

Tacrolimus – renal transplant

	Recommendations		Notes/Evidence																	
Initiation	Post-operative day 1		<ul style="list-style-type: none"> Initiation of tacrolimus should start before or at the time of transplant, rather than delayed until the onset of graft function (UW Health, Very Low, Conditional) 																	
Dosing (initial)	Decreased sensitivity (African-American, >80kg)	0.1 mg/kg/day (use ABW), by mouth divided in 2 doses twice daily, rounded to nearest capsule size	<ul style="list-style-type: none"> Capsules and suspension may be taken with or without food. Since the presence of food affects the bioavailability of tacrolimus, if taken with food, it should be taken consistently the same way each time. (UW Health, Very Low, Conditional) 																	
	Increased sensitivity (NPO, <80kg)	Fixed dose 2 mg by mouth twice daily																		
Drug-drug Interactions (not an all-inclusive list)	<p>Increases tacrolimus concentration *Check Lexicomp for dose adjustments* <u>Adjust tacrolimus dose empirically:</u></p> <ul style="list-style-type: none"> Fluconazole Posaconazole Voriconazole Ritonavir Letermovir <p><u>Monitor tacrolimus levels and adjust as needed:</u></p> <ul style="list-style-type: none"> Clarithromycin Erythromycin 	<p>Decreases tacrolimus concentration *Check Lexicomp for dose adjustments* <u>Monitor tacrolimus levels and adjust as needed:</u></p> <ul style="list-style-type: none"> Rifampin Phenytoin Carbamazepine Phenobarbital 	<ul style="list-style-type: none"> Tacrolimus may be given sublingually in patients unable to adequately absorb enteral formulations or in those unable to take oral. If a patient is being transitioned to tacrolimus sublingual from tacrolimus IR, each dose should be divided by 2 and given sublingually. (UW Health, Very Low, Conditional) Use of IV tacrolimus is reasonable for patients unable to adequately absorb enteral formulations, and conversion from IV to oral tacrolimus is recommended as soon as enteral therapy can be tolerated to minimize risk of anaphylactic reactions that occur with injectables containing castor oil derivatives. (UW Health, Very Low, Conditional) Tacrolimus ER may be utilized in patients with documented intolerable adverse effects with tacrolimus IR or who are unable to obtain a therapeutic drug concentration with the IR formulation. If a patient is being transitioned to tacrolimus ER (Envarsus®) from tacrolimus IR, the total daily dose should be multiplied by 0.8, then rounded to the nearest capsule size. (UW Health, Very Low, Conditional) 																	
Target levels	Concurrent use of mycophenolate +/- prednisone	<p><u>Laboratory Monitoring:</u> Tacrolimus (trough), potassium, and creatinine Inpatient: Daily Post-Discharge:</p> <table border="1"> <thead> <tr> <th>Day</th> <th>Frequency</th> </tr> </thead> <tbody> <tr> <td>0-90</td> <td>Not less than weekly</td> </tr> <tr> <td>91-180</td> <td>Not less than twice monthly</td> </tr> <tr> <td>181-2 years</td> <td>Not less than once monthly</td> </tr> <tr> <td>>2 years</td> <td>Not less than quarterly</td> </tr> </tbody> </table> <p>As Needed:</p> <ul style="list-style-type: none"> Change in medication formulation, patient status, or creatinine increase ≥ 0.3 mg/dL above baseline 3 to 7 days (ideally 4 days) following dose adjustment 	Day	Frequency	0-90	Not less than weekly	91-180	Not less than twice monthly	181-2 years	Not less than once monthly	>2 years	Not less than quarterly								
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Adverse effects	Acute kidney injury	<ul style="list-style-type: none"> Assess tacrolimus trough level for correlation with elevated creatinine If trough level is above goal and creatinine has increased ≥ 0.3 mg/dL above baseline: <ul style="list-style-type: none"> Decrease tacrolimus dose if trough is <4 ng/mL above goal Hold tacrolimus if trough ≥ 5 ng/mL above goal and consider increasing current prednisone dose
	Neurological symptoms (tremor, headache)	<ul style="list-style-type: none"> Assess tacrolimus trough level for correlation with tremors or headache If trough level is above goal, adjust tacrolimus dose and follow up with patient if trough level within target range, no dose adjustment is recommended, follow-up with patient in 1 week If adverse effects are intolerable or interacting with daily activities and there is no other known cause of symptom: <ul style="list-style-type: none"> Consult the transplant physician to consider converting the patient to tacrolimus ER, belatacept, cyclosporine, or refer to primary care provider for supportive therapy, such as addition of low dose beta blocker (propranolol)
	New onset diabetes after transplantation (NODAT) <i>Diagnosis</i> <ul style="list-style-type: none"> Sx of DM + casual PG concentrations ≥ 200 mg/dL FPG ≥ 126 mg/dL 2-hr PG ≥ 200 mg/dL during an oral glucose tolerance test 	<ul style="list-style-type: none"> No tacrolimus dose adjustment is recommended Consider consulting diabetes management & nutrition services Diagnosis of new onset diabetes after transplant (NODAT) is defined by the World Health Organization (WHO) and American Diabetes Association (ADA) that develops for the first time after transplantation If there is no improvement in glucose control 6 months after transplant (NODAT requiring insulin OR A1c $>7\%$ with glucose lowering agent) and there have been 3 months of minimal glucocorticoid doses <ul style="list-style-type: none"> Consult transplant physician and consider converting the patient to cyclosporine

