UCSF Joint Hepatology/Transplant ID Guidelines For Anti-HBc+ Management In Organ Transplantation and Immunosuppression

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PART I: Management of HBsAg– anti-HBc+ Patients Receiving Immunosuppression (anti-HBs– or +)[1]

Type of Immunosuppression	Prophylaxis?	Duration of Prophylaxis	Monitoring (HBsAg, HBV DNA, ALT)
High risk of Reactivation (>10%) • B-cell depleting agents (e.g.,rituximab) • HSCT (auto or allo) • CAR T cell therapy • Hematologic malignancy with myelosuppressive chemotherapy	Yes	• 24 mo after last dose of rituximab or after CAR T cell infusion • At least 2 years after HSCT or after completion of myelosuppressive chemo for heme malignancy (consider indefinite ppx)	q3mo until 1 yr after ppx is stopped
Moderate risk of Reactivation (1-10%) • Anti-TNF inhibitors • Cytokine or integrin inhibitors (e.g., abatacept, ustekinumab, natalizumab, vedolizumab) • Tyrosine kinase inhibitors (e.g., imatinib, nilotinib) • Steroids (≥10mg/d prednisone x ≥4 wks) • Anthracyclines (e.g.doxorubicin) • SOT recipients	Yes (this is a controversial area given risk of reactivation is not clearly defined for this population; monitoring with q3mo HBsAg, ALT, and HBV DNA and "on-demand" therapy can also be considered)	• 6 mo after last dose of immunosuppression • For SOT recipients: ○ 12 mo for non-liver SOT recipients (Thymoglobulin treatment for rejection should restart the clock. Pulse dose steroids for rejection should extend prophylaxis for an additional 6 months.) ○ No ppx for liver SOT recipients[2]	q3mo until 1 yr after ppx is stopped (or equivalent time period if monitoring only)
Low risk of reactivation (<1%) • Azathioprine, methotrexate • <10mg prednisone for ≥4 weeks	No	n/a	q3mo x 6 mo after last dose of immunosuppression

[1]Hepatology should be consulted for patients who are HBsAg+ and undergoing immunosuppression.
[2]Liver SOT recipients of an anti-HBc+ donor receive life-long prophylaxis with lamivudine 100 mg po daily, adjusted for renal function, as per post-liver transplant protocol. Entecavir, TDF, or TAF are also acceptable but LAM is preferred due to its low cost and need for lifelong prophylaxis.

General Principles for Prophylaxis

- Entecavir is the preferred antiviral (TDF or TAF are also first line agents, but used less commonly); Lamivudine is considered second line given high risk of resistance. Prophylactic dosing of entecavir is 0.5mg PO daily in patients ≥ 16 years (needs renal dosing adjustment if CrCl <50).
- The presence of anti-HBs is not protective against reactivation and should not influence prophylaxis decisions.
- Prophylaxis, when given, should be started as soon as possible before (when possible) or simultaneously with the onset of immunosuppression.
- For HIV-positive patients requiring prophylaxis: follow DHHS guidelines for the treatment of HIV/HBV coinfection: use tenofovir (TDF or TAF) with FTC or 3TC. If TDF or TAF cannot be used, then use entecavir with a fully suppressive ARV regimen. Do not use 3TC or FTC alone for prophylaxis given the risk of resistance.

PART II: Management of HBsAg– and anti-HBc– Transplant Recipients with HBsAg–, anti-HBc+ Donors (Non-liver)

Recipient Status	Prophylaxis?	Duration	Monitoring (HBsAg, HBV DNA, ALT)
anti-HBc– anti-HBs–	Kidney: yes[1]	At least 1 year[1]	q3mo until 1 yr after d/c antivirals
	Heart or lung: no	n/a	q3mo x 1 yr
anti-HBc– anti-HBs+	No	n/a	q3mo x 1 yr (also check for loss of anti-HBs)

[1]Only kidney and liver recipients have been shown to reactivate in this situation. Ultimate duration of ppx depends on results of monitoring labs and patient's net state of immunosuppression.

Note: Pediatric organ transplantation from anti-HBc+ donors is NOT currently recommended due to lack of data for safety in children; if transplantation from an anti-HBc+ donor is being considered under exceptional circumstances, consult with Pediatric ID.

References/Guidelines:

- Reddy et al, AGA Institute Guideline of the Prevention and Treatment of Hepatitis B Virus Reactivation During Immunosuppressive Therapy. Gastroenterology 2015; 148:215.
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