failure, brady arrhythmias, and those taking certain antiarrhythmic medications or other medication that lead to QT prolongation, and those with electrolyte disturbances such as hypocalcemia, hypokalemia, or hypomagnesemia electrocardiograms and electrolytes monitoring should be considered. Frequent monitoring of tacrolimus whole blood concentrations and monitoring for QT prolongation is recommended, when co-administering tacrolimus with other substrates and/or inhibitors of CYP3A4 that have the potential to prolong the QT interval. It has been reported to result in elevated tacrolimus whole blood concentrations with or without concurrent QT prolongation when tacrolimus is used with amiodarone.

4.5 DRUG INTERACTIONS

No.	Drug	Drug Interaction	Remarks
1.	Mycophenolic Acid Products	With a given dose of mycophenolic acid (MPA) products, exposure to MPA is higher with tacrolimus co-administration than with cyclosporine co-administration because cyclosporine interrupts the enterohepatic recirculation of MPA while tacrolimus does not	Clinicians should be aware that there is also a potential for increased MPA exposure after crossover from cyclosporine to tacrolimus in patients concomitantly receiving MPA-containing products.
2.	Grapefruit Juice	Grapefruit juice inhibits CYP3A-enzymes which results in elevated tacrolimus whole blood trough concentrations.	patients should avoid eating grapefruit or drinking grapefruit juice with tacrolimus
3.	Protease Inhibitors	Tacrolimus whole blood concentrations are elevated as most of the protease inhibitors inhibit CYP3A enzymes. When protease inhibitors agents like telaprevir or boceprevir are co-administered with tacrolimus it markedly increases the blood concentration of tacrolimus.	Tacrolimus-associated adverse reactions and tacrolimus whole blood concentrations should be monitored and when tacrolimus and protease inhibitors (e.g., ritonavir, telaprevir, boceprevir) are used co-administered appropriate adjustments in the dosing regimen of tacrolimus are recommended
4.	Antifungal Agents	1. Antifungal agents like Azoles: posaconazole, fluconazole itraconazole,	Based on the tacrolimus whole blood concentrations, patients

		ketoconazole, Voriconazole, and clotrimazole inhibit CYP3A metabolism of tacrolimus and increase tacrolimus whole blood concentrations. 2. Caspofungin is an inducer of CYP3A and decreases whole blood concentrations of tacrolimus.	already receiving tacrolimus and when initiating therapy with voriconazole or posaconazole in, it is recommended that the tacrolimus dose be initially reduced to one-third of the original dose and the subsequent tacrolimus doses be adjusted
5.	Calcium Channel Blockers	Verapamil, nifedipine, diltiazem, and nicardipine inhibit CYP3A metabolism of tacrolimus and may elevate tacrolimus whole blood concentrations.	when these calcium channel blocking drugs and tacrolimus are used concomitantly, monitoring of whole blood concentrations and appropriate dosage adjustments of tacrolimus are recommended
6.	Antibacterials	Tacrolimus whole blood concentrations are elevated when Erythromycin, clarithromycin, troleandomycin and chloramphenicol inhibit CYP3A metabolism of tacrolimus.	When these drugs and tacrolimus are used co-administered, monitoring of blood concentrations and appropriate dosage adjustments of tacrolimus are recommended
7.	Antimycobacterials	Antimycobacterial agents like Rifampin and rifabutin are inducers of CYP3A enzymes and may reduce tacrolimus whole blood concentrations.	When these antimycobacterial drugs and tacrolimus are co-administered, monitoring of whole blood concentrations and appropriate dosage adjustments of tacrolimus are recommended.
8.	Anticonvulsants	Anticonvulsants agents like Phenobarbital, Phenytoin, and carbamazepine induce CYP3A enzymes and may decrease tacrolimus whole blood concentrations.	Phenytoin plasma concentrations can be increased when tacrolimus and phenytoin are used concomitantly therefore frequent monitoring of phenytoin is recommended and appropriate adjustment of phenytoin are needed.

