

**Guidelines for management of hepatitis B for patients requiring  
immunosuppressive treatment  
Version 3.1: July 2020**

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These guidelines apply to adults in whom immunosuppressive treatment is planned and focuses on those with either current or past (“cleared”) hepatitis B infection,

These guidelines will predominantly apply, although not exclusively, to patients under the care of the following clinical teams: Dermatology, Gastroenterology, Hepatology, Haematology, Neurology, Neurosurgery, Oncology, Renal Medicine, Respiratory Medicine, Rheumatology

These guidelines **do not** apply to HIV co-infected patients

These guidelines can also be accessed on an NHS computer via  
<http://tinyurl.com/SVSHBVIS>

### Summary of changes in Version 3:

1. Reformatting of document into sections which include: background, principles of treatment and prophylaxis, screening patients, patient management, anti-HBV drugs and monitoring
2. Background virology and summary of hepatitis B markers provided
3. Table 1 updated. Drug groups named as Group A to G
4. Inclusion of relevant drugs with unknown risk into a new risk group (G)
5. Inclusion of guidance for renal transplant patients/ other solid organ transplant types
6. Defining responsibilities of parent and viral hepatitis team
7. Incorporation of latest recommendations from EASL 2017 (and review of other literature)
8. Emphasis made on exclusion of passively acquired antibodies
9. A new algorithm 1 has been defined to help Parent Teams
10. Incorporating parts of previous version into algorithm 1
11. Adding a new algorithm 2 to help Specialist Viral hepatitis
12. Made explicit recommendation about low risk patients not needing a formal referral to specialist clinic

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## Section 1: Introduction

- Hepatitis B virus (HBV) causes infection in humans and has a predilection for liver cells. It can transmit from infected individuals via exposure to infected blood & body fluids and sexual contact but the commonest mode of transmission globally is exposure of newborn to infected mother's blood at time of birth. Around 90% of infections acquired as infants become chronic and remain largely asymptomatic. The immune system is not mature enough at this age to mount responses required to resolve this infection. Adults on the other hand *are* able to mount such responses and clear infection in around 95% of cases. Once replication has resolved, the virus lives in liver cells for the rest of patient's life as 'latent infection'. The immune system ensures HBV does not escape from this phase of latency.
- Hepatitis B virus is not cytopathic. This means that in an ongoing active infection the virus lives in liver cells but does not kill them. Liver inflammation and secondary fibrosis which complicate infection are primarily immune mediated. This is a continuous but unproductive attempt of the body to get rid of the virus.
- Three main types of proteins are seen during HBV's life cycle. The main one which is produced in all cases of a typical infection is the **surface antigen** (referred to as s antigen and denoted by HBsAg). The presence of HBsAg defines HBV infection. People are said to clear HBV infection once HBsAg is no longer detectable.
- HBV core antigen (HBcAg) is essential for viral survival but its presence in blood is transient and is not used as a diagnostic marker. In contrast, **e antigen** (HBeAg) is a protein produced in large amounts where infection dynamics are very rapid and replicative rates of the virus are high.
- Early in infection, antibody to core antigen (HBcAb) develops and remains detectable lifelong. This is a useful marker for exposure to the virus, but does not help stage the HBV infection as it is present in both active and resolved infections.

Natural Clearance: Some patients clear virus naturally. Over the course of infection, antigens are lost and antibodies to them develop which heralds resolution of the infection. First to disappear is HBeAg followed by HBsAg. This usually correlates to disappearance of HBV DNA. Antibody to HBeAg (referred to as HBeAb) develops first followed by antibody

### **Box 1: Definitions**

#### **Current hepatitis B (HBV) infection**

All HBsAg+ve cases (irrespective of other HBV markers)

At risk of virological & biochemical 'flare-ups'

Presence of HBsAg for at least 6 months establishes the chronicity of infection

#### **Latent, past or cleared HBV infection**

HBsAg -ve, **HBcTotal antibody +ve**, HBV DNA -ve, (HBsAb + or -ve)

At risk of 'reactivation'

#### **Active HBV**

This term is no longer used. Current/Past infection should be used instead. For further differentiation, use the term 'highly replicating' virus (eAg+ve or high level of DNA)

#### **Flare-ups**

Occur in cases of current hepatitis B infection, where DNA levels shoot up with or without transaminitis.

