**Policy: Post-Liver Transplant Concomitant Medications**

**Statement: 1. Activation** **date**: 12/11/08

**2. Affected Department**: Liver transplant program
**3. Vision strategy**: Patient care
**4. Policy Statement**: The Emory Transplant Center will comply with all applicable federal, state and local laws, regulations and policies regarding the management of prescribing medications and refills.
**5. Basis**: This policy is necessary for the protection of patients, physicians and staff.
**6. Administrative Responsibility**: Section heads, physicians, practitioners, and staff are responsible for compliance with this policy.

**Scope/Procedure:**

**Protocol**:

I. Anti-viral prophylaxis

a. Herpes prophylaxis

i. Post-transplant: Acyclovir 400mg po TID

a. Refer to CMV protocol in liver transplantation for more information.

ii. Consider extended prophylaxis if history of HSV.

II. Antibacterial surgical prophylaxis

a. Ampicillin/sulbactam q6hr x 24 hours starting prior to incision

i. Antibiotics should be redosed for surgery > 4 hours or if large amount of blood products are given

b. For patients with severe PCN allergy: Vancomycin 1.5 grams IV x 1 and levofloxacin 750mg IV x 1. Severe PCN allergy is defined as hives or other rash occurring within 24 hours of starting drug, angioedema, bronchospasm, anaphylaxis or exfoliative dermatitis.

III. Empiric antimicrobial coverage for biliary complications and/or fever

a. Piperacillin/tazobactam 4.5 grams IV q8hr
b. Vancomycin 1.5 grams IV x 1 , then dosed per PK if MRSA suspected
c. Fluconazole 800mg x 1, then 400mg PO/IV daily if high risk fungal infection. Fluconazole to be continued for 3 weeks post-transplant if high risk.

i. Definition of high risk for fungal infection

1. Re-operation
2. Transfusion requirements > 20 units
3. Dialysis, or chronic kidney disease
4. Broad spectrum antibiotic use > 14 days
5. Biliary leakage

d. For fever > 24 hours and history of multi-drug resistant organism(s) or fever persisting > 24 hours, consult Transplant ID.

IV. Empiric antimicrobial coverage for biliary procedure

Piperacillin/tazobactram 4.5 grams IV x 1

If PCN allergy, levofloxacin 750mg IV x 1

V. Anti-pneumocystis prophylaxis

Sulfamethoxazole/trimethoprim (SMZ/TMP) single strength tablet daily x 6 months. Dose to be adjusted for renal insufficiency/dialysis, severe leucopenia (WBC < 3).

If estimated CrCl is < 30ml/min, administer SMZ/TMP SS 1 tab po Mon/Wed/Fri

If persistent hyperkalemia and patient is on SMZ/TMP, consider reducing to MWF or holding medication.

b. Patients with documented sulfa allergy may receive one of the following (listed in order of preference):

Atovaquone 1500mg po daily

Inhaled pentamadine 300mg via inhalation q month

Dapsone 100mg po daily

1. Check G6PD prior to initiation

Possible side effects: methemoglobinemia

VI. Anti-fungal prophylaxis

a. Nystatin swish and swallow 500,000 units (5ml) po four times daily x 3 months. Patients receiving fluconazole do not need to receive nystatin prophylaxis until after fluconazole is discontinued.

VII. Antihypertensive therapy

a. Hypertension is defined as a sitting systolic blood pressure (SBP) of greater than or equal to 140mmHg or a diastolic blood pressure (DBP) of greater than or equal to 90mmHg. Severity ratings as follows:

i. Mild: SBP > 140 mmHg or DBP 90-104 mmHg
ii. Moderate: SBP > 160 mmHg or DBP 105-114 mmHg
iii. Severe: SBP > 200 mmHg or DBP > 115 mmHg

b. Patients already on antihypertensives may be treated with alterations in their current regimen or the regimen outlined for new-onset hypertension.
c. A diagnosis of mild hypertension is to be if three consecutive readings taken on different days are SBP > 140 mmHg or DBP 90-104 mmHg. Treatment may be initiated upon findings of mild to severe hypertension after confirmation with repeat determinations on the same day with treatments as follows (in order of preference):

i. Calcium channel blocker of the dihydroperidine class (amlodipine or nifedipine XL)

