Abdominal Transplant Immunosuppression Management – Adult– Inpatient/Ambulatory Clinical Practice Guideline

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Pharmacy and Therapeutics Committee: June, 2014
Lab Practice Committee: July, 2014

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Executive Summary

Guideline Overview
This document is intended to guide the use of immunosuppressive agents in both the inpatient and outpatient setting for abdominal transplant patients. Medications used for stress ulcer prophylaxis and supplementation are also addressed.

Immunosuppressive agents in this guideline include:

1. Azathioprine (Imuran®)
2. Belatacept (Nulojix®)
3. Cyclosporine (Neoral®, Gengraf®)
4. Dexamethasone
5. Everolimus (Zortress®)
6. Mycophenolic acid (Myfortic®, Cellcept®)
7. Prednisone
8. Sirolimus (Rapamune®)
9. Tacrolimus (Prograf®, Hecoria®)

Target Population
Adult inpatient and outpatient kidney, pancreas and liver transplant recipients. Patients enrolled in investigational studies and patients with delayed graft function are not included.

Practice Recommendations
Immunosuppression should be patient and organ specific, incorporating multiple factors to determine the optimal regimen.

Companion Documents
1. Desensitization, induction and rejection for kidney recipients based on DSA

Pertinent UW Health Policies & Procedures
1. Multidisciplinary Patient Care- Abdominal

Patient Resources:
1. Transplant medication class handout
Scope

Disease/Condition(s):
Adult kidney, pancreas, and liver transplant recipients

Clinical Specialty:
Transplant, Nephrology, Hepatology

Intended Users:
Physicians, Physician Assistants, Nurse Practitioners, Nurses, Pharmacists

CPG objective(s):
To provide recommendations for managing maintenance immunosuppression in an inpatient and outpatient setting.

Target Population:
Adult kidney, pancreas, and liver transplant recipients

Interventions and Practices Considered:
This guideline recommends immunosuppression management for abdominal transplant patients in order to help standardize care in both the inpatient and outpatient settings. It also incorporates stress ulcer prophylaxis, and recommendations for the use of supplements post-transplant.

Major Outcomes Considered:
Rejection, toxicity, graft survival, patient survival, and graft function

Guideline Metrics:
Rates of rejection, graft survival, patient survival, and graft function

Methodology

Description of Methods Used to Collect/Select the Evidence:
1. Searches of electronic databases (e.g., national and international guidelines for immunosuppression management)
2. Hand-searches of Published Literature (Primary Sources)
3. Hand-searches of Published Literature (Secondary Sources)

Methods Used to Assess the Quality and Strength of the Evidence:
Weighing according to rating scheme (scheme given below).

Rating Scheme for the Strength of the Evidence:
A modified Grading of Recommendations Assessment, Development and Evaluation (GRADE) developed by the American Heart Association and American College of Cardiology (Figure 1) have been used to assess the Quality and Strength of the Evidence in this Clinical Practice Guideline.

Figure 1: Quality of Evidence and Strength of Recommendation Grading Matrix*

Description of the Methods Used to Analyze the Evidence:
Systemic Reviews
Expert Opinion

Description of Methods Used to Formulate the Recommendations:
A review of current literature, survey of provider preferences, and trends from current practice were all incorporated into the formulation of recommendations.
Rating Scheme for the Strength of the Recommendations:
See the “Rating Scheme for the Strength of Evidence”

Cost Analysis:
Not Applicable

Introduction
Maintenance immunosuppression regimens vary based on patient specific factors, provider preference, and institutional policies and guidelines. This document is intended to guide the use of maintenance immunosuppressive agents in both the inpatient and outpatient setting for abdominal transplant patients. Induction immunosuppression regimens, medications used for guler prophylaxis, medications to prevent thrombosis, and vitamins and supplements are also addressed.

Agents for maintenance immunosuppression:
1. Calcineurin Inhibitors (CNI)
   a. Tacrolimus (Prograf®, Hecoria®)
   b. Cyclosporine (Neoral®, Gengraf®)
2. Anti-Proliferatives
   a. Mycophenolic acid (Myfortic®, Cellcept®)
   b. Azathioprine (Imuran®)
3. Corticosteroids
   a. Prednisone
4. Mammalian Target of Rapamycin (mTOR) Inhibitors
   a. Sirolimus (Rapamune®)
   b. Everolimus (Zortress®)
5. Costimulation Blocker
   a. Belatacept (Nulojix®)

Recommendations
Renal transplant immunosuppression:
1. Induction therapy, utilizing a combination of immunosuppressive medications, is recommended to start before, or at the time of kidney transplantation. (Desensitization, induction and rejection for kidney recipients based on DSA) (Class I, Level of Evidence A)
2. Maintenance immunosuppression consists of a combination of immunosuppressive medications which may include a CNI or costimulation blocker (belatacept) and anti-proliferative agent with or without corticosteroids (Class I, Level of Evidence A)
3. The preferred maintenance regimen consists of tacrolimus or belatacept and mycophenolic acid, with or without prednisone (Class I, Level of Evidence A)
4. Recipients from living HLA-matched (HLA-identical) donors are not continued on steroid maintenance immunosuppression (Class I, Level of Evidence A)
5. Recipients that receive alemtuzumab induction therapy are not continued on steroid maintenance immunosuppression (Class I, Level of Evidence A)
6. Maintenance medications used for immunosuppression include the following:

a. Tacrolimus (Class IIa, Level of Evidence C)
   i. Tacrolimus is the preferred CNI for use in renal transplant patients
   ii. Initiate tacrolimus on POD 1 for all patients with a target discharge tacrolimus level of 8 ng/mL by POD 5
   iii. If a patient received thymoglobulin, initiation may be delayed if renal function has not shown significant improvement (<30% decline in serum creatinine from POD 1 to POD2)¹
   iv. There is no evidence that delaying the initiation of tacrolimus results in decreased duration of delayed graft function
   v. Intravenous tacrolimus is not indicated for use
   vi. Tacrolimus should be administered with food
   vii. Initial tacrolimus dosing:
       1. If patient receives basiliximab induction:
          a. Tacrolimus: 0.05 mg/kg/day (in two divided doses)
             for max MFI <500
          b. Tacrolimus 0.1 mg/kg/day (in two divided doses)
             for max MFI >500 in two divided doses
       2. If patient receives anti-thymocyte globulin induction:
          a. Tacrolimus dosing should be tailored based on potential sensitivity to tacrolimus and goal tacrolimus level
          b. If a patient meets any of the criteria for decreased sensitivity to tacrolimus (Table 1), the initial dose will be 2 mg twice daily
          c. All other patients will be initiated on 1 mg twice daily