HBV virological flare-up is defined as one of the following <sup>1</sup>:

- (1) 2 log (100-fold) increase in HBV DNA compared to the baseline level, or
- (2) HBV DNA >3 log (1,000) IU/mL in a patient with previously undetectable level, or
- (3) HBV DNA >4 log (10,000) IU/mL if the baseline level is not available

A hepatitis (biochemical) flare is defined as an ALT increase to 3 times the baseline level and >100 U/L.

#### **Reactivation**

Recurrence of hepatitis B in previously cleared infection. It covers scenarios where in a previously cleared infection :

- (1) HBV DNA becomes detectable or
- (2) reverse HBsAg seroconversion occurs (reappearance of HBsAg).

**HBV-associated liver failure**<sup>1</sup> is defined as one of the following:

- (1) impaired synthetic function (total bilirubin >3 mg/dL or international normalized ratio > 1.5)
- (2) ascites
- (3) encephalopathy or
- (4) death following HBV-associated liver failure attributed to HBV reactivation

#### **Sero-reversion**

Same as reactivation

#### **Occult HBV**

Presence of HBV DNA in the absence of HBsAg (very rare). Always rule out sample contaminations. True occult infections are repeatable, in more than one sample

#### **Isolated core antibody**

Presence of total core antibody in absence of sAg/ sAb/ e-Ab. Treat as past exposure to HBV however false positivity should be considered/ excluded.

#### **Oral nucleoside analogues**

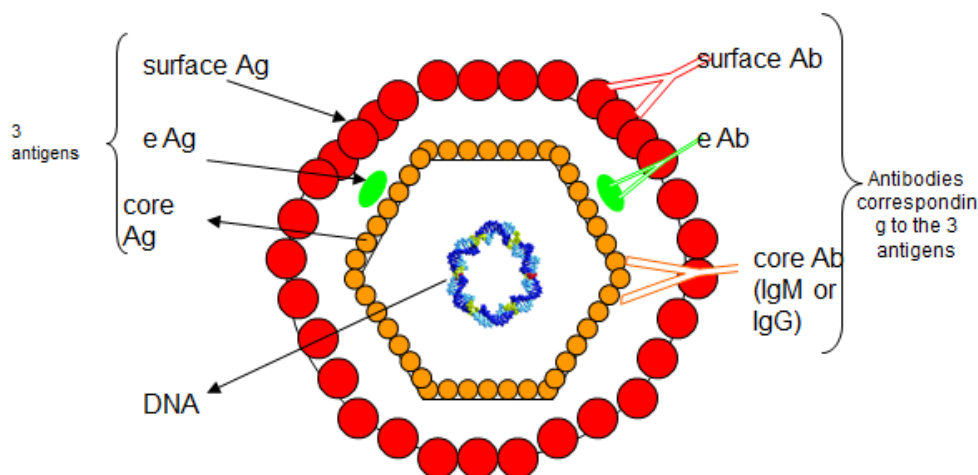
Drugs with anti-HBV activity which act by competing with naturally occurring nucleosides

#### **Oral nucleotide analogues**

Drugs with anti-HBV activity which act by competing with naturally occurring nucleotides

to HBsAg (referred to as HBsAb). These antibodies persist for a very long time, if not for the whole life of the patient.

- Patients who successfully clear HBV infection and confine the virus to latency do so with the help of T-cells and B-cells. Lapses in this control pose a risk of hepatitis B reactivation. This is initially seen as resurgence/come back of the virus (much higher DNA or sAg sero-reversion) which goes unchecked. Liver damage, with fulminant hepatic failure and death in severe cases, occurs once immune system starts coming back (withdrawal of immunosuppressants / recovery e.g. after initial phase of stem cell transplantation) and efficiently recognizes the presence of the virus<sup>2-6</sup>.
- The risk of reactivation, flare-ups, fulminant liver failure and death is increased in patients receiving specific immunosuppressive agents, especially B-cell depleting agents like rituximab<sup>1,5</sup> and ofatumumab<sup>1</sup> (see Table 1).
- Hepatitis B reactivation or flare-ups can be prevented by commencing anti-HBV drugs (i.e. lamivudine, entecavir or tenofovir) when indicated<sup>2, 7-12</sup>.
- Figure below shows a summary of HBV markers.