Cyclosporine – renal transplant

	Recommendations		Notes/Evidence																				
Initiation	Post-operative day 1		<ul style="list-style-type: none"> The initiation of cyclosporine should start before or at the time of transplantation, rather than delayed until the onset of graft function (UW Health, Very Low, Conditional) 																				
Dosing (initial)	Decreased sensitivity (African-American, >80kg)	Fixed dose 150 mg by mouth twice daily	<ul style="list-style-type: none"> Neoral/Gengraf (cyclosporine modified) and Sandimmune (cyclosporine non-modified) are not bioequivalent and cannot be used interchangeably (UW Health, Very Low, Conditional) Capsules and suspension may be taken with or without food. However, since the presence of food affects the bioavailability of cyclosporine, if taken with food, it should be taken consistently the same way each time. (UW Health, Very Low, Conditional) 																				
	Increased sensitivity (NPO, <80kg)	Fixed dose 100 mg by mouth twice daily																					
Drug-Drug Interactions (not an all-inclusive list)	<p>Increases cyclosporine concentration *Check Lexicomp for dose adjustments* <u>Adjust cyclosporine dose empirically:</u></p> <ul style="list-style-type: none"> Fluconazole Posaconazole Voriconazole Ritonavir Letermovir <p><u>Monitor cyclosporine levels and adjust as needed:</u></p> <ul style="list-style-type: none"> Clarithromycin Erythromycin 	<p>Decreases cyclosporine concentration *Check Lexicomp for dose adjustments* <u>Monitor cyclosporine levels and adjust as needed:</u></p> <ul style="list-style-type: none"> Rifampin Phenytoin Carbamazepine Phenobarbital 																					
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Belatacept – renal transplant

	Recommendation		Notes/Evidence
Dosing	Induction dosing (starting post-transplant or converting from CNI <6 months from transplant)	Day 0, day 4: 10 mg/kg/dose Ends of weeks 2, 4, 8, 12: 10 mg/kg/dose 5 mg/kg/dose every 4 weeks (± 3 days) starting at week 16	<ul style="list-style-type: none"> Indicated for use in patients who are EBV seropositive as a replacement for CNIs or to allow for CNI minimization (UW Health, Very Low, Conditional) EBV serostatus should be evaluated prior to initiation of belatacept (UW Health, Very Low, Strong)
	Conversion dosing w/ CNI taper (converting from CNI to belatacept >6 months from transplant)	Initial phase: - Day 0: 5 mg/kg/dose - End of weeks 2, 4, 6, and 8: 5 mg/kg/dose Maintenance phase: - 5 mg/kg/dose every 4 weeks (± 3 days) starting end of week 12 CNI taper: - 100% of previous dose on days 1-14 - 50% of previous dose on days 15-28 - 25% of previous dose on days 29-41 - Discontinue CNI on day 42	
	Conversion dosing with no CNI taper (converting from CNI to belatacept >6 months from transplant)	Initial phase: - Day 0: 10 mg/kg/dose - End of weeks 2, 4, 6, and 8: 10 mg/kg/dose Maintenance phase: - 5 mg/kg/dose every 4 weeks (± 3 days) starting end of week 12	
Labs	<u>Laboratory Monitoring:</u> Prior to initiation: EBV serostatus		
Adverse effects	Post-transplant lymphoproliferative disorder (PTLD)	<ul style="list-style-type: none"> Consult transplant provider if concerns for PTLN (weight loss, fatigue, unexplained anemia/thrombocytopenia/leukopenia, hypercalcemia) 	