1. First line agent in new onset hypertension. Doses should be maximized (by labeled dose or tolerance) prior to adding second line therapy
2. Avoid the use of non-dihydroperidine class such as verapamil, nicardipine, and diltiazem due to the effect on tacrolimus (will increase tacrolimus levels)

ii. Beta blockers (metoprolol, atenolol, labetalol, carvedilol)

1. May be considered drug of choice for htn, if patient is also tachycardic, has atrial fibrillation, or another compelling indication

2. Avoid beta blockers if HR < 60 bpm

iii. ACE-Inhibitors (ACE-I) or angiotensin receptor blockers (ARBs) if patient is 6 months or more from transplant (ex: lisinopril, losartan)

1. Potential cardioprotection and renal protection. May be drug of choice in some patients with diabetes mellitus and/or cardiovascular disease or low EF.

2.Avoid if K > 5.5
3. Avoid if SCr > 3 mg/dL
4. Second line therapy

iv. Alpha agonist (Clonidine) tablets or patches

v. Vasodilators (Hydralazine)

vi. Alpha blockers (tamsulosin, doxazosin, etc)

May be of benefit in patients with urinary retention and/or benign protstate hypertrophy (BPH)

vii. Diuretics

Loop diuretics (furosemide, torsemide)should be used carefully in liver transplant recipients because of their tendency to cause volume depletion and worsening renal function.

Indications may include ascites, edema, volume overload post-transplant or patients with congestive heart failure.

Potassium sparing diuretics (spironolactone, amiloride) should generally be avoided post-transplant due to their tendency to hyperkalemia which can be potentiated by calcineurin inhibitors (tacrolimus and cyclosporine) and sulfamethoxazole/trimethoprim.

VIII. Aspirin

Aspirin 81mg po qday starting post transplant for all patients unless contraindicated. Initiation will start after platelet count is > 50,000 and stable. Contraindications may include concomitant warfarin and/or clopidogrel (Plavix) treatment.

Aspirin does not need to be held for liver biopsy.

If the patient has a history of PUD, consider initiation of a PPI (pantoprazole, esomeprazole, omeprazole, etc).

IX. DVT Prophylaxis

a. Alternating leg pressure/sequential compression devices
b. Heparin

i. Heparin 5000 units SQ q8hr

X. Supplements

a. Multivitamin 1 tablet po qday in all patients unless contraindicated
b. Calcium and Vitamin D supplements should be considered in patients on long-term prednisone therapy.
c. Magnesium oxide 400mg po BID as indicated for low magnesium or medically necessity