9.	St. John's Wort (Hypericumperforatum)	Whole blood concentration of tacrolimus may reduce as St. John's Wort induces CYP3A enzymes	Whole blood concentration should be monitored, and appropriate dosage adjustments of tacrolimus are recommended when St. John's Wort and tacrolimus are co-administered.
1(	Gastric Acid Suppressors/Neutralizers	1.Lansoprazole and omeprazole, as CYP2C19 and CYP3A4 substrates, which may potentially inhibit the CYP3A4 metabolism of tacrolimus and there by tacrolimus whole blood concentrations is elevated, especially in transplant patients who are intermediate or poor CYP2C19 metabolizers, as compared to those patients who are efficient CYP2C19 metabolizers. 2. Whole blood concentrations of tacrolimus are substantially elevated as Cimetidine may also inhibit the CYP3A4 metabolism of tacrolimus. 3. Whole blood concentration of tacrolimus is increased when magnesium and aluminium hydroxide antacids are co-administered.	Appropriate dose adjustment and monitoring of whole blood concentration is recommended when these drugs and tacrolimus are used concomitantly.
1	Others	Bromocriptine, danazol, ethinylestradiol, amiodaronenefazodone, metoclopramide, and methylprednisolone may inhibit CYP3A metabolism of tacrolimus and increase tacrolimus whole blood concentrations	When these drugs are co-administered with tacrolimus proper monitoring of whole blood concentration and appropriate dose adjustment is recommended.
1	Cannabidiol	Drug interaction with cannabidiol may lead to increased concentrations& toxicity of calcineurin inhibitors like Tacrolimus &	Adopted by European Medicines Agency 23 November 2020 EMA/PRAC/570588/2020 Corr

		Cyclosporin and mTOR inhibitors like Everolimus & sirolimus.	Pharmacovigilance Risk Assessment Committee (PRAC)

4.6 USE IN SPECIAL POPULATIONS (SUCH AS PREGNANT WOMEN, LACTATING WOMEN, PAEDIATRIC PATIENTS, GERIATRIC PATIENTS ETC.)

Pregnancy: In clinical trial it was reported that tacrolimus crosses the placenta. There was no evidence of elevated adverse reaction on the course and outcome of pregnancy during the tacrolimus treatment when compared with other immunosuppressant. However, it was reported to have spontaneous absorption of tacrolimus. In pregnant women tacrolimus treatment can be considered when there is no safe alternative. New-born monitoring is recommended for potential adverse event of tacrolimus in case of in utero exposure. Premature delivery is one of the risk factor however, it was reported that majority of the new-borns had normal birth weight. Hyperkalaemia in the new-born was observed which, however, normalises spontaneously. In preclinical studies at doses which demonstrated maternal toxicity tacrolimus caused embryofoetal toxicity.

Breast-feeding: Tacrolimus is excreted in breast milk according to the clinical data. Women should not breast-feed during tacrolimus treatment detrimental effects on the new-born cannot be excluded.

Fertility: On male fertility a negative effect of tacrolimus was observed in the form of reduced sperm counts and motility as reported during preclinical studies.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Tacrolimus may cause visual and neurological disturbances. This association may be enhanced in case if it is administered along with alcohol. Patient should be advised to avoid alcohol consumption while on Tacrolimus. Additionally, patient should be informed to share any adverse events with their healthcare provider.

4.8 UNDESIRABLE EFFECTS

Nervous System: Haemorrhagic stroke, hallucinations, hypertonia, incoordination, abnormal dreams, agitation, amnesia, anxiety, confusion, thinking abnormal, convulsion, crying, depression, elevated mood, emotional lability, encephalopathy, nervousness, neuralgia, neuropathy like monoparesis, myoclonus, nerve compression, paralysis flaccid, psychomotor skills impaired, psychosis, quadriparesis, somnolence, vertigo, writing impaired

Special Senses

Ear pain, otitis media, abnormal vision, amblyopia, and tinnitus

Gastrointestinal

Oesophagitis ulcerative, oral moniliasis, Cholangitis, GOT increase, GI disorders cholestatic jaundice, duodenitis, dysphagia, esophagitis,flatulence, gastritis, gastroesophagitis, gastrointestinal hemorrhage, liver damage, pancreatic pseudocyst, rectal disorder, GI perforation, hepatitis, hepatitis granulomatous, ileus, increased appetite, jaundice, stomatitis

Cardiovascular

Congestive heart failure, abnormal ECG, heart rate decreased, hypotension, angina pectoris, cardiopulmonary failure, arrhythmia, atrial fibrillation, atrial flutter, bradycardia, cardiac fibrillation, peripheral vascular disorder, cardiovascular disorder, deep

thrombophlebitis, echocardiogram abnormal, electrocardiogram QRS complex abnormal, electrocardiogram ST segment abnormal, heart failure, hemorrhage, phlebitis, postural hypotension, syncope, tachycardia, thrombosis, vasodilatation

Urogenital
Urinary retention, toxic nephropathy hydronephrosis, hematuria, vaginitis, acute kidney failure albuminuria, BK nephropathy, bladder spasm, cystitis, kidney failure, kidney tubular necrosis, dysuria, nocturia, pyuria, urge incontinence, urinary frequency, urinary incontinence,