Mycophenolate – renal transplant

		Recommendation	Notes/Evidence
Initiation	Post-operative day 1		<ul style="list-style-type: none"> Full dose mycophenolic acid is the preferred anti-proliferative medication used for renal transplant patients (UW Health, Very Low, Conditional) IV mycophenolate mofetil is indicated if the patient has an acute condition that affects gastrointestinal absorption (i.e., GI bleed or obstruction, malabsorption syndromes, severe diarrhea or severe vomiting) (UW Health, Very Low, Conditional) Mycophenolate mofetil suspension is utilized for patients receiving medications via nasogastric or orogastric tube
Dosing (initial)	Mycophenolate sodium (Myfortic)	720 mg by mouth twice daily	
	Mycophenolate mofetil (Cellcept)	1000 mg by mouth twice daily	
Drug-drug interactions (not an all-inclusive list)	Decreases mycophenolate concentration *Check Lexicomp for dose adjustments* <ul style="list-style-type: none"> Cyclosporine 		
Target levels			<ul style="list-style-type: none"> MPA AUC is a better predictor of clinical events than MPA trough. Trough levels are poorly correlated with AUC and are not recommended (UW Health, Very Low, Conditional)
Labs		Goal MPA Trough	
	CsA based regimens:	1.3-2.8 mg/L	
	TAC based regimens:	1.9-2.8 mg/L	
	Laboratory Monitoring: <ul style="list-style-type: none"> Lab monitoring of MPA levels is not recommended to assess for toxicity or efficacy If levels are requested, they are only appropriate for mycophenolate mofetil and should be drawn as a trough 		
Adverse effects	Diarrhea If a patient has ≥50% increase in their frequency of daily bowel movements for ≥ 5-7 days <ul style="list-style-type: none"> 0-3 months post-transplant: <ul style="list-style-type: none"> C. difficile, C. difficile toxin B PCR CMV PCR ≥3 months post-transplant: <ul style="list-style-type: none"> CMV PCR Complete blood count Clostridium difficile toxin B PCR Cryptosporidium Giardia PCR Norovirus PCR Rotavirus AG Stool culture, with E. Coli (Shiga) toxin Stool O&P (parasitology, isospora, cyclospora, pinworm) Consider colonoscopy if diarrhea persists and all stool studies are negative 		<ul style="list-style-type: none"> If diarrhea work-up is negative for an infectious cause of diarrhea and it is affecting activities of daily living or the patient is having limited and/or decreased oral intake: <ul style="list-style-type: none"> Decrease mycophenolate by 25% and increase dosing frequency (ex. 720 mg BID → 360 mg TID) <ul style="list-style-type: none"> If fails, decrease mycophenolate by 50% Follow up with patient in 1 week If dose is decreased to 180 mg twice daily (MYF) or 250 mg twice daily (MMF) consult provider to determine if other immunosuppression needs to be adjusted Consider adding the following: <ul style="list-style-type: none"> Add loperamide (Imodium®) 2 mg as needed after each loose stool (max dose: 16 mg daily) Diphenoxylate/atropine (Lomotil®) 5 mg four times daily as needed (max dose: 20 mg/day) Psyllium fiber (Metamucil®) 3.4 g daily as needed
	Heartburn/nausea		<ul style="list-style-type: none"> Counsel patient on taking MYF or MMF with food if not already doing so Convert from MMF to MYF if only upper GI complaints (heartburn, nausea) Add calcium carbonate as needed, or the addition of an H2RA or PPI if not already on If symptoms continue following 1 week of daily therapy increase H2RA or PPI dose to twice daily, reassess in 1 week If symptoms persist for ≥1 week, consider EGD to rule out infection vs. ulceration