• Figure 1: Schematic diagram of hepatitis B showing various markers

## Section 2: Principles of prophylaxis, treatment and monitoring<sup>10</sup>

- Risk categorisation: This policy uses the recommendations of the American Gastroenterological Association<sup>12</sup> to classify immunosuppressive / chemotherapy agents into high, moderate and low risk. Management of

hepatitis B is based on these risk groups. *[Note variation from NICE guideline CG165 (2013) which does not use such classification<sup>13</sup>.]*

- **HBV+ve patients and treatment:** Immunosuppressed patients known to have current hepatitis B infection (ie HBsAg+ve) should be started on anti-HBV drugs **irrespective** of their eAg/DNA/LFTs status. This contrasts management of immunocompetent patients where these parameters are used to determine need for treatment.
- **Latent infection:** Patients with serological profile consistent with latent infection are further evaluated with a risk assessment based on drugs used. This is shown in Table 1 and used in Algorithm 1. Where indicated, anti-HBV drugs are used independent of ALT levels<sup>6</sup>. *[Note variation from NICE guideline CG165 (2013) around prophylaxis in latent infection<sup>13</sup>, where it is only advised for those on B-cell depleting agents. HBV reactivation in latent infection from other classes of immunosuppressant agents is well described, and the AGA guideline better reflects this knowledge].*
- **Is HBsAb important?:** The role of HBsAb (anti-HBS, hepatitis B surface Antibody) in protection against reactivation of virus is controversial and cases occur despite its presence. For this reason this marker is not used in making management decisions. *[Note variation from NICE guideline CG165 (2013)<sup>13</sup>.]*  
However, HBsAb may be added by Virology to determine if someone has true past exposure to HBV infection versus false positive results.

**Table 1. Comparative risk of hepatitis B flare-ups / reactivation with different immunosuppressive agents<sup>2,12</sup>:**

Planned immunosuppressant agent/therapy**
<b>High risk agents</b>
<b>Group A</b> <ul style="list-style-type: none"> <li>• B-cell depleting agents, e.g. rituximab, ofatumumab, ocrelizumab, daratumumab</li> <li>• Allogeneic Stem Cell Transplant patients<sup>6</sup></li> <li>• Autologous Stem Cell Transplant<sup>6</sup></li> <li>• Patients undergoing anti CD-19/22 CAR-T cell therapy<sup>14,15</sup></li> </ul>
<b>Moderate risk agents</b>
<b>Group B</b> <ul style="list-style-type: none"> <li>• Systemic corticosteroids <math>\geq 10\text{mg}</math> prednisolone (or equivalent), daily for <math>\geq 4</math> weeks*</li> <li>• Anthracycline derivatives, e.g. doxorubicin, epirubicin</li> </ul>
<b>Group C</b> <ul style="list-style-type: none"> <li>• Any other drugs used in treatment of myeloma<sup>16</sup></li> </ul>

