VENTURA COUNTY
HEALTH CARE PLAN

Prior Authorization DRUG Guidelines

PROGRAF (tacrolimus)

Effective Date: 10/20/14
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Last Approval Date: 1/26/16, 1/24/17, 4/20/17, 1/23/18, 1/22/19

(Archived 1/22/19)

Description: Tacrolimus is a macrolide derivative which inhibits T-lymphocyte activation. The exact mechanism of action is not known. Experimental evidence suggests that tacrolimus binds to an intracellular protein, FKBP-12. A complex of tacrolimus-FKBP-12, calcium, calmodulin, and calcineurin is then formed and the phosphatase activity of calcineurin inhibited. This effect may prevent the dephosphorylation and translocation of nuclear factor of activated T-cells (NF-AT), a nuclear component thought to initiate gene transcription for the formation of lymphokines (such as interleukin-2, gamma interferon). The net result is the inhibition of T-lymphocyte activation (i.e., immunosuppression).

Authorization Criteria: Prophylaxis of organ rejection in kidney, liver and heart transplants.

Unlabeled Use: Graft-versus-host disease, lung transplant.

NOTE: Per VCHCP policy, unlabeled uses are not covered unless specific information is submitted. See VCHCP Policy for Coverage of Prescription Medications for Off-Label Use.

Dosing: The initial postoperative dose of tacrolimus (immediate release) should begin no sooner than 6 hours after liver and heart transplant and within 24 hours of kidney transplant (but may be delayed until renal function has recovered).

Kidney 0.2 mg/kg/day as bid; **liver** 0.10-0.15 mg/kg/day as bid; **heart** 0.075 mg/kg/day as bid; **Continuous IV** (if oral not tolerated): **renal/liver** 0.03-0.05 mg/kg/day; **heart** 0.01 mg/kg/day

Note: sublingual dosing is an off label route of administration.

How Supplied: Capsule: 0.5, 1, 5 mg; IV: 5 mg (in 1 mL ampules)

Contraindications/Warnings: Adjust dosage in patients with renal or liver impairment; initiate therapy orally if possible, otherwise use a continuous IV infusion; initiate therapy no sooner than six hours after transplantation; avoid live vaccines

Major Adverse Reactions: Serious infections, lymphoma and skin cancer, Post-Transplant Lymphoproliferative Disorder (PTLD), Polyoma virus infections, CMV infections, new onset diabetes after transplant, nephrotoxicity, neurotoxicity (posterior reversible encephalopathy

syndrome (PRES), delirium, and coma), hyperkalemia, hypertension, anaphylaxis, Torsades de Pointes due to Q-T interval, pure red cell aplasia; hypertrophic cardiomyopathy (mostly pediatric); **Only physicians experienced in immunosuppressive therapy and management of organ transplant patients should use Prograf.**

Major Drug Interactions: When coadministering Prograf with strong CYP3A4-inhibitors (e.g., telaprevir, boceprevir, ritonavir, ketoconazole, itraconazole, voriconazole, clarithromycin) and strong inducers (e.g., rifampin, rifabutin) adjustments in the dosing regimen of Prograf and subsequent frequent monitoring of tacrolimus whole blood trough concentrations and tacrolimus-associated adverse reactions are recommended.

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Revision History:

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HEALTH CARE PLAN

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1/24/17	No	Catherine Sanders, MD; Robert Sterling, MD	Annual review
4/20/17	Yes	Catherine Sanders, MD; Robert Sterling, MD	Added lung transplant to unlabeled use; added information on dosing.
1/23/18	No	Catherine Sanders, MD; Robert Sterling, MD	Annual review
1/22/19	No	Catherine Sanders, MD; Robert Sterling, MD	Archived – check ESI