<table>
<thead>
<tr>
<th>Increased Tacrolimus Sensitivity</th>
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</tr>
</thead>
<tbody>
<tr>
<td>NPO</td>
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<td>Weight &gt;80 kg</td>
</tr>
<tr>
<td>Significant drug interactions</td>
<td>African-American</td>
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</table>

3. Target trough levels should be utilized for all subsequent dose adjustments using the goals found below
   a. These goals are based on concurrent use of tacrolimus with mycophenolate

<table>
<thead>
<tr>
<th>Table 2. Goal Tacrolimus (FK) Levels</th>
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<tbody>
<tr>
<td>Goal FK Level</td>
</tr>
<tr>
<td>0-3 months: 8-11 ng/mL</td>
</tr>
<tr>
<td>3-6 months: 7-9 ng/mL</td>
</tr>
<tr>
<td>6-12 months: 6-8 ng/mL</td>
</tr>
<tr>
<td>&gt;12 months: 5-7 ng/mL</td>
</tr>
</tbody>
</table>
4. Dose adjustments:
   a. Dose adjustments will occur after a patient has received 4 doses of the current regimen.
   b. Below goal:
      i. If a patient is >50% below their target goal, the daily dose will be increased by 25-50%
      ii. If a patient is <50% below their target goal, the daily dose will be increased by 25%.
   c. Above goal:
      i. If a patient is >50% above their target goal, the daily dose will be decreased by 25-50%
      ii. If a patient is <50% above their target goal, the daily dose will be decreased by 25%.
      iii. May consider holding tacrolimus to facilitate decrease in trough concentration.

viii. Laboratory Monitoring:
  1. Tacrolimus levels will be ordered daily while inpatient and patient is receiving daily tacrolimus doses (either post-operatively or during readmission)
  2. Once discharged, tacrolimus levels will be monitored at the following frequency:
     a. Day 0-90: not less than once weekly
     b. Day 91-180: not less than twice monthly
     c. Day 181-240: not less than one time monthly
  3. Additional monitoring of tacrolimus trough levels is warranted if there is a change in medication formulation or patient status that may affect levels or if the creatinine has increased 0.3 mg/dL above baseline
  4. Check level in 3-7 days following dose adjustment
  5. Check potassium and creatinine with each tacrolimus level
  6. A minimum of 2 levels should be within the goal range before resuming the previous monitoring frequency

ix. Adverse effects due to tacrolimus:
  1. Acute kidney injury:
     a. Inpatient Management:
        i. Assess tacrolimus trough level for correlation with elevated creatinine
        ii. If trough level is above goal and creatinine has increased 0.3 mg/dL above baseline, hold tacrolimus
        iii. While tacrolimus is held, double current prednisone dose
     b. Outpatient Management:
i. Assess tacrolimus trough level for correlation with elevated creatinine

ii. If trough level is above goal and creatinine has increased 0.3 mg/dL above baseline, adjust tacrolimus dose as follows:
   1. If a patient is >50% above their target goal, the daily dose will be decreased by 25-50%
   2. If a patient is <50% above their target goal, the daily dose will be decreased by 25%.
   3. May consider holding tacrolimus to facilitate decrease in trough concentration.

2. Neurological symptoms (tremor, headache)
   a. Assess tacrolimus trough level for correlation with tremors or headache
   b. If trough level is above goal, adjust tacrolimus dose and follow up with patient after the subsequent tacrolimus lab draw
   c. No dose adjustment is recommended if trough level within target range
      i. Follow up with patient in 1 week if no dose adjustment is made
   d. If adverse effects are intolerable or interacting with daily activities and there is no other known cause of symptoms, consult the transplant physician and consider converting the patient to cyclosporine or refer to primary care provider for supportive therapy

3. Hyperglycemia
   a. No dose adjustment is recommended
   b. Consider diabetes management & nutrition services for patient
   c. 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 kidney transplantation
   d. 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:
i. Consult transplant physician and consider converting the patient to cyclosporine\textsuperscript{2,3}

b. Cyclosporine (Neoral): (Class IIa, Level of Evidence C)
   i. Cyclosporine will be initiated post-transplant in patients who were previously intolerant of tacrolimus or were on cyclosporine prior to transplant
   ii. Initiate cyclosporine on POD 1
   iii. If a patient received thymoglobulin, initiation may be delayed if renal function has not shown significant improvement (<30\% decline in serum creatinine from POD 1 to POD\textsuperscript{2}1)
   iv. Initial dosing recommendation of 100-150 mg twice daily
      1. Cyclosporine dosing should be tailored based on potential sensitivity to cyclosporine and goal cyclosporine level
      2. If a patient meets any of the criteria for decreased sensitivity to cyclosporine (Table 1), the initial dose will be 150 mg twice daily
      3. All other patients will be initiated on 100 mg twice daily

Table 3. Factors for Identifying Cyclosporine Sensitive Patients\textsuperscript{2}

<table>
<thead>
<tr>
<th>Increased Cyclosporine Sensitivity</th>
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</tr>
</tbody>
</table>

4. Target trough levels should be utilized for all subsequent dose adjustments using the goals below:

Table 4. Goal Cyclosporine (CSA) Levels

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Goal CSA Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-3 months:</td>
<td>200-300 ng/mL</td>
</tr>
<tr>
<td>3-6 months:</td>
<td>150-250 ng/mL</td>
</tr>
<tr>
<td>6-12 months:</td>
<td>100-200 ng/mL</td>
</tr>
<tr>
<td>&gt;12 months:</td>
<td>50-100 ng/mL</td>
</tr>
</tbody>
</table>