<p><b>Group D</b></p> <ul style="list-style-type: none"> <li>• <b>Tumour necrosis factor (TNF)-α inhibitors</b>, e.g. etanercept, adalimumab, certolizumab, infliximab</li> <li>• <b>Cytokine or integrin inhibitors</b>, e.g. abatacept, ustekinumab, natalizumab, vedolizumab</li> <li>• <b>Tyrosine kinase inhibitors</b>, e.g. imatinib, nilotinib</li> <li>• <b>High-dose methotrexate</b> &gt;100mg/m<sup>2</sup> (excluding intrathecal use)</li> <li>• <b>Everolimus at Oncology doses (see Group G for renal transplant)</b></li> <li>• <b>Other chemotherapy drugs</b></li> </ul>
<p><b>Low risk agents</b></p>
<p><b>Group E</b></p> <ul style="list-style-type: none"> <li>• <b>Systemic corticosteroids, &lt;10mg daily prednisolone (or equivalent), for ≥4 weeks</b></li> </ul>
<p><b>Group F</b></p> <ul style="list-style-type: none"> <li>• <b>Systemic corticosteroids for &lt;4 weeks</b></li> <li>• <b>“Traditional” agents</b>, e.g. azathioprine, low-dose methotrexate, 6-mercaptopurine</li> <li>• <b>Cyclosporine (see Group G for guidance on renal transplant)</b></li> <li>• <b>Other agents used in solid organ transplant eg mTOR inhibitors, mycophenolate derivatives (see Group G for guidance on renal transplant)</b></li> </ul>
<p><b>Other agents</b></p>
<p><b>Group G:</b></p> <ul style="list-style-type: none"> <li>• <b>Unclassified/ unknown: Refer to Algorithm 1</b></li> <li>• <b>Renal transplant: See above for particular agents e.g. Rituximab, Alemtuzumab, corticosteroids, and follow respective advice if any 1 drug is identified as high risk.</b>                      Most classical immunosuppressives used in renal Tx carry a low risk of HBVr when used on their own (Cyclosporin, azathioprine, sirolimus) or have an unknown risk but are not identified to date as high risk (tacrolimus). The mTOR inhibitor Everolimus has caused HBVr when used at higher doses in Oncology, but has unknown risk at standard transplant dosing.<sup>17</sup> Mycophenolate acid derivatives are likely low risk in isolation, but are usually used as combination therapy.  <b>Duration and additive effect of combination immunosuppression is likely most critical factor. The overall immunosuppressive effect of the regimen must be decided by the parent team. If unsure of the risk of a drug/ combination, advise to follow guidance for highest considered risk. Suggest to treat all Renal Tx as moderate risk or higher whilst on combination immunosuppression (to at minimum facilitate monitoring and pre-emptive treatment if needed, as per EASL guidance).<sup>6</sup></b></li> <li>• <b>Other solid organ transplants: Patients needing other transplant types (performed elsewhere) should be screened where necessary by the parent team as part of transplant work up. If for some reason they are tested in STH as part of their transplant work-up, the results must be relayed back to the transplant team.</b></li> </ul>

\*Consider screening +/- consideration of prophylaxis in patients requiring frequent high dose pulsed steroids, e.g. methylprednisolone)

**Section 3: Screening patients (who to screen and what tests to send)<sup>2,11-12,16</sup>**

Use table 1 to determine the group of the planned immunosuppressive treatment (e.g. Group A= B-cell depleting agents).

**1. Groups A-D (±G): High and moderate risk immunosuppression**

All patients should be tested for:

- Hepatitis B surface antigen (HBsAg), and
- Hepatitis B total core antibody (HBcTotal Ab)



Results should be reviewed by parent team and actioned **prior** to initiation of immunosuppressive treatment. <sup>10-12</sup>

## 2. **Group E and F (±G): Low risk immunosuppression**

### a) Group E

Low dose steroids are generally considered to carry a low risk of reactivation. However, this may be increased in patients with a current HBV infection, who are deemed to be at moderate risk according to the AGA. In order to identify those with a current infection, all patients in this group should be screened for:

- Hepatitis B surface antigen (HBsAg), and
- Hepatitis B total core antibody (HBcTotal Ab)

### b) Group F: All other low risk agents

Although patients taking these other agents are classed as having a low risk of HBV flare/ reactivation, some may still require testing to identify those with a current infection and allow viral hepatitis specialist input.

Patients falling into any of the risk groups listed below, should be tested for Pre-Steroids Virology Screen (see Box 2) at baseline, **regardless of immunosuppression planned** and in accordance with 2012 NICE Public Health Guidance PH43<sup>18</sup>. Testing for hepatitis B serology otherwise is not indicated.

- People born/raised in a country with intermediate or high prevalence (≥2%) of chronic HBV. This includes all countries in Africa, Asia, the Caribbean, Central and South America, Eastern Europe, the Middle East and the Pacific islands
- Patients infected with HIV and/or hepatitis C (HCV) infection
- History of injecting drug use, prison contact, homeless people, young people living in care
- Immigration detainees
- Contacts of HBV infected people (sexual partners, household contacts, children of HBV infected mothers)
- Unprotected sexual contact in, or with partner from, intermediate/high prevalence country (see above); sexual contact of injecting drug user; man who has sex with men; commercial sex workers
- Medical exposure, including: receiving blood products in the UK before 1970; medical treatment abroad in areas of intermediate/high prevalence

(see above); recipients of a needle-stick injury if donor is HBsAg detected or unknown HBV status

### **Box 2: Requesting Hepatitis B tests**

#### **ICE requests:**

HBsAg and HBcTotal Ab tests may be ordered as individual tests on ICE but this is actively discouraged. Special ICE profiles created for use in context of this guideline enable the laboratory to perform additional tests and tackle results as appropriate. Choosing these ensures additional tests are not missed on samples when indicated, smooth laboratory workflow and timely results to the end-user.

