**Tacrolimus (oral, IV)** (ta-krö-li-mus)

**Drug Class**
Immunosuppressant

**Pregnancy Category** C

**Indications**
Prevention of organ rejection in patients who have undergone allogenic liver, kidney, or heart transplantation (used concurrently with corticosteroids).

**Action**
Inhibits T-lymphocyte activation.

**Pharmacokinetics**
Absorption following oral administration is erratic and incomplete (5-67%).

**Metabolism and Excretion:**
99% metabolized by the liver; 1% excreted unchanged in the urine.

**Distribution:**
Crosses the placenta and enters breast milk.

**Half-life:**
11.7 hr; 21.2 hr.

**Contraindications/Precautions**
- Hypersensitivity to tacrolimus or to castor oil (a component of the injection).
- Anticoagulants: Thrombocytopenia should be avoided.

**Use Cautiously in:**
Renal or hepatic impairment (dose may be required; if oliguria occurs, wait 48 hr before initiating tacrolimus). Concurrent use with cyclosporine should be avoided; Exposure to sunlight/V light (may risk of malignant skin changes).  

**Adverse Reactions/Side Effects**
- CNS: headache, dizziness, depression, hallucinations, psychoses, somnolence, seizures, tremor.
- CV: edema, hypertension, peripheral edema.
- Derm: rash, pruritus.
- Endo: acne, hirsutism, sweating, photosensitivity.
- GU: ascites, constipation, dysuria, hematuria, aphthous stomatitis.
- Hem: anemia, leukopenia, thrombocytopenia, purpura.
- HIV: weight gain, hyperglycemia, nausea, vomiting.
- Hemat: anemia, leukopenia, thrombocytopenia, purpura.
- Hypersensitivity: angioedema, rash, pruritus.
- Misc: allergic reactions including Stevens-Johnson syndrome, erythema multiforme, abnormal testicular growth.

**Interactions**
- Drug-Diet: Risk of nephrotoxicity is increased by concurrent use of amino-glycosides, amphotericin B, cyclosporine, or echinacea (allow 24 hr to pass after stopping cyclosporine before starting tacrolimus). Concentration of potassium-sparing diuretics, ACE inhibitors, or angiotensin II receptor antagonists may be less effective if given concurrently with tacrolimus (may increase risk of malignant skin changes).  

**Drug-Drug:**
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**Drug-Natural Products:**
- Risk of nephrotoxicity is increased by concurrent use of garlic, echinacea, or St. John's wort (allow 24 hr to pass after stopping garlic before starting tacrolimus). Concentration of potassium-sparing diuretics, ACE inhibitors, or angiotensin II receptor antagonists may be less effective if given concurrently with tacrolimus (may increase risk of malignant skin changes).

**Drug-Other Drugs:**
- Risk of nephrotoxicity is increased by concurrent use of aminoglycosides, amphotericin B, cyclosporine, or echinacea (allow 24 hr to pass after stopping cyclosporine before starting tacrolimus). Concentration of potassium-sparing diuretics, ACE inhibitors, or angiotensin II receptor antagonists may be less effective if given concurrently with tacrolimus (may increase risk of malignant skin changes).  

**Contraindications:**
Hypersensitivity to tacrolimus or to castor oil (a component of the injection).

**Precautions:**
- Use cautiously in patients who have undergone allogenic liver, kidney, or heart transplantation (used concurrently with corticosteroids).

**Route Onset Peak Duration**
- PO: Rapid 1.3–3.2 hr† 12 hr† 12 hr
- IV: Rapid unknown 8–12 hr

**Half-life:**
11.7 hr; 21.2 hr.

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**Genetic Implication**
CAPITALS indicate life-threatening, underlines indicate most frequent.
Drug-Food: Food decreases the rate and extent of GI absorption. Grapefruit juice decreases absorption.

Route/Dosage

Because of the potential risk for anaphylaxis, the IV route of administration of tacrolimus should be reserved for those patients unable to take the drug orally.

Kidney Transplantation

PO (Adults): Initial dose—0.2 mg/kg/day in 2 divided doses; titrate to achieve recommended blood concentration.