5. Dose adjustments:
   a. Dose adjustments will occur after a patient has received 4 doses of the current regimen
   b. Below goal:
      i. If a patient is >50\% below their target goal, the daily dose will be increased by 25-50\%
      ii. If a patient is <50\% below their target goal, the daily dose will be increased by 25%.
   c. Above goal:
i. If a patient is >50% above their target goal, the daily dose will be decreased by 25-50%
ii. If a patient is <50% above their target goal, the daily dose will be decreased by 25%.
iii. May consider holding tacrolimus to facilitate decrease in trough concentration.

v. Laboratory monitoring:
1. Cyclosporine levels will be ordered daily while inpatient and receiving daily cyclosporine doses (either post-operatively or during readmission)
2. Once discharged, cyclosporine levels will be monitored at the following frequency:
   a. Day 0-90: not less than once weekly
   b. Day 91-180: not less than twice monthly
   c. Day 181-240: not less than one time monthly
3. Check level in 5-7 days following dose adjustment
4. Check potassium and creatinine with each cyclosporine level
5. A minimum of 2 levels should be within the goal range before resuming the previous monitoring frequency

vi. Adverse effects:
1. Management of adverse effects for cyclosporine is the same as the management of adverse effects for tacrolimus

c. Mycophenolic Acid (MPA): (Class IIa, Level of Evidence C)
   i. Mycophenolic acid is the preferred anti-proliferative medication used for renal transplant patients
   ii. Initiate mycophenolate sodium 720 mg PO twice daily on POD 1
      1. Equivalent mycophenolate mofetil dosing: 1000 mg PO twice daily
      2. African-American patients may be initiated on 720 mg PO three times daily
   iii. IV mycophenolate mofetil is indicated if the patient has an acute condition that affects gastrointestinal absorption (i.e., gastrointestinal bleed or obstruction, malabsorption syndromes, severe diarrhea or severe vomiting)
   iv. Mycophenolate mofetil suspension is utilized for patients receiving medications via nasogastric or orogastric tube
   v. Laboratory monitoring of mycophenolic acid levels is not recommended to assess for toxicity or efficacy
   vi. Adverse effects:
      1. Diarrhea:
a. If a patient has $\geq 50\%$ increase in their frequency of daily bowel movements for $\geq 5$-7 days
   i. 0-3 months post-transplant:
      1. Check *Clostridium difficile*, *Clostridium difficile* toxin B PCR
   ii. CMV PCR
   iii. $\geq 3$ months post-transplant, obtain the following studies:
      1. CMV PCR
      2. Complete blood count
      3. *Clostridium difficile* Clostridium difficile toxin B PCR
      4. *Cryptosporidium*
      5. Giardia PCR
      6. Norovirus PCR
      7. Rotavirus AG
      8. Stool culture, with E. Coli (Shiga) toxin
      9. Stool O&P (ova & parasite studies including: parasitology, isospora, cyclospora, pinworm) – do not order for inpatients who have been in house for $>48$-$72$ hours
   iv. If the above studies are 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:
      1. Decrease mycophenolate by 50% to a minimum dose of 180 mg twice daily or 250 mg twice daily
      2. Follow up with patient in 1 week
      3. 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
      4. Add loperamide 2 mg as needed after each loose stool (max dose: 16 mg daily) or diphenoxylate/atropine (Lomotil®) 5 mg four times daily as needed (max dose: 20 mg/day)

2. Heartburn/nausea:
   a. Counsel patient on taking MYF or MMF with food if not already doing so
b. Convert from MMF to MYF if only upper GI complaints (heartburn, nausea)
c. Add calcium carbonate as needed, or the addition of an H2RA or PPI if not already on
d. If symptoms continue following 1 week of daily therapy increase H2RA or PPI dose to twice daily, reassess in 1 week
e. If symptoms persist for ≥1 week, consider EGD to rule out infection vs. ulceration

d. **Prednisone:** (Class IIa, Level of Evidence C)
   i. Prednisone 30 mg daily will be started on POD 4 following dexamethasone and prednisone taper and will continue on discharge for patients that receive thymoglobulin or basiliximab for induction
   ii. Patients that receive alemtuzumab for induction should finish a steroid taper on POD 4 and not continue on prednisone for maintenance immunosuppression
   iii. Prednisone doses should be split to twice daily dosing for patients requiring insulin for glucose control
   iv. Assessment for prednisone taper should occur at 2 week post-operative clinic visit
      1. Factors that may influence the ability to taper prednisone at that time include:
         a. Current and historical tacrolimus/cyclosporine levels
         b. Current MPA dose
         c. Current renal function
         d. Episodes of rejection
   v. If deemed appropriate for a prednisone taper at that time, patients should decrease prednisone doses from 30 mg daily by 5 mg per week to a maintenance dose of 5 mg daily (if tacrolimus levels are within goal and the patient is on full dose mycophenolate)

e. **Azathioprine:** (Class I, Level of Evidence A)
   i. Indicated for use in patients unable to tolerate adverse effects of MPA
   ii. Dosing:
      1. 1-3 mg/kg/day as a single daily dose
   iii. There is no recommended azathioprine level for monitoring purposes.
   iv. Recommend either discontinuation of allopurinol if azathioprine is initiated or decreasing the allopurinol dose by 1/3 (33%) or 1/4 (25%).
v. Recommend discontinuation of febuxostat if azathioprine is initiated.
vi. If allopurinol or febuxostat is continued, close hematological monitoring is warranted.

f. Sirolimus/Everolimus: (Class IIa, Level of Evidence C)
i. Indicated for use in patients as a replacement for azathioprine, MPA or CNIs
ii. Dosing:
   1. Sirolimus: 2 mg PO one time daily
   2. Everolimus: 0.75 mg twice daily
iii. Subsequent doses should be adjusted based on trough levels
iv. Consult managing provider to determine dosing plan