Azathioprine – renal transplant

	Recommendation	Notes/Evidence
Initiation	Failure to tolerate mycophenolate	
Dosing (initial)	1-2 mg/kg by mouth daily	<ul style="list-style-type: none"> • Azathioprine is recommended for use in patients unable to tolerate adverse effects of mycophenolate (UW Health, Very Low, Conditional) • Azathioprine is considered to be less effective than MPA in preventing rejection. Prior to initiating azathioprine, consider the total immunosuppression for the patient and timing out from transplant
Drug-drug interactions (not an all-inclusive list)	<p>Increases azathioprine concentration: *Check Lexicomp for dose adjustments*</p> <p><u>Avoid concurrent use:</u></p> <ul style="list-style-type: none"> • Febuxostat <p><u>Adjust azathioprine dose empirically:</u></p> <ul style="list-style-type: none"> • Allopurinol 	
Labs	<p><u>Laboratory Monitoring:</u></p> <ul style="list-style-type: none"> • There is no recommended azathioprine level for monitoring purposes. However, if toxicity is suspected, check thiopurine methyltransferase (TPMT) 	
Adverse effects	Leukopenia	<ul style="list-style-type: none"> • Consult transplant provider if WBC <3 • See diarrhea work-up algorithm
	<p>Gastrointestinal</p> <p>If a patient has ≥50% increase in their frequency of daily bowel movements for ≥ 5-7 days</p> <ul style="list-style-type: none"> • 0-3 months post-transplant: <ul style="list-style-type: none"> ○ C. difficile, C. difficile toxin B PCR ○ CMV PCR • ≥3 months post-transplant: <ul style="list-style-type: none"> ○ CMV PCR ○ Complete blood count ○ Clostridium difficile toxin B PCR ○ Cryptosporidium ○ Giardia PCR ○ Norovirus PCR ○ Rotavirus AG ○ Stool culture, with E. Coli (Shiga) toxin ○ Stool O&P (parasitology, isospora, cyclospora, pinworm) <p>Consider colonoscopy if diarrhea persists and all stool studies are negative</p>	

Sirolimus/everolimus – renal transplant

	Recommendations		Notes/Evidence
Initiation	For use in patients with: <ul style="list-style-type: none"> CNI toxicity Skin cancer Quadruple therapy		<ul style="list-style-type: none"> Sirolimus/everolimus may impair or delay wound healing, and should be used with caution in the peri-surgical period (UW Health, Very Low, Conditional) Indicated for use in patients with recurrent skin cancers as a replacement for azathioprine, MPA, or CNIs (UW Health, Very Low, Conditional)
Dosing (initial)	Sirolimus	6 mg load on day 1, followed by 2 mg by mouth once daily	
	Everolimus	0.75 mg by mouth twice daily	
Drug-drug interactions (not an all-inclusive list)	Increase mTOR concentration (not an all-inclusive list): *Check Lexicomp for dose adjustments* <u>Avoid concurrent use:</u> <ul style="list-style-type: none"> Posaconazole Voriconazole Ritonavir <u>Monitor mTOR levels and adjust as needed:</u> <ul style="list-style-type: none"> Fluconazole Ritonavir Letermovir Clarithromycin Erythromycin 	Decrease mTOR concentration (not an all-inclusive list) *Check Lexicomp for dose adjustments* <u>Monitor mTOR levels and adjust as needed:</u> <ul style="list-style-type: none"> Rifampin Phenytoin Carbamazepine Phenobarbital 	
Target levels		Goal Trough Levels (SIRO/EVR+TAC)	Goal Sirolimus Level (SIRO/EVR+MPA)
Dose Adjustments	0-3 months:	TAC: 5-7 ng/mL SIRO/EVR: 4-7 ng/mL	SIRO/EVR: 8-10 ng/mL
Labs	3-6 months:	TAC: 5-7 ng/mL SIRO/EVR: 4-7 ng/mL	SIRO/EVR: 8-10 ng/mL
	6-12 months:	TAC: 3-5 ng/mL SIRO/EVR: 3-5 ng/mL	SIRO/EVR: 5-8 ng/mL
	>12 months:	TAC: 3-5 ng/mL SIRO/EVR: 3-5 ng/mL	SIRO/EVR: 5-8 ng/mL
	<u>Laboratory Monitoring:</u> <ul style="list-style-type: none"> Recommended once weekly upon initiation and with any dose changes When the target trough level has been attained, recommend monitoring levels once monthly 		