Choose from one of the following two screens:

#### **1. Pre-Immunosuppression Virology Screen**

- Indicated where immunosuppression with Group A-E agent has been planned
- Contains: HBsAg; HBcTotal Ab; HIV Ag/Ab; HCV Ab; CMV IgG; EBV IgG and VZV IgG
- Please ensure verbal consent from patient obtained and documented prior to HIV screening.

#### **2. Pre-Steroids Virology Screen**

- Not generally indicated and is for use only in patients receiving Group F immunosuppressants who are identified to be in a risk group (as described in Section 3.2)
- Contains: HBsAg and HBcTotal Ab
- If additional risk factors for HIV or HCV infection exist, you'll have to order these separately.

Please be aware of some other haematology / renal / specialty-specific screens which already contain both HBV sAg/cAb (e.g. **Pre Auto / Allo Recipient Screen (Haem), Renal Tx screens, Pre-Immunosuppression virology screen**). If these have been previously requested, there is no need to re-order.

#### **Paper requests:**

Only to be used when ICE is not accessible. In clinical details specify whether "High/Moderate/Low risk" for HBV reactivation and ask for screens as named above (no need to specify tests individually)

# Algorithm 1: Parent Team's guide to management of HBV in immunosuppressed patients

Perform relevant Virology Pre-Immunosuppression Screen via ICE requesting (see section 3 for details)

If sample is already in the Lab, use [online test requesting portal](#) to request Pre-Immunosuppression virology screen ("ATNF screen")

## HBV NEGATIVE:

HBsAg	Not detected
HBcTotal Antibody	Not Detected
HBsAntibody	(any result)

**Action Required:** No further action

## CURRENT HBV INFECTION:

HBsAg	DETECTED
HBcTotal Antibody	DETECTED
HBsAntibody	(any result)

### Risk:

- 41%-53% risk of aggravating HBV with some monoclonal antibodies. May lead to fulminant hepatic failure
- Mitigated by anti-HBV medication if patient deemed to be at risk due to immunosuppression

**Action Required:** follow below box for **ALL patients** with current HBV infection

## LATENT HBV INFECTION:

HBsAg	Not detected
HBcTotal Antibody	DETECTED

PLEASE NOTE INTERPRETATIONS GIVEN BELOW DO NOT APPLY IF PATIENT HAS RECEIVED BLOOD PRODUCTS OR IMMUNOGLOBULIN IN THE LAST 3 months. CONTACT VIROLOGY IF THIS IS THE CASE

### Interpretation:

- HBs Antibody or HBe Antibody DETECTED = Past & cleared HBV infection. Virus latent in liver
- HBs Antibody or HBe Antibody BOTH Not Detected = Isolated core Total Antibody. Unable to exclude past infection. To be dealt as if this was past infection

Always exclude possibility of passive serological profile due to transfusion, and if required discuss further with a virologist.

### Risk:

- 1.7%-18% risk of HBV reactivation. This is characterised by re-appearance of HBsAg, HBV DNA or both
- Mitigated either by anti-HBV medication or by regular blood monitoring of viral markers/ pre-emptive treatment

**Action Required:** Actions depend on immunosuppressive regimen (as per Table 1)

**Group A-D agents**

**Group E/F agents:** Low risk of reactivation. Referral to Specialist clinic not needed/ no prophylaxis/ no monitoring (discuss with ID/hepatology/ virology only if concerned)