<table>
<thead>
<tr>
<th></th>
<th>Goal Trough Levels (SIRO/EVR+FK)</th>
<th>Goal Sirolimus Level (SIRO/EVR+MPA)</th>
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<tbody>
<tr>
<td>0-3 months:</td>
<td>FK: 5-7 ng/mL SIRO/EVR: 4-7 ng/mL</td>
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v. Laboratory monitoring:
   1. Recommended one time weekly upon initiation and with any dose changes
   2. When the target trough level has been attained, it is recommended to monitor levels one time monthly

g. Belatacept (Class I, Level of Evidence A)
i. Indicated for use in patients who are EBV seropositive as a replacement for CNIs in combination with basiliximab induction, mycophenolate and corticosteroids
ii. Dosing:
   1. Initial phase:
      a. Day 1/POD 0: 10 mg/kg/dose
      b. Day 5: 10 mg/kg/dose
      c. End of week 2, 4, 8, 12: 10 mg/kg/dose
   2. Maintenance phase:
      a. 5 mg/kg/dose every 4 weeks (±3 days)
Pancreas transplant maintenance immunosuppression:

1. Induction therapy, utilizing a combination of immunosuppressive medications, is recommended to start before, or at the time of pancreas transplant alone (PTA), pancreas after kidney transplant (PAK) or simultaneous kidney pancreas (SPK) transplant. (Desensitization, induction and rejection for kidney recipients based on DSA) (Class IIa, Level of Evidence C)

2. Maintenance immunosuppression consists of a combination of immunosuppressive medications which may include a CNI and anti-proliferative agent with or without corticosteroids. (Class IIa, Level of Evidence C)

3. The preferred maintenance regimen consists of tacrolimus and mycophenolic acid, with or without prednisone (Class IIa, Level of Evidence C)

4. Recipients that receive alemtuzumab induction therapy are not continued on steroid maintenance immunosuppression. (Class IIa, Level of Evidence C)

5. Maintenance medications used for immunosuppression include the following:

   a. Tacrolimus: (Class IIa, Level of Evidence C)
      i. Tacrolimus is the preferred CNI for use in pancreas transplant alone, pancreas after kidney and simultaneous kidney pancreas transplants.
      ii. Initiate tacrolimus on POD 1 for all patients.
      iii. If a patient received thymoglobulin induction, tacrolimus initiation may be delayed if renal function has not shown significant improvement in SPK transplants (<30% decline in creatinine from POD 1 to POD2).  
      iv. There is no evidence that delaying the initiation of tacrolimus results in decreased duration of delayed graft function.
      v. Intravenous tacrolimus is not indicated for use.
      vi. Tacrolimus should be administered with food.
      vii. Initial tacrolimus dosing:
         1. If patient receives basiliximab induction:
            a. Tacrolimus: 0.05 mg/kg/day (in two divided doses) for max MFI <500
            b. Tacrolimus 0.1 mg/kg/day (in two divided doses) for max MFI >500 in two divided doses.
         2. If patient receives anti-thymocyte globulin induction:
            a. Tacrolimus dosing should be tailored based on potential sensitivity to tacrolimus and goal tacrolimus level
            b. If a patient meets any of the criteria for decreased sensitivity to tacrolimus (Table 1), the initial dose will be 2 mg twice daily
c. All other patients will be initiated on 1 mg twice daily

Table 6. Factors for Identifying Tacrolimus Sensitive Patients

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2. Target trough levels should be utilized for all subsequent dose adjustments using the goals found below
   a. These goals are based on concurrent use of tacrolimus with mycophenolate

Table 7. Goal Tacrolimus (FK) Levels (SPK, PTA, PAK)

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3. Dose adjustments:
   a. Dose adjustments will occur after a patient has received 4 doses of the current regimen
   b. Below goal:
      i. If a patient is >50% below their target goal, the daily dose will be increased by 25-50%
      ii. If a patient is <50% below their target goal, the daily dose will be increased by 25%.
   c. Above goal:
      i. If a patient is >50% above their target goal, the daily dose will be decreased by 25-50%
      ii. If a patient is <50% above their target goal, the daily dose will be decreased by 25%.
      iii. May consider holding tacrolimus to facilitate decrease in trough concentration.

i. Laboratory Monitoring:
   1. Tacrolimus levels will be ordered daily while inpatient and patient is receiving daily tacrolimus doses (either post-operatively or during readmission)
   2. Once discharged, tacrolimus levels will be monitored at the following frequency:
a. Day 0-90: not less than once weekly
b. Day 91-180: not less than twice monthly
c. Day 181-240: not less than one time monthly
3. Additional monitoring of tacrolimus trough levels is warranted if there is a change in medication formulation or patient status that may affect levels or if the creatinine has increased 0.3 mg/dL above baseline
4. Check level in 3-7 days following dose adjustment
5. Check potassium and creatinine with each tacrolimus level
6. A minimum of 2 levels should be within the goal range before resuming the previous monitoring frequency

ii. Adverse effects due to tacrolimus:
1. Acute kidney injury:
   a. Inpatient Management:
      i. Assess tacrolimus trough level for correlation with elevated creatinine
      ii. If trough level is above goal and creatinine has increased 0.3 mg/dL above baseline, hold tacrolimus
      iii. While tacrolimus is held, double current prednisone dose
   b. Outpatient Management:
      i. Assess tacrolimus trough level for correlation with elevated creatinine
      ii. If trough level is above goal and creatinine has increased 0.3 mg/dL above baseline, adjust tacrolimus dose as follows:
         1. If a patient is >50% above their target goal, the daily dose will be decreased by 25-50%
         2. If a patient is <50% above their target goal, the daily dose will be decreased by 25%.
         3. May consider holding tacrolimus to facilitate decrease in trough concentration.

2. Neurological symptoms (tremor, headache)
   a. Assess tacrolimus trough level for correlation with tremors or headache
   b. If trough level is above goal, adjust tacrolimus dose and follow up with patient after the subsequent tacrolimus lab draw
c. No dose adjustment is recommended if trough level within target range
   i. Follow up with patient in 1 week if no dose adjustment is made
d. If adverse effects are intolerable or interacting with daily activities and there is no other known cause of symptoms, consult the transplant physician and consider converting the patient to cyclosporine or refer to primary care provider for supportive therapy

3. Hyperglycemia
   a. No dose adjustment is recommended
   b. Consider diabetes management & nutrition services for patient
   c. 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 kidney transplantation
   d. 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:
      i. Consult transplant physician and consider converting the patient to cyclosporine