Metabolic/Nutritional
ALT (SGPT) increased, AST (SGOT) increased, lactic dehydrogenase increase, weight gain acidosis, alkaline phosphatase increased, alkalosis, hypocalcemia, bicarbonate decreased, bilirubinemia, dehydration, GGT increased, gout, hypercalcemia, hypercholesterolemia, hyperphosphatemia, healing abnormal, hyperuricemia, hypervolemia, hypoglycemia, hyponatremia, hypoproteinemia,

Endocrine
Cushing's syndrome

Hemic/Lymphatic
Leukocytosis, haemoglobin abnormal, coagulation disorder, ecchymosis, polycythemia vera, prothrombin decreased haematocrit increased, hypochromic anaemia, serum iron decreased

Miscellaneous
Generalized edema, flu syndrome, cellulitis, abdomen enlarged, photosensitivity reaction, abscess, peritonitis, accidental injury, allergic reaction, chills, fall, feeling abnormal, hernia, mobility decreased, sepsis, temperature intolerance, ulcer

Musculoskeletal
Generalized spasm, arthralgia, myalgia, myasthenia, cramps, joint disorder, leg cramps, osteoporosis

Respiratory
Rhinitis, sinusitis, asthma, emphysema, pneumonia, pneumothorax, hiccups, pulmonary edema, lung disorder, lung function decreased, pharyngitis, respiratory disorder, voice alteration

Skin
Acne, skin discoloration, skin disorder alopecia, hirsutism, exfoliative dermatitis, herpes zoster, fungal dermatitis, herpes simplex, neoplasm skin benign, , skin ulcer, sweating

4.9 OVERDOSE
It has been reported in acute overdosages of up to 30 times the intended dose. And in almost all cases have been asymptomatic and all patients recovered with no sequelae. Sometimes acute overdosage was followed by adverse reactions consistent which include abnormal renal function, tremors, hypertension, peripheral edema increases in blood urea nitrogen, serum alanine aminotransferase and creatinine levels. In some case of acute overdosage, transient urticaria and lethargy were reported.

Treatment
An acute overdose can be treated with the oral use of activated charcoal and/or gastric lavage, but experience has not been sufficient to warrant recommending its use. Tacrolimus is not dialyzable to any significant extent due to poor aqueous solubility and extensive erythrocyte and plasma protein binding. To tacrolimus therapy no specific antidote is available. General supportive measures and symptomatic treatment should be followed in all cases of over dosage. Haemofiltration or -diafiltration have been effective in reducing toxic concentrations in isolated patients with very high plasma levels.

5.0 PHARMACOLOGICAL PROPERTIES

5.1 MECHANISM OF ACTION

At the molecular level, the effects of tacrolimus appear to be mediated by binding to a cytosolic protein (FKBP12) which is responsible for the intracellular accumulation of the compound. The FKBP12-tacrolimus complex specifically and competitively binds to and inhibits calcineurin, leading to a calcium-dependent inhibition of T-cell signal transduction pathways, thereby preventing transcription of a discrete set of lymphokine genes.

5.2 PHARMACODYNAMIC PROPERTIES

Tacrolimus is reported to act via several ways with the central mechanism for its immunosuppressive action being inhibition of the activated threonine phosphatase, serine, calcineurin, in T-lymphocytes. Formations of cytotoxic lymphocytes are inhibited by tacrolimus which are mainly responsible for graft rejection. T-helper-cell dependent B-cell proliferation, T-cell activation, the expression of the interleukin-2 receptor and the formation of lymphokines (such as interleukins-2, -3, and γ-interferon) are suppressed by the drug tacrolimus. It has been reported tacrolimus have an ability to affect ventricular repolarisation. ECG monitoring on a routine basis during the initial post-transplant period are recommended.

5.3 PHARMACOKINETIC PROPERTIES

Parameters	Tacrolimus
Absorption	Rapid absorption of tacrolimus is found by gastrointestinal in particular in the jejunum and duodenum but bioavailability was low and variable. Various factor contributing to low and variable bioavailability are p-glycoprotein mediated efflux, extensive first pass metabolism and presence of food. Improved absorption is found during fasting and adsorption profile can be improved by the development of a once daily dose which reduce variability and is more convenient to the patients.
Distribution	The distribution of tacrolimus between whole blood and plasma depends on several factors, such as drug concentration, plasma protein concentration and hematocrit temperature at the time of plasma separation. In the preclinical studies, the major organ of distribution was found to be lung, adrenal gland and heart which showed 29 times the plasma concentration. Liver, kidney and gastrointestinal tract were other orangs for distribution. Over the first week tacrolimus accumulates quickly and increase becoming gradual by three week and after 4–5-week steady state is reached.
Protein Binding	The plasma protein binding of tacrolimus is approximately 99%. Tacrolimus is bound mainly to albumin and alpha-1-acid glycoprotein, and has a high level of association with erythrocytes.
Half-life	The half-life is long and variable of tacrolimus. The mean half-life in whole blood is approximately 43 hours as reported in clinical studies.

