**Policy: Post Liver Transplant Protocol for Hepatitis B Prophylaxis in HBV Positive Recipients**

**Statement:**
**Vision Strategy**: Patient Care
**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.

**Basis**: This policy is necessary for the protection of patients, physicians, and staff.

**Administrative Responsibility**: Section heads, physicians, practitioners, and staff are responsible for compliance with this policy:

**Scope/Procedure:**

**Hepatitis B Prophylaxis Protocol in HBsAg-Positive Liver Transplant Recipients**

**I. Background**: Recurrent hepatitis B virus (HBV) infection following orthotopic liver transplantation (OLT) was initially associated with significant morbidity and mortality. However since the late 1980’s, effective measures to prevent and treat reinfection using hepatitis B immune globulin (HBIG) and subsequently nucleos(t)ide analogs have significantly improved the graft and patient survival after liver transplantation. Lamivudine was traditionally used to suppress viral activity but has been associated with relatively high resistance rates. As our ability to effectively prevent HBV recurrence after OLT has improved due to the improved nucleoside analog resistance profiles, this protocol reflects the our current strategy with less dependence on HBIG and more use of nucleotide analogs such as entecavir, periodic lab surveillance, and use of high-dose HBV vaccinations when appropriate.

**II. Purpose:** To prevent hepatitis B virus recurrence (re-infection of the allograft) by maintaining therapeutic hepatitis B surface antibody titers (anti-HBS) with the use of HBIG and to maintain undetectable HBV DNA with nucleoside analogs.

**III. Persons Affected:** Transplant Nurse Coordinator, mid-level providers, and all physicians.

**IV: Pre-Liver Transplant:** Oral anti-viral therapy (nucleoside or nucleotide analog) is often prescribed to patients with active HBV awaiting OLT. Indications for treatment prior to OLT include: ALT greater than 2 times normal due to active HBV, HBs-Ag positive patients with decompensated cirrhosis, and/or HBV DNA greater than 20,000 IU/ml.

Check Hepatitis B surface antigen (HBsAg) and HBV DNA immediately prior to transplant***.***

If the patient is already on oral anti-viral therapy at the time of transplant with a suppressed viral load, continue the same agent(s) post-OLT in combination with HBIG. Goal of treatment is to prevent further HBV-related complications and to reduce HBV DNA to at least < 2 x 104 IU/mL or undetectable levels prior to transplant to reduce the risk of recurrence.

If HBV DNA is negative at the time of transplant, continue same antiviral therapy.

If HBV DNA results are positive at the time of transplant, consult hepatology regarding therapy recommendation.

**V. Intraoperative Liver Transplant:** Administer 10,000 IUnits of HBIG (Hepagam B) over two hours during the anhepatic phase intraoperatively.

**VI. Postoperative Liver Transplant:** All laboratory results are to be discussed with a hepatologist.

**HBIG Dosing and duration:**

Post-operative days 1-6: HBIG (Hepagam B) 10,000 IU infused over 2 hours to be given DAILY x 6 days.

**If the HBV DNA was** **NEGATIVE** at time of transplant, **then no further HBIG** is to be given after day 6. The patient should be maintained on oral anti-viral therapy (see below).

**If the HBV DNA was** **POSITIVE** at the time of transplant, then HBIG should be continued for a **total of 6 months** as outlined below:

The HBIG administration will be based on the anti-HBs trough titers checked. Check anti-HBs trough titers based on the schedule listed in the laboratory monitoring section (VII).

If anti-HBs trough titer is > 100 mIU/mL, no HBIG may be needed.

If anti-HBs trough titer is < 100 mIU/mL, give HBIG 5ml (>1560 IU/5ml) IM x 1 dose. If significantly or consistently low, consider consulting hepatologist and/or transplant pharmacist.

Discontinue after 24 weeks.

**Oral anti-viral therapy:** Oral anti-viral therapy should be started immediately post-operatively via NG tube or orally (dose adjusted for renal-insufficiency; recommendations based on CrCl).

a. If the HBV DNA was **NEGATIVE** at the time of transplant, resume the same pre-transplant oral anti-viral therapy indefinitely.

b. If the HBV DNA was **POSITIVE** at the time of transplant, recommend the use of combination nucleoside/tide unless the patient newly started treatment and resistance is not expected; Descovy (tenofovir alafenamide (TAF) 25 mg/emtricitabine 200 mg) preferred but can also use Truvada (tenofovir disoproxil fumarate (TDF) 300 mg/emtricitabine 200 mg) or entecavir and tenofovir). Monotherapy with drugs associated with unacceptably high long-term resistance rates (lamivudine, telbivudine, adefovir) is not recommended as first-line. Long-term (> 1 year post-OLT) anti-viral therapy is at the discretion of the treating transplant hepatologist.

**VII. Laboratory Monitoring:** **Anti-HBs** should be drawn immediately prior to administration on day 6 and the following intervals ONLY IN PATIENTS GIVEN HBIG AFTER THE FIRST WEEK (I.E. HBV DNA POSITIVE AT TRANSPLANT):

0-3 months after transplant: every 2 weeks

3-6 months after transplant: every month

Titers: Goal anti-HBs for first 6 months post-transplant should be over 100 mIU/mL.

**HBV DNA Ultraquant PCR** and **Hepatitis B Surface Antigen** (HBsAg) should both be drawn pre-operatively and then at the following intervals:

0-12 months post-transplant: every 3 months

After 1 year post-transplant: every 6 months indefinitely

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**Hepatitis B Prophylaxis Protocol in HBcAb-Positive (HBsAg-negative)**

**Liver Transplant Recipients**

For transplant recipients that are HBcAb-positive and HBsAg-negative, ***NO*** HBIG or oral anti-viral therapy after transplant is indicated if receiving an HBV negative donor (i.e. the donor is HBcAb-negative and HbsAg-negative) Recommend administration of HBV vaccine at 1 year post-OLT if HBsAb is negative using **the high-dose vaccine** (40 mcg) at 0, 1, and 6 months. Then check HBsAb over 1 month after last dose.

**References:**

Pilmore H, Gane E. Hepatitis B-positive donors in renal transplantation: increasing the deceased donor pool. Transplantation 2012; 94(3):205-10.

Approved by: Liver Transplant Leadership Group

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