**d. Cyclosporine (Neoral):** (Class IIa, Level of Evidence C)
   i. Cyclosporine will be initiated post-transplant in patients who were previously intolerant of tacrolimus or were on cyclosporine prior to transplant
   ii. Initiate cyclosporine on POD 1
   iii. If a patient received thymoglobulin, initiation may be delayed if renal function has not shown significant improvement (<30% decline in serum creatinine from POD 1 to POD2)
   iv. Initial dosing recommendation of 100-150 mg twice daily
      1. Cyclosporine dosing should be tailored based on potential sensitivity to cyclosporine and goal cyclosporine level
      2. If a patient meets any of the criteria for decreased sensitivity to cyclosporine (Table 8), the initial dose will be 150 mg twice daily
      3. All other patients will be initiated on 100 mg twice daily
Table 8. Factors for Identifying Cyclosporine Sensitive Patients

<table>
<thead>
<tr>
<th>Increased Cyclosporine Sensitivity</th>
<th>Decreased Cyclosporine Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>NPO</td>
<td>General Diet</td>
</tr>
<tr>
<td>Weight &lt; 80 kg</td>
<td>Weight &gt; 80 kg</td>
</tr>
<tr>
<td>Significant drug interactions</td>
<td>African-American</td>
</tr>
</tbody>
</table>

Table 9. Goal Cyclosporine (CSA) Levels (SPK, PAK, PTA)

<table>
<thead>
<tr>
<th>Goal CSA Level</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>0-3 months:</td>
<td>200-300 ng/mL</td>
</tr>
<tr>
<td>3-6 months:</td>
<td>150-250 ng/mL</td>
</tr>
<tr>
<td>6-12 months:</td>
<td>100-200 ng/mL</td>
</tr>
<tr>
<td>&gt;12 months:</td>
<td>100-200 ng/mL</td>
</tr>
</tbody>
</table>

4. Dose adjustments:
   a. Dose adjustments will occur after a patient has received 4 doses of the current regimen
   b. Below goal:
      i. If a patient is >50% below their target goal, the daily dose will be increased by 25-50%
      ii. If a patient is <50% below their target goal, the daily dose will be increased by 25%.
   c. Above goal:
      i. If a patient is >50% above their target goal, the daily dose will be decreased by 25-50%
      ii. If a patient is <50% above their target goal, the daily dose will be decreased by 25%.
      iii. May consider holding tacrolimus to facilitate decrease in trough concentration.

v. Laboratory Monitoring:
   1. Cyclosporine levels will be ordered daily while inpatient and patient is receiving daily cyclosporine doses (either post-operatively or during readmission)
   2. Once discharged, cyclosporine levels will be monitored at the following frequency:
      a. Day 0-90: not less than once weekly
      b. Day 91-180: not less than twice monthly
      c. Day 181-240: not less than one time monthly
   3. Additional monitoring of cyclosporine trough levels is warranted if there is a change in medication formulation or patient status that may affect levels or if the creatinine has increased 0.3 mg/dL above baseline
   4. Check level in 3-7 days following dose adjustment
   5. Check potassium and creatinine with each cyclosporine level
6. A minimum of 2 levels should be within the goal range before resuming the previous monitoring frequency

vi. Adverse effects due to cyclosporine:
   1. Management of adverse effects for cyclosporine is the same as the management of adverse effects for tacrolimus.

b. Mycophenolate dosing: (Class IIa, Level of Evidence C)
   i. Mycophenolic acid is the preferred anti-proliferative medication used for PTA, PAK and SPK transplant patients.
   ii. Initiate mycophenolate sodium 720 mg PO three times daily on POD 1.
      1. Equivalent mycophenolate mofetil dosing: 1000 mg PO three times daily
      2. Mycophenolate will be decreased to BID dosing at 1 month post-transplant
   iii. IV mycophenolate mofetil is administered for the first 4 doses after transplant and may also be indicated if the patient has an acute condition that affects gastrointestinal absorption (i.e., gastrointestinal bleed or obstruction, malabsorption syndromes, severe diarrhea or severe vomiting).
   iv. Mycophenolate mofetil suspension is utilized for patients receiving medications via nasogastric or orogastric tube.
   v. Laboratory monitoring of mycophenolic acid levels is not recommended to assess for toxicity or efficacy.
   vi. Adverse effects:
      1. Diarrhea:
         a. If a patient has ≥50% increase in their frequency of daily bowel movements for ≥5-7 days
            i. 0-3 months post-transplant:
               1. Check *Clostridium difficile*, CMV PCR
            ii. ≥3 months post-transplant, obtain the following studies::
               1. CMV PCR
               2. Complete blood count
               3. *Clostridium difficile* toxin B PCR
               4. *Cryptosporidium*
               5. Giardia PCR
               6. Norovirus PCR
               7. Rotavirus AG
               8. Stool culture, with *E. Coli* (Shiga) toxin
9. Stool O&P (ova & parasite studies including: parasitology, isospora, cyclospora, pinworm) – do not order for inpatients who have been in house for >48-72 hours

   iii. If the above studies are 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:
      1. Decrease mycophenolate by 50% to a minimum dose of 180 mg twice daily or 250 mg twice daily
      2. Follow up with patient in 1 week
      3. 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
      4. Add loperamide 2 mg as needed after each loose stool (max dose: 16 mg daily) or diphenoxylate/atropine (Lomotil®) 5 mg four times daily as needed (max dose: 20 mg/day)

2. Heartburn/nausea:
   a. Counsel patient on taking MYF or MMF with food if not already doing so.
   b. Convert from MMF to MYF if only upper GI complaints (heartburn, nausea).
   c. Add calcium carbonate as needed, or the addition of an H2RA or PPI if not already on.
   d. If symptoms continue following 1 week of daily therapy increase H2RA or PPI dose to twice daily, reassess in 1 week.
   e. If symptoms persist for ≥1 week, consider EGD to rule out infection vs. ulceration.

c. Predisone (Class IIa, Level of Evidence C)
   i. Prednisone 15 mg twice daily will be started on POD 4 following dexamethasone and prednisone taper and will continue on discharge for patients that receive thymoglobulin or basiliximab for induction.
ii. Patients that receive alemtuzumab for induction should finish a steroid taper on POD 4 and not continue on prednisone for maintenance immunosuppression.

iii. Assessment for prednisone taper should occur at 2 week post-operative clinic visit.
   1. Factors that may influence the ability to taper prednisone at that time include:
      a. Current and historical tacrolimus/cyclosporine levels
      b. Sensitization status
      c. Primary vs. non-primary transplant
      d. Current MPA dose
      e. Current renal function
      f. Episodes of rejection

iv. If deemed appropriate for a prednisone taper at that time, patients should decrease prednisone doses from 30 mg daily by 5 mg every 2 weeks to a maintenance dose of 10 mg daily. Further tapering to be determined by managing provider.