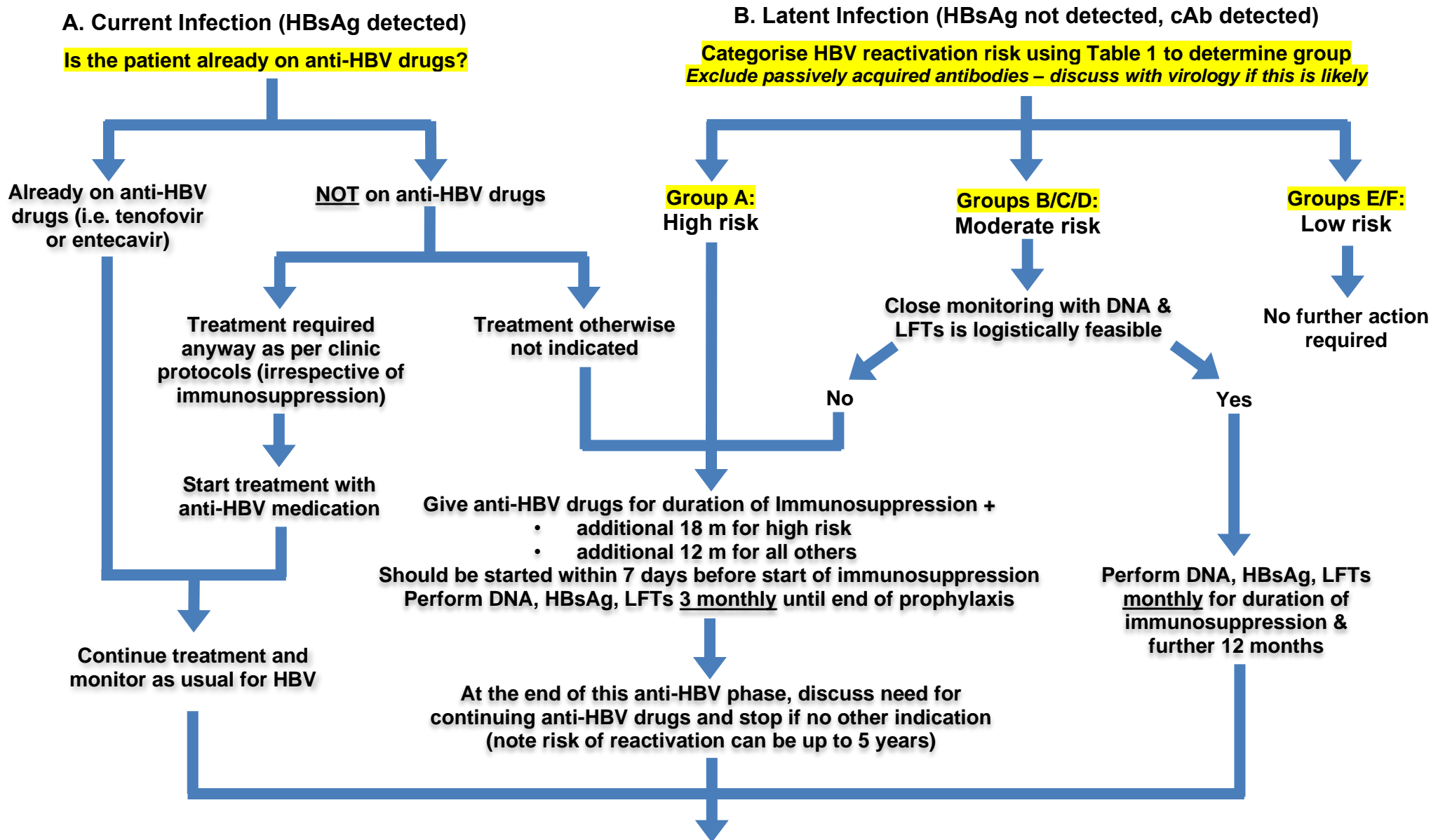
**Group G:** The number of immunosuppressants (including monoclonal antibodies) where risk of viral reactivations is not known is quite high. We advise checking product information sheet, recommendations from professional bodies & published literature. If it is still unclear but you are worried, specify drug mechanism & seek advice from either a Virologist, Hepatologist or ID Specialist. Chances are there will be paucity of data to make a solid recommendation and a pragmatic decision will have to be taken. This will be heavily driven by the degree of your concern regarding level of immunosuppression.

### Actions Required from Specialty Parent Team:

- Formally refer to Viral Hepatitis Specialist: patient needs to be seen at least 2 weeks before immunosuppression start date where able. If patient is already on immunosuppression/ urgent need to start, contact ID SpR via switch. If transplant patient, inform parent transplant team.
- If patient already under care of Hepatitis Specialist, inform them of impending immunosuppression
  - Details of immunosuppression and planned start date will be required by their clinic
- If not already performed by Lab, request HBV DNA test on sample already in Lab ([online test requesting portal](#))
- After initial referral, report any new derangement in LFTs to Viral Hepatitis Specialist team

**Note:** Newly diagnosed HIV or HCV RNA positive patient should be referred to Infectious Diseases or Viral Hepatitis Clinic