Metabolism	Cytochrome P-450 (CYP3A) enzymes in the small intestine and liver metabolize tacrolimus extensively. 8 possible metabolites can be formed by metabolic pathway. Primary mechanisms of biotransformation in vitro are demethylation and hydroxylation. 13-demethyl tacrolimus is the major metabolite identified in incubations with human liver microsomes. It has been reported that in in-vitro studies, a 31-demethyl metabolite has same activity as tacrolimus.
Excretion	Unchanged tacrolimus amount excreted was found to be less than 2% with biliary secretion and major route of elimination is faecal excretion (80-90%). Some results were obtained with repeated administration. After oral administration of tacrolimus at, it was found in milk at similar levels to those observed in the plasma eight hours post administration.

6.NONCLINICAL PROPERTIES

6.1 ANIMAL TOXICOLOGY OR PHARMACOLOGY

The kidneys and the pancreas were the primary organs affected in toxicity studies performed in rats and baboons. In rats, tacrolimus caused toxic effects to the nervous system and the eyes. Reversible cardiotoxic effects were observed in rabbits following intravenous administration of tacrolimus.

When tacrolimus is administered intravenously as rapid infusion/bolus injection at a dose of 0.1 to 1.0 mg/kg, QTc prolongation has been observed in some animal species. Peak blood concentrations achieved with these doses were above 150 ng/ml which is more than 6-fold higher than mean peak concentrations observed with Tacrolimus in clinical transplantation.

Embryofoetal toxicity was observed in rats and rabbits and was limited to doses that caused significant toxicity in maternal animals. In rats, female reproductive function including birth was impaired at toxic dosages and the offspring showed reduced birth weights, viability and growth.

A negative effect of tacrolimus on male fertility in the form of reduced sperm counts and motility was observed in rats.

7.DESCRIPTION

Rengarf™ 0.5 - RENGRAF is supplied for oral administration, as a hard gelatin capsule of Tacrolimus. Each hard gelatin capsule of RENGRAF contains Tacrolimus 0.5mg.

Rengarf™ 1 - RENGRAF is supplied for oral administration, as a hard gelatin capsule of Tacrolimus. Each hard gelatin capsule of RENGRAF contains Tacrolimus 1mg.

8.PHARMACEUTICAL PARTICULARS

8.1 INCOMPATIBILITIES

Not Applicable

8.2 SHELF-LIFE

Refer peck

8.3 PACKAGING INFORMATION

Refer peck

8.4 STORAGE CONDITION AND HANDING INSTRUCTIONS
Refer peck

9. PATIENT COUNSELLING INFORMATION

- Patient should be advised to take Tacrolimus at the same 12-hour intervals every day to achieve consistent blood concentrations.
- Patient should be advised to take Tacrolimus consistently either with or without food because the presence and composition of food decreases the bioavailability of Tacrolimus.
- Patient should be advised not to eat grapefruit or drink grapefruit juice in combination with Tacrolimus.
- Patients should be informed that they are at increased risk of developing a variety of infections, including opportunistic infections, due to immunosuppression and to contact their physician if they develop any symptoms of infection.
- Patients should be informed that Tacrolimus can cause diabetes mellitus and should be advised to contact their physician if they develop frequent urination, increased thirst or hunger.
- Patients should be instructed to inform their healthcare provider if they plan to become pregnant or breast-feed their infant.
- Patients should be informed that Tacrolimus can cause high blood pressure which may require treatment with anti-hypertensive therapy

10. DETAILS OF MANUFACTURER
Refer Pack for manufacturer details.

Marketed By:
Abbott Healthcare Pvt. Ltd.
Angel Space, Bldg. D-4, Gala No. 1 to 3 &
11 to 13 Ground Floor, 101 to 106 &
111 to 116 First Floor, 201 to 206 & 211 to 216
2nd Floor, Pimplas, Dist. Thane, Bhiwandi - 421 302,
Maharashtra, India.

11. DETAILS OF PERMISSION OR LICENCE NUMBER
Refer Pack for Permission/License details.

12. DATE OF REVISION
Version 5.0, Dated 04th June 2025

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