Liver transplant immunosuppression:
1. Induction therapy with antithymocyte globulin is recommended for patients receiving a deceased after circulatory death (DCD) liver transplant. (Class IIb, Level of Evidence C)
   a. Antithymocyte globulin should be administered daily for 3 days at a dose of 1.5 mg/kg/day or for a total cumulative dose of 4.5 mg/kg

2. Maintenance immunosuppression consists of a combination of immunosuppressive medications that includes a CNI with or without an anti-proliferative agent and corticosteroids. (Class IIa, Level of Evidence B)

3. The goal of treatment is to maintain hepatic integrity and minimize overall immunosuppression. (Class IIa, Level of Evidence A)

4. The preferred CNI is tacrolimus and the preferred anti-proliferative agent is mycophenolic acid. (Class IIa, Level of Evidence C)

5. Patients with an autoimmune (primary sclerosing cholangitis, primary biliary cirrhosis, autoimmune hepatitis) cause of liver failure will be maintained on prednisone and mycophenolic acid in combination with a CNI for maintenance immunosuppression therapy. (Class IIa, Level of Evidence C)

6. Patients without an autoimmune mediated disease will be tapered off of prednisone 2 months post-transplant and mycophenolic acid will be reduced to half dose 3-6 months post-transplant. Exceptions to this include patients with normal renal function and patients who have experienced rejection. (Class IIa, Level of Evidence C)
   a. Patients with normal renal function may be tapered off prednisone and mycophenolate and continued on tacrolimus monotherapy. (Class IIa, Level of Evidence C)
7. Patients who have received a DCD liver transplant and have hepatitis C will not be initiated on mycophenolate as part of the immunosuppression regimen. (Class IIb, Level of Evidence C)

8. Maintenance immunosuppression medications include the following:

a. **Tacrolimus** (Class IIa, Level of Evidence C)
   i. Tacrolimus is the preferred CNI for use in liver transplant patients
   ii. Initiate tacrolimus on POD 1 for all patients
   iii. If a patient received induction therapy, initiation may be delayed if renal function has not shown significant improvement on POD 1
   iv. Initial dosing:
      1. Tacrolimus dosing should be tailored based on potential sensitivity to tacrolimus and goal tacrolimus level
      2. If a patient meets any of the criteria for decreased sensitivity to tacrolimus (Table 1), the initial dose will be 2 mg twice daily
      3. All other patients will be initiated on tacrolimus 1 mg twice daily

Table 10. Factors for Identifying Tacrolimus Sensitive Patients

<table>
<thead>
<tr>
<th>Increased Tacrolimus Sensitivity</th>
<th>Decreased Tacrolimus Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>NPO</td>
<td>General Diet</td>
</tr>
<tr>
<td>Weight &lt;80 kg</td>
<td>Weight &gt;80 kg</td>
</tr>
<tr>
<td>Significant drug interactions</td>
<td>African-American</td>
</tr>
</tbody>
</table>

4. Target trough levels should be utilized for all subsequent dose adjustments using the goals found below:
   a. Autoimmune disease patients include those with a diagnosis of primary sclerosing cholangitis (PSC), autoimmune hepatitis (AIH) and/or primary biliary cirrhosis (PBC)

Table 11. Goal Tacrolimus Levels (Liver)

<table>
<thead>
<tr>
<th>Time from Tx</th>
<th>Autoimmune disease and not on mycophenolate</th>
<th>NOT autoimmune disease OR on mycophenolate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Goal FK Level</td>
<td>Goal FK Level</td>
</tr>
<tr>
<td>0-3 months:</td>
<td>8-10 ng/mL</td>
<td>5-7 ng/mL</td>
</tr>
<tr>
<td>3-6 months:</td>
<td>8-10 ng/mL</td>
<td>3-5 ng/mL</td>
</tr>
<tr>
<td>6-12 months:</td>
<td>6-8 ng/mL</td>
<td>3-5 ng/mL</td>
</tr>
<tr>
<td>&gt;12 months:</td>
<td>4-6 ng/mL</td>
<td>2-5 ng/mL</td>
</tr>
</tbody>
</table>
5. Dose adjustments (0-90 days post-transplant):
   a. Dose adjustments will occur after a patient has received 4 doses of the current regimen
   b. Below goal:
      i. If a patient is >50% below their target goal, the daily dose will be increased by 25-50%
      ii. If a patient is <50% below their target goal, the daily dose will be increased by 25%.
   c. Above goal:
      i. If a patient is >50% above their target goal, the daily dose will be decreased by 25-50%
      ii. If a patient is <50% above their target goal, the daily dose will be decreased by 25%.
      iii. May consider holding tacrolimus to facilitate decrease in trough concentration.
   ii. Laboratory Monitoring:
      1. Tacrolimus levels will be ordered daily while inpatient and patient is receiving daily tacrolimus doses (either post-operatively or during readmission).
      2. Once discharged, tacrolimus levels will be monitored at the following frequency:
         a. Day 0-90: not less than once weekly
         b. Day 91-180: not less than twice monthly
         c. Day 181-240: not less one time monthly
      3. Additional monitoring of tacrolimus trough levels is warranted if there is a change in medications or patient status that may affect levels or if there is a decline in kidney function.
      4. Check level in 3-7 days following dose adjustment.
      5. Check potassium and creatinine with each tacrolimus level.
      6. A minimum of 2 levels should be within the goal range before resuming the previous monitoring frequency.
   iii. Adverse effects of tacrolimus:
      1. Acute kidney injury:
         a. Inpatient Management:
            i. Assess tacrolimus trough level for correlation with elevated creatinine
            ii. If trough level is above goal and creatinine has increased 0.3 mg/dL above baseline, hold tacrolimus
            iii. While tacrolimus is held, double current prednisone dose
         b. Outpatient Management:
i. Assess tacrolimus trough level for correlation with elevated creatinine

ii. If trough level is above goal and creatinine has increased 0.3 mg/dL above baseline, adjust tacrolimus dose as follows:
   1. If a patient is >50% above their target goal, the daily dose will be decreased by 25-50%
   2. If a patient is <50% above their target goal, the daily dose will be decreased by 25%.
   3. May consider holding tacrolimus to facilitate decrease in trough concentration.