PO (Children): 0.15–0.15 mg/kg/day in 2 divided doses.

IV (Adults): Initial dose—0.05–0.1 mg/kg/day as a continuous infusion; titrate to achieve recommended blood concentration.

IV (Children): 0.05–0.15 mg/kg/day.

Liver Transplantation

PO (Adults): Initial dose—0.1–0.15 mg/kg/day in 2 divided doses; titrate to achieve recommended blood concentration.

PO (Children): Initial dose—0.15–0.2 mg/kg/day in 2 divided doses; titrate to achieve recommended blood concentration.

IV (Adults and Children): Same as for kidney transplant.

Heart Transplantation

PO (Adults): Initial dose—0.075 mg/kg/day in 2 divided doses; titrate to achieve recommended blood concentration.

IV (Adults): Initial dose—0.01 mg/kg/day as a continuous infusion; titrate to achieve recommended blood concentration.

NURSING IMPLICATIONS

Assessment

● Prevention of Organ Rejection: Monitor blood pressure closely during therapy. Hypertension is a common complication of tacrolimus therapy and should be treated.

● Observe patients receiving IV tacrolimus for the development of anaphylaxis (rash, pruritus, laryngeal edema, wheezing) for at least 30 min and frequently thereafter. If signs develop, stop infusion and institute treatment.

● Lab Test Considerations: Tacrolimus blood level monitoring may be helpful in the evaluation of rejection and toxicity, dose adjustments, and assessment of compliance. For liver transplantation, most patients are stable when tacrolimus trough whole blood concentrations are maintained between 5–20 ng/mL. For kidney transplantation, during the first 3 mo, most patients maintained tacrolimus whole blood trough levels between 5–15 ng/mL and then between 5–10 ng/mL. For heart transplantation, from wk 1 to 3 mo, most patients maintained tacrolimus trough whole blood concentrations between 8–20 ng/mL and then between 10–15 ng/mL post-transplant. Serum creatinine, potassium, and glucose were monitored and urine output noted in the transplant nursery. May also cause mild to dependent post-transplant diabetes melitus (incidence is higher in African American and Hispanic patients)

● May also cause hyperkalemia, hypocalcemia, hyperglycemia, hyperuricemia, metabolic alkalosis, metabolic acidosis, hyperphosphatemia, hyperglyceridemia, hyperphosphatemia, hypocalcemia, and hypomagnesemia.

● Monitor CBC. May cause anemia, leukocytosis, and thrombocytopenia.

Potential Nursing Diagnoses

Anxiety (Side Effects)

Implementation

● Do not confuse Prograf with Prozac.

● Therapy should be provided by clinicians and in facilities experienced in transplant management.

● Therapy with tacrolimus should be started no sooner than 6 hr post-transplantation. Concurrent therapy with corticosteroids is recommended in the early postoperative period.

● Tacrofile should be continued until at least 24 hr after starting the other.

● Tacrofile is preferred because of the risk of anaphylaxis reactions with IV tacrolimus. IV therapy should be replaced with oral therapy as soon as possible.

● Serum creatinine and glucose should be monitored closely.

● Tacrofile should be started at the lower end of the dose range. PO: Children require higher doses to maintain blood trough concentrations similar to adults.

● PO: Oral doses can be started 8–12 hr after discontinuation of IV doses. May be taken with or without food, but with or without food should be consistent, 12 hrs apart, at the same time each day.

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CONTINUOUS INFUSION:

- Dilute in 0.9% NaCl or D5W for a concentration of 0.004–0.02 mg/mL prior to use. May be stored in polyethylene or glass containers.
- Administer daily dose as a continuous infusion over 24 hr.