XI. Antihyperlipidemic therapy

a. Hyperlipidemia is defined as a total serum cholesterol of > 200 mg/dL or a LDL cholesterol of > 100 mg/dL.
b. Therapy for fasting hyperlipidemia should be initiated at three months if lipid levels exceed those listed above and do not respond to lifestyle modifications. Lifestyle modifications may include a change in diet, increased exercise and/or weight loss.
c. Statins such as pravastatin (Pravachol) 20mg po qhs, atorvastatin (Lipitor) 10 mg qhs, rosuvastatin (Crestor) 5mg po qhs or simvastatin (Zocor) 5 mg qhs should be used to treat elevated cholesterol. The dose of simvastatin should not exceed 40mg po qday if used concurrently with CNIs or mTOR inhibitors due to increased risk of adverse effects.
d. Dose should be increased as necessary to decrease triglyceride and/or serum cholesterol levels by at least 20%.
e. Check a baseline CPK (statins and immunosuppressants = increase risk of rhabdomyolisis) and LFTs, if not done. Recheck LFTs and CPK at no more than 6 weeks after initiation of statin therapy. Increases in LFTs are not an absolute contraindication to continuing statin therapy as a detrimental increase in LFTs is a rare adverse effect.
f. For patients unable to tolerate statins, alternative therapy includes fibric acid derivatives such as fenofibrate (Tricor), gemfibrozil (Lopid) or ezetimibe (Zetia) and other agents as appropriate.
g. For triglycerides > 200 mg/dL start a fibric acid derivative such as fenofibrate (Tricor) 54 mg po daily or gemfibrozil (Lopid) 600mg po BID and increasing after 6 weeks of therapy to maintain triglycerides below 200mg/dL. LFTs should be checked no less than 6 weeks after initiation of fibric acid derivative treatment. Blood glucose should be controlled to help decrease hypertriglyercidemia. If a patient is receiving sirolimus with increased triglycerides, consider changing immunosuppression if triglycerides unable to be controlled. When fibric acid derivatives are added to statin therapy, there is an increased risk of side effects, including rhabdomolysis. Monitoring is warranted.
h. For patients unable to tolerate statins or fibric acid derivatives, consider bile acid sequesterants such as cholestyramine (Questran) 4 grams daily or colestipol 5 grams daily and increase doses to achieve desired effect. Instruct patient to take bile acid sequestrants 4 hours apart from immunosuppressants and other medications.

XII. Antacid, H-2 blocker or proton pump inhibitor prophylaxis

For occasional heartburn (non-daily), patient may take calcium carbonate (Tums) or magnesium hydroxide (Maalox). If the patient is receiving mycophenolate, these medications need to be separated by at least 1 hour.

Consider prophylaxis in patients with a history of PUD or on concomitant aspirin and prednisone therapy.

Proton pump inhibitor prophylaxis is the first line agent. Drugs include esomeprazole (Nexium) 20-40mg daily, lansoprazole (Prevacid) 15-30 mg daily, omeprazole (Prilosec) 20 mg daily and pantoprazole (Protonix) 40mg po daily.

H2-blockers are second line agents. Drugs include famotidine (Pepcid) 20mg po BID or ranitidine (Zantac)150 mg po BID.

Cimetidine (Tagamet) should be avoided due to potential drug interactions.

XIII. Inpatient Hyperglycemia management

Blood glucose should be maintained at < 150 mg/dl. Patients may be managed on insulin drip or SQ insulin. See insulin infusion protocol for more information.
b. Insulin is the preferred agent
c. Consult endocrine for difficult to manage hyperglycemia

XIV. Outpatient Hyperglycemia management

Oral agents are not typically recommended for the first month post transplant

Consult endocrine for difficult to manage hyperglycemia.

XV. New Onset Diabetes after Transplantation (NODAT)

a. Obtain endocrine consult.
b. Refer to the new onset diabetes after transplant (NODAT) protocol (under development)

XVI. Pain management and controlled substances

a. Please refer to link below for more information regarding the policy

[http://euhnotes.eushc.org/tec/tecpolcy.nsf/6a0cc13319de9f7f852569310054e7c5/b88e600f503ff7f185257b2100675cf5?OpenDocument](http://euhnotes.eushc.org/tec/tecpolcy.nsf/6a0cc13319de9f7f852569310054e7c5/b88e600f503ff7f185257b2100675cf5?OpenDocument-)

b. Please refer to the link below for the patient agreement document

[http://euhnotes.eushc.org/tec/tecpolcy.nsf/6a0cc13319de9f7f852569310054e7c5/b88e600f503ff7f185257b2100675cf5/$FILE/PC-16%20attachment%20EHC%20TEC%20ESA%20Pain%20Agreement%2010%2023%2012%20v4.pdf](http://euhnotes.eushc.org/tec/tecpolcy.nsf/6a0cc13319de9f7f852569310054e7c5/b88e600f503ff7f185257b2100675cf5/%24FILE/PC-16%20attachment%20EHC%20TEC%20ESA%20Pain%20Agreement%2010%2023%2012%20v4.pdf-)

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Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (ATP III Final Report) <http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3_rpt.htm> Accessed 4.28.08

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Approved by: Liver Transplant Leadership Group

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