2. Neurological symptoms (tremor, headache)
   a. Assess tacrolimus trough level for correlation with tremors or headache
   b. If trough level is above goal, adjust tacrolimus dose and follow up with patient after the subsequent tacrolimus lab draw
   c. No dose adjustment is recommended if trough level within target range
      i. Follow up with patient in 5-7 days if no dose adjustment is made
   d. If adverse effects are intolerable or interacting with daily activities and there is no other known cause of symptoms, consult transplant physician to consider converting the patient to cyclosporine.

3. Hyperglycemia
   a. No dose adjustment is recommended
   b. Consider diabetes management & nutrition services for patient
   c. 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 kidney transplantation
   d. 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:
      i. Consult transplant physician to consider converting patient to cyclosporine.
b. **Cyclosporine:** (Class IIa, Level of Evidence C)
   
   i. Cyclosporine will be initiated post-transplant in patients who were previously intolerant of tacrolimus.
   
   ii. Initiate cyclosporine on POD 1.
   
   iii. If a patient received induction therapy, initiation may be delayed until if renal function has not shown significant improvement on POD 1.
   
   iv. Initial dosing recommendation of 100-150 mg twice daily.
      
      a. Cyclosporine dosing should be tailored based on potential sensitivity to cyclosporine and goal cyclosporine level.
      
      b. If a patient meets any of the criteria for decreased sensitivity to cyclosporine (Table 1), the initial dose will be 150 mg twice daily.
      
      c. All other patients will be initiated on 100 mg twice daily.

   
   Table 12. Goal Cyclosporine Levels
   
<table>
<thead>
<tr>
<th>Time from Tx</th>
<th>Autoimmune disease and not on mycophenolate</th>
<th>NOT autoimmune disease OR on mycophenolate</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-3 months:</td>
<td>Goal CSA Level</td>
<td>Goal CSA Level</td>
</tr>
<tr>
<td></td>
<td>150-200 ng/mL</td>
<td>125-175 ng/mL</td>
</tr>
<tr>
<td>3-6 months:</td>
<td>125-150 ng/mL</td>
<td>100-125 ng/mL</td>
</tr>
<tr>
<td>6-12 months:</td>
<td>100-125 ng/mL</td>
<td>75-100 ng/mL</td>
</tr>
<tr>
<td>&gt;12 months:</td>
<td>100 ng/mL</td>
<td>50-75 ng/mL</td>
</tr>
</tbody>
</table>

   v. Dose adjustments (0-90 days post-transplant):
      
      a. Dose adjustments will occur after a patient has received 4 doses of the current regimen.
      
      b. If a patient is >50% below their target goal, the dose will be increased by 25-50% per dose.
      
      c. May consider holding tacrolimus to facilitate decrease in trough concentration.
      
      d. If a patient is <50% below their target goal, the total daily dose will be increased by 25%.

   vi. Laboratory monitoring:
      
      1. Cyclosporine levels will be ordered daily while inpatient and receiving daily cyclosporine doses (either post-operatively or during readmission).
      
      2. Once discharged, cyclosporine levels will be monitored at the following frequency:
         
         a. Day 0-90: not less than once weekly
b. Day 91-180: not less than twice monthly 
  c. Day 181-240: not less than one time monthly 
3. Check level in 5-7 days following dose adjustment 
4. Check potassium and creatinine with each cyclosporine level 
5. A minimum of 2 levels should be within the goal range before resuming the previous monitoring frequency 

vii. Adverse effects: 
  1. Management of adverse effects for cyclosporine is the same as the management of adverse effects for tacrolimus 

c. Mycophenolic acid (Class IIa, Level of Evidence C) 
  i. Mycophenolic acid is the preferred anti-proliferative medication used for liver transplant patients 
  ii. Initiate mycophenolate sodium 720 mg PO twice daily on POD 1 
      1. Equivalent mycophenolate mofetil dosing: 1000 mg PO twice daily 
  iii. IV mycophenolate mofetil is indicated in the immediate post-transplant setting if the patient has an acute condition that affects gastrointestinal absorption (i.e., gastrointestinal bleed or obstruction, malabsorption syndromes, severe diarrhea or severe vomiting). 
  iv. Mycophenolate mofetil suspension is utilized for patients receiving medications via nasogastric or orogastric tube. 
  v. Mycophenolate will be reduced to half dose between 3-6 months post-transplant with the exception of patients with normal renal function and patients who have not experienced rejection. 
  vi. Mycophenolate will be discontinued between 3-6 months post-transplant in patients with normal renal function and in patients who have not experienced rejection. 
  vii. Laboratory monitoring of mycophenolic acid levels is not recommended to assess for toxicity or efficacy. 
  viii. Adverse effects: 
      1. Diarrhea: 
         a. If a patient has $\geq$50% increase in their frequency of daily bowel movements for $\geq$ 5-7 days 
            i. 0-3 months post-transplant: 
               1. Check Clostridium difficile, CMV PCR 
            ii. $\geq$3 months post-transplant, obtain the following studies: 
               1. CMV PCR 
               2. Complete blood count
3. *Clostridium difficile* Clostridium difficile toxin B PCR
4. *Cryptosporidium*
5. Giardia PCR
6. Norovirus PCR
7. Rotavirus AG
8. Stool culture, with E. Coli (Shiga) toxin
9. Stool O&P (ova & parasite studies including: parasitology, isospora, cyclospora, pinworm) – do not order for inpatients who have been in house for >48-72 hours

iii. If the above studies are 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:
   1. Decrease mycophenolate by 50% to a minimum dose of 180 mg twice daily or 250 mg twice daily
   2. Follow up with patient in 1 week
   3. 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
   4. Add loperamide 2 mg as needed after each loose stool (max dose: 16 mg daily) or diphenoxylate/atropine (Lomotil®) 5 mg four times daily as needed (max dose: 20 mg/day)