Y-SITE COMPATIBILITY:

- alemtuzumab, alfentanil, amifostine, amikacin, aminocaproic acid, aminophylline, amiodarone, amphotericin B colloidal, amphotericin B lipid complex, amphotericin B liposome, anidulafungin, argatroban, atracurium, azithromycin, aztreonam, benztropine, bivalirudin, bleomycin, bumetanide, buprenorphine, busulfan, butorphanol, calcium acetate, calcium chloride, calcium gluconate, carboplatin, carmustine, caspofungin, cefazolin, cefperazone, cefotaxime, cefotetan, cefoxitin, ceftazidime, ceftriaxone, cefuroxime, chloramphenicol, chlorpromazine, ciprofloxacin, cisatracurium, cisplatin, clindamycin, cyclophosphamide, cyclosporine, cytarabine, dactinomycin, daptomycin, dexmedetomidine, dexrazoxane, digoxin, diltiazem, diphenhydramine, dobutamine, docetaxel, dolasetron, dopamine, doripenem, doxacurium, doxorubicin, doxycycline, droperidol, enalaprilat, ephedrine, epinephrine, etoposide, etoposide phosphate, famotidine, fenoldopam, fentanyl, fluconazole, fludarabine, foscarnet, fosphenytoin, gemcitabine, gentamicin, glycopyrrolate, granisetron, haloperidol, heparin, hetastarch, hydralazine, hydrocortisone sodium succinate, hydromorphone, ibuprofen, indomethacin, impetigo, vitamin K, insulin, irinotecan, isoproterenol, ketorolac, leucovorin, levofloxacin, levorphanol, lidocaine, linezolid, lorazepam, magnesium sulfate, mannitol, mechlorethamine, meperidine, meropenem, mesna, metaraminol, methotrexate, methyldopate, methylprednisolone, metoclopramide, metoprolol, micronutrients, miconazole, mycophenolate, nalidixic acid, sodium thiosulfate, nafcillin, naloxone, neostigmine, necarbamyl, norepinephrine, nitroglycerin, nitroprusside, norepinephrine, nortriptyline, ondansetron, oxacillin, oxytocin, paclitaxel, palonosetron, pamidronate, pamcuronium, pemetrexed, penicillin G potassium, pentamidine, pentazocine, perphenazine, phentolamine, phenylpropanolamine, phenylalanine, piperacillin/tazobactam, potassium acetate, potassium chloride, potassium phosphates, procainamide, prochlorperazine, promethazine, propranolol, quinupristin/dalfopristin, ranitidine, remifentanil, ranolazine, sodium acetate, sodium bicarbonate, sodium phosphate, streptomycin, sucralfate, sulfa, suproxin sodium succinate, succinylcholine, sufenil, teniposide, theophylline, thiotepa, ticarcillin/clavulanate, tigecycline, ticlopidine, tobramycin, tolazoline, trimethoprim/sulfamethoxazole, vancomycin, vecuronium, verapamil, vinblastine, vincristine, vinorelbine, voriconazole, zidovudine, zolendronic acid.

Y-SITE INCOMPATIBILITY:

- acyclovir, allopurinol, azathioprine, caffeine, cephalosporin, ceftriaxone, chlorpromazine, cyclosporine, diazepam, diazoxide, esomeprazole, folic acid, ganciclovir, iron sucrose, levothyroxine, omeprazole, phenytoin, thiopental.

PATIENT/FAMILY TEACHING:

- Instruct patient to take tacrolimus at the same time each day, as directed. Do not skip or double up on missed doses. Do not discontinue medication without advice of health care professional. A follow-up is essential.
- Reinforce the need for lifelong therapy to prevent transplant rejection. Be aware of symptoms of rejection for transplanted organ and stress need to seek health care professional immediately if they occur.
- Advise patient to avoid grapefruit or grapefruit juice and eating raw oysters or other shellfish; make sure they are fully cooked before eating.
- Advise patient to wear protective clothing and sunscreen to avoid photosensitivity reactions.
- Instruct patient to avoid exposure to chickenpox, measles, mumps, and rubella. If exposed, see health care professional for prophylactic therapy.
- Inform patient of the risk of lymphoma with tacrolimus therapy.
- Emphasize the importance of repeated lab tests during tacrolimus therapy.

EVALUATION/DESIRABLE OUTCOMES:

- Prevention of transplant rejection.
- Prevention of transplant liver, kidney, or heart rejection.

WHY WAS THIS DRUG PRESCRIBED FOR YOUR PATIENT?