

Appendix 1 (as supplied by the authors): HBV reactivation

Diagnostic Criteria for HBV Reactivation

Table 1 - Diagnosis of HBV Reactivation by Serologies and HBV DNA levels¹

HBsAg+, anti-HBc+	HBsAg-, anti-HBc+
1) A 2 log (100-fold) increase in HBV DNA compared to the baseline OR 2) HBV DNA \geq 3 log (1,000) IU/mL in a patient with previously undetectable level OR 3) HBV DNA \geq 4 log (10,000) IU/mL if baseline level is unavailable	1) HBV DNA is detectable OR 2) Reverse HBsAg seroconversion (reappearance of HBsAg)

Factors for Increased Risk of HBV Reactivation

Table 2 shows the risk for each class of immunosuppressive therapies with respect to virologic profile. Host factors (male, cirrhosis, older age, other underlying disease) and other virological factors (high baseline HBV DNA and HBeAg) have also been associated with increased risk.²

Table 2 – Risk of HBV Reactivation by Class of Immunosuppressants and Virologic Profile²

Low risk (<1%) Prophylaxis not recommended	Moderate risk (1-10%) Prophylaxis suggested	High Risk (>10%) Prophylaxis recommended
- Azathioprine - 6-mercaptopurine - Methotrexate - Intra-articular steroids - Any dose of oral corticosteroids daily for \leq 1 week - <10mg prednisone* \geq 4 weeks	- TNF-alpha inhibitors and other biologics (eg. etanercept, adalimumab, certolizumab, infliximab) - Cytokine or integrin inhibitors (eg. abatacept, ustekinumab, natalizumab, vedolizumab) - Tyrosine Kinase inhibitors (eg. imatinib, nilotinib) - <10 mg prednisone* daily \geq 4 weeks - Anthracyclines (eg. doxorubicin, epirubicin) - \geq 10mg prednisone* daily \geq 4 weeks	- B-cell depleting agents (eg. rituximab, ofatumumab) - Anthracyclines (eg. doxorubicin, epirubicin) - \geq 10mg prednisone* daily \geq 4 weeks

*prednisone or equivalent doses of another oral corticosteroid

Red: HBsAg+/anti-HBc+ or HBsAg-/anti-HBc+ (Surface antigen negative or positive, and core positive)

Blue: HBsAg+/anti-HBc+ (Surface antigen and core positive)

Green: HBsAg-/anti-HBc+ (Surface antigen negative and core positive)

References

1. Terrault NA, Lok ASF, McMahon BJ, et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. *Hepatology* 2018; 67:1560.
2. Reddy KR, Beavers KL, Hammond SP, et al. American Gastroenterological Association Institute guideline on the prevention and treatment of hepatitis B virus reactivation during immunosuppressive drug therapy. *Gastroenterology* 2015; 148: 215-219.