2. Heartburn/nausea:
   a. Counsel patient on taking MYF or MMF with food if not already doing so
   b. Convert from MMF to MYF if only upper GI complaints (heartburn, nausea)
   c. Add calcium carbonate as needed, or the addition of an H2RA or PPI if not already on
   d. If symptoms continue following 1 week of daily therapy increase H2RA or PPI dose to twice daily, reassess in 1 week
   e. If symptoms persist for ≥1 week, consider EGD to rule out infection vs. ulceration
d. **Prednisone** (Class IIa, Level of Evidence C)
   i. Predisone 10 mg twice daily will be started on POD 5 following dexamethasone taper and will continue on discharge
   ii. Prednisone doses should be split to twice daily dosing for patients who require insulin for glucose control
   iii. Assessment for prednisone taper should occur at 3-4 weeks post-operatively for patients without autoimmune disease
      1. Factors that may influence the ability to taper prednisone at that time include:
         a. Current and historical tacrolimus/cyclosporine levels
         b. Current liver function
         c. Episodes of rejection
   iv. If deemed appropriate for a prednisone taper at that time, patients should decrease prednisone doses from 10 mg twice daily using the following schedule:
      1. Prednisone 10 mg every morning and 5 mg every evening for 2 weeks
      2. Prednisone 5 mg twice daily for 2 weeks
      3. Prednisone 5 mg daily for 2 weeks and then STOP
         a. Patients with a history of autoimmune disease should be tapered down to 5 mg daily and continued on that dose

e. **Azathioprine**: (Class IIa, Level of Evidence C)
   i. Indicated for use in patients unable to tolerate adverse effects of MPA
   ii. Thiopurine methyltransferase (TPMT) genotyping is recommended prior to azathioprine initiation to determine dose.
   iii. Dosing:
      1. 1-3 mg/kg/day as a single daily dose
   iv. There is no recommended azathioprine level for monitoring purposes.
   v. Recommend either discontinuation of allopurinol if azathioprine is initiated or decreasing the allopurinol dose by 1/3 (33%) or 1/4 (25%).
   vi. Recommend discontinuation of febuxostat if azathioprine is initiated.
   vii. If allopurinol or febuxostat is continued, close hematological monitoring is warranted.

f. **Sirolimus/Everolimus**: (Class IIa, Level of Evidence C)
   i. Indicated for use in patients as a replacement for azathioprine, MPA or CNIs and for patients with recurrent hepatocellular carcinoma
ii. Sirolimus should not be used within 30 days of liver transplant

iii. Dosing:
   1. Sirolimus: 2 mg PO one time daily
   2. Everolimus: 0.75 mg twice daily

iv. Subsequent doses should be adjusted based on the following goal trough levels:

<table>
<thead>
<tr>
<th></th>
<th>Goal Sirolimus Level (Monotherapy)</th>
<th>Goal Sirolimus Level (+FK or MPA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-3 months:</td>
<td>8-10 ng/mL</td>
<td>5-8 ng/mL</td>
</tr>
<tr>
<td>3-6 months:</td>
<td>5-8 ng/mL</td>
<td>5-8 ng/mL</td>
</tr>
<tr>
<td>6-12 months:</td>
<td>5-8 ng/mL</td>
<td>3-5 ng/mL</td>
</tr>
<tr>
<td>&gt;12 months:</td>
<td>3-5 ng/mL</td>
<td>3-5 ng/mL</td>
</tr>
</tbody>
</table>

v. Laboratory monitoring:
   1. Recommended one time weekly upon initiation and with any dose changes.
   2. When the target trough level has been attained, it is recommended to monitor levels one time monthly.

General Transplant Recommendations:

a. Gastric ulcer prophylaxis: (Class IIa, Level of Evidence C)
   i. It is recommended that patients with no prior history of gastroesophageal reflux disease (GERD) who were not taking a proton pump inhibitor prior to transplant should be started on an H2 receptor antagonist (H2RA) post-transplant
   ii. Ranitidine is the preferred H2RA for use:
      1. Dosing: Ranitidine 150 mg PO twice daily (requires renal dose adjustment).
   iii. Patients that were on a PPI prior to transplant or have a history of GERD should be started on a PPI post-transplant
   iv. Pantoprazole is the preferred PPI for use.
      1. Dosing: Pantoprazole 40 mg PO daily
   v. If a patient complains of heartburn on daily dosing of the H2RA or PPI, frequency may be increased to twice daily (pending renal function).
   vi. If a patient continues to experience heartburn or reflux symptoms on twice daily H2RA, it is recommended to change to a PPI.
   vii. It is recommended to discontinue prophylaxis in patients with no history of heartburn/GERD prior to transplant when the dose of prednisone is ≤10 mg daily.
b. **Thrombosis prophylaxis:** (Class I, Level of Evidence A)
   i. All transplant recipients should receive aspirin 81 mg PO daily for thrombosis prophylaxis.
   ii. Liver transplant recipients should not be started on aspirin until platelets are >50,000.

c. **Vitamins and supplements:** (Class Ia, Level of Evidence B)
   i. All transplant recipients are recommended to take a daily multivitamin appropriate for their age & gender.
   ii. All transplant recipients are recommended to take calcium 1000 mg daily (based on elemental calcium dosing).
   iii. All transplant recipients are recommended to take vitamin D 1000 units daily.

**UW Health Implementation**

**Potential Benefits:**
This guideline is intended to help standardize care for medication management in adult kidney, pancreas and liver transplant recipients.

**Potential Harms:**
Side effects and adverse events associated with various medications and drug treatments.

**Implementation Plan and Tools**
1. Guideline will be housed on UConnect in a dedicated folder for Clinical Practice Guidelines.
2. Links to this guideline will be created in appropriate Health Link or equivalent tools.

**References**
Disclaimer
CPGs are described to assist clinicians by providing a framework for the evaluation and treatment of patients. This Clinical Practice Guideline outlines the preferred approach for most patients. It is not intended to replace a clinician’s judgment or to establish a protocol for all patients. It is understood that some patients will not fit the clinical condition contemplated by a guideline and that a guideline will rarely establish the only appropriate approach to a problem.