Adverse effects	Proteinuria	<ul style="list-style-type: none"> • Monitor at 6 months and then annually post-transplant per standard lab monitoring • Consider administration of angiotensin-converting enzyme (ACE)-inhibitors and angiotensin II receptor antagonists and reducing mTOR levels
	Mouth ulcers	<ul style="list-style-type: none"> • Development of mouth ulcers also seems to be dose-related, because they usually appear after the loading dose and often improve after a dose reduction • Addition of a high-potency topical steroid may be considered
	Hyperlipidemia	<ul style="list-style-type: none"> • Monitor cholesterol and lipids • If hyperlipidemia occurs, follow current guidelines for management (diet, exercise, lipid lowering agents) • Immunosuppressive strategies minimizing doses of mTORs, CNIs, or corticosteroids may help in controlling hyperlipidemia
	Thrombocytopenia	<ul style="list-style-type: none"> • Consider dose reduction or temporary drug suspension if appropriate



Prednisone – renal transplant

	Recommendations			Notes/Evidence	
Initiation	Post-operative day 4 following dexamethasone taper			<ul style="list-style-type: none"> Prednisone 30 mg once daily will be started on POD 4 following dexamethasone taper and may be continued on discharge 	
Dosing (initial)	Standard steroid taper <ul style="list-style-type: none"> Prednisone taper should occur following POD4 Factors that may influence the duration of prednisone taper: <ul style="list-style-type: none"> Current and historical CNI levels Current MPA dose Current renal function Episodes of rejection 	Dexamethasone	100 mg	POD0	<ul style="list-style-type: none"> Steroid withdrawal can be considered for patients who receive alemtuzumab for induction (UW Health, Very Low, Conditional) Rapid steroid taper can be considered for patients who receive alemtuzumab or thymoglobulin for induction (UW Health, Very Low, Conditional) Prednisone doses should be split to twice daily dosing for patients requiring insulin for glucose control (UW Health, Very Low, Conditional)
			50 mg	POD1	
		Dexamethasone or Prednisone	18 mg (dex) or 90 mg (pred)	POD2	
	12 mg (dex) or 60 mg (pred)	POD3			
Prednisone	30 mg	POD4			
	Discharge on 30 mg and decrease dose by 5 mg each week to a target dose of 10 mg daily				
Rapid steroid taper	Dexamethasone	100 mg	POD0		
		50 mg	POD1		
	Dexamethasone or Prednisone	18 mg (dex) or 90 mg (pred)	POD2		
	12 mg (dex) or 60 mg (pred)	POD3			
Prednisone	30 mg	POD4			
	10 mg	POD5			
	Discharge on 10 mg and consider reduction to 5 mg at week 3 to target dose of 5 mg daily				
Early steroid withdrawal	Dexamethasone	100 mg	POD0		
		50 mg	POD1		
	Dexamethasone or Prednisone	18 mg (dex) or 90 mg (pred)	POD2		
		12 mg (dex) or 60 mg (pred)	POD3		
	Prednisone	30 mg	POD4		
	Steroid withdrawal on POD5				
Labs	<u>Laboratory Monitoring:</u> Glucose, bone mineral density				
Adverse effects	Hyperglycemia	<ul style="list-style-type: none"> Prednisone doses should be split to twice daily dosing for patients requiring insulin for glucose control 			
	Heartburn/reflux	<ul style="list-style-type: none"> Start a proton pump inhibitor (PPI) at time of transplant If a patient complains of heartburn on daily dosing of the PPI, frequency may be increased to twice daily (pending renal function) Discontinue PPI in patients with no history of heartburn/gastroesophageal reflux disease (GERD) prior to transplant if prednisone is discontinued 			
	Osteoporosis	<ul style="list-style-type: none"> Recommend calcium 2000 mg daily (based on elemental calcium dosing) Recommend vitamin D 2000 units daily For patients that are on an early steroid withdrawal maintenance immunosuppression regimen, calcium and vitamin D supplementation are not required 			