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Transplant Medications: Timing is Everything

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ptimal immunosuppression therapy is a cornerstone to successful transplantation and requires that patients take a complex, lifelong regimen of anti-rejection medications. Without these lifesaving medications, we would not be able to perform transplants.

The multidisciplinary team at UC San Diego Health, which includes our transplant pharmacists, works together to optimize medication regimens to improve the survival of patients and grafts. In the immediate post-transplant period, induction therapy is utilized. This involves the use of high dose and more intense immunosuppressive regimens, given over a short course. Medications used for induction include thymoglobulin, basiliximab and high-dose steroids. We also use some of these highintensity medications to treat acute-rejection episodes after transplant. Patients are transitioned to maintenance immunosuppression for long-term management, which usually includes three different anti-rejection medications. Careful balancing and close monitoring are necessary to avoid the potentially harmful side-effects of these powerful medications and to prevent rejection.

The medication regimens that patients take long-term to prevent rejection are referred to as maintenance therapy. It is tailored to the patient depending on how far out they are post-transplant, the transplant type, and whether they have had any post-transplant complications, including rejection or infection complications. Most

often, these regimens consist of a triple drug therapy comprised of a calcineurin inhibitor (tacrolimus or cyclosporine), an antiproliferative agent (mycophenolate or azathioprine) and a steroid (prednisone). In select patients, we add, or replace one of these medications with, an mTOR inhibitor (sirolimus or everolimus); however, these medications are not used in the early post-transplant phase as they are known to delay wound healing. Common side effects and special instructions or monitoring parameters for each of these medications are listed below in Table 1.

It is very important that patients take the right dose of the immunosuppressant medications at the right time. These medications have a narrow therapeutic index and large inter-patient variability, meaning that each patient requires a different dose to get the same effect of the medication. For these reasons, we check medication blood concentrations in all of our posttransplant patients. In the early post-transplant phase, we check a medication level each day. We target specific concentrations of the medications depending on the type of transplant and length of time post-transplant to achieve optimal outcomes and to prevent toxic side effects or rejection. Below are some tips for helping our team to optimize the administration and monitoring of transplant medications.



Ashley Feist, Pharm.D., BCPS graduated from University of Nebraska Medical Center in 2005 and competed her residency training at UC San Diego Health. Since completing her training, she has been working as a Pharmacist Specialist in Solid Organ Transplantation at UC San Diego Health focusing in heart and lung transplantation in the inpatient and clinic settings.



Tips for Transplant Medication Administration and Monitoring:

- Trough levels for tacrolimus, cyclosporine, sirolimus and everolimus should be drawn as a trough level between 0600-0630, prior to the morning dose. Please ensure the level has been collected prior to administering the morning dose.
- Do not draw a level from a line that is infusing or was ever used to infuse IV tacrolimus or cyclosporine.
- Occasionally, a lab draw to evaluate peak levels of tacrolimus or cyclosporine is ordered to help assess the absorption of these medications. Peak levels should be drawn 2 hours after the dose is administered.
- Tacrolimus and cyclosporine are dosed twice daily. Standardized administration times in the hospital are 0700 and 2000 so that it can be administered on an empty stomach (1 hour before meals or 2-3 hours after meals). Food can reduce the absorption by 30-50% and consistency of administration with or without food is very important.

	Name	Strength	Side Effects/Toxicity	Special Instructions
Calcineurin Inhibitors	Tacrolimus (Prograf) Tacrolimus Ext.	0.5 mg, 1 mg, 5 mg capsules	Headache and tremor Kidney dysfunction Increased blood sugar Nausea Increased BP and cholesterol High Potassium Hair loss	 Take twice a day, on empty stomach (1hr before eating or 2-3 hrs after eating) Avoid grapefruit and pomegranate
	Release (Envarsus XR)	and 4mg tablets		
	Cyclosporine (Gengraf, Neoral)	25 mg, 100 mg capsules	Kidney dysfunction Increased BP and cholesterol High potassium Increased hair growth Increased growth of gum tissues Increased blood sugar Tremor and headache	 Take twice a day, on empty stomach (1hr before eating or 2- 3 hrs after eating) Avoid grapefruit and pomegranate
Antimetabolite Agents	Mycophenolate Mofetil (Cellcept)	250 mg capsule 500 mg tablet	Diarrhea Nausea/vomiting Decreased WBC	Best taken on empty stomach (If can tolerate) Separate dosing time of calcium, magnesium, zinc, iron-containing products (including antacids) Teratogenic – women of childbearing age must be counseled and use approved contraception
	Mycophenolic Acid (Myfortic)	180 mg, 360 mg tablets		
	Azathioprine (Imuran)	50 mg tablet	Decreased WBC Nausea/vomiting Elevated liver function tests	
mTOR Inhibitors	Sirolimus (Rapamune)	0.5 mg, 1 mg, 2 mg tablets	Delayed wound healing Increased cholesterol Decreased WBC & platelets Anemia Edema Mouth ulcers Skin rash	Must separate dosing time from cyclosporine by 4 hours
	Everolimus (Zortress)	0.25 mg, 0.5 mg, 0.75 mg, and 1 mg tablets		
Steroids	Prednisone	5 mg, 10mg, 20 mg, 50 mg tablet	Increased appetite Thin skin/bruise easily/acne Restlessness/insomnia Elevated blood sugar Slow wound healing Moon face/fat deposits Mood swings Increased blood pressure Osteoporosis	Take with food to prevent upset stomach