## Algorithm 2: Specialist in Viral Hepatitis's guide to management of HBV in immunosuppressed patients



Any new abnormality in liver function tests should prompt full clinical assessment and further investigation in liaison with virology. HBV reactivations should be dealt in the same way as current infection in this algorithm

## Section 4: Patient Management

### **Responsibilities of Parent Team** (follow *Algorithm 1*)

- Prompt patient testing to identify patients at risk of hepatitis B flare-ups, reactivations and those infected with HIV or Hepatitis C.
- Classification of the reactivation risk of the immunosuppressive regimen the patient will receive (examples listed in Table 1). This may require checking the product information insert/ literature search, particularly for new drugs.
- Note there may be an additive effect with multiple drugs. On occasions it may be safer to classify the drug in a higher risk group if the risk is unknown or there are other patient factors to consider. The table is only a guide.
- Ensure infected or patients at risk are referred to viral hepatitis / HIV clinic so that they are seen well before start of the planned immunosuppression (ideally refer 2 or more weeks ahead to allow time for referral/ any further testing that may be needed). Any treatment / prophylaxis required should be started no longer than in the week preceding start of immunosuppression.
- Ensure details of immunosuppression along with start dates are provided to specialist clinic at the time of referral.
- If the patient is already on immunosuppression when the need for specialist input is identified, ensure urgent discussion with a viral hepatitis specialist (contact ID SpR via switch).
- Transplant patients should be screened where necessary by the parent transplant team as part of transplant work up, but could be tested by other services for HBV for other reasons. Any new HBV diagnosis in a transplant patient should be urgently discussed with the patient's transplant team to determine HBV reactivation risk and any other transplant concerns.
- Report any new abnormality of transaminitis to viral hepatitis specialist.

### **Responsibilities of Specialist Viral Hepatitis Clinic** (follow *Algorithm 2*)

- Where the patient is referred prior to starting immunosuppression, arrange to see patients in clinic well in advance, and no later than one week before start of immunosuppressive therapy. If the patient is unable to attend clinic for logistical or health-related reasons, consider alternative means of review/ guiding a parent team to allow information to be gathered/ investigations to be completed (e.g. by phone consult).
- If the patient is already on immunosuppression, review how quickly the patient can be seen, e.g. are they a current STH in-patient and could be reviewed at that site. If there is likely to be a delay, consider a decision on risk of reactivation and need for any antivirals with available information.
- If the patient is a transplant patient, ensure the parent transplant team has been notified.
- Arrange initiation of and follow up for anti-hepatitis B drugs as appropriate.
- Follow up patients and organize necessary blood tests for appropriate management of the patient. This could be in conjunction with other teams

STH guidelines on management of HBV in immunocompromised patients (V3) July 2019  
involved in the patient's care including their GP but should be directed by hepatitis clinic.

- Take full responsibility for management of patients' hepatitis B in context of this policy.
- Liaise with virology to ensure all necessary workup has been performed.

## Section 5: Anti-HBV drugs<sup>12,16</sup>

### When to start anti-HBV drugs

- HBsAg+ patients who need treatment anyway as per clinic protocols:  
Patients should be started on treatment as soon as practically possible, and at the very latest, simultaneously with the onset of immunosuppressive therapy.
- Patients who only require anti-HBV drugs only because of immunosuppression: (e.g. who do not otherwise warrant treatment as per clinic protocols, or those with latent infection and receiving high/moderate risk immunosuppressive agents. Anti-HBV drug should be initiated as soon as possible before or, at the latest, simultaneously with the onset of immunosuppressive therapy.  
Anti-HBV drug should be prescribed under the direction of a viral hepatitis specialist clinic (i.e. Infectious Diseases or Hepatology).

### What drug to start:

- Start (or switch to) treatment with either tenofovir disoproxil 245mg once daily or entecavir 0.5mg once daily (renal dose adjustment as outlined in Table 2). *[Note variation from NICE guideline CG165 (2013)<sup>13</sup> which advises lamivudine in some patients; due to risk of resistance this antiviral is not recommended in STH]*

**Table 2. Dose adjustments of oral nucleos(t)ide drugs in patients with impaired creatinine clearance**

\* indicates doses applicable to haemodialysis or continuous ambulatory peritoneal dialysis (CAPD) patients

#### Entecavir:

Creatinine clearance (ml/min)	Entecavir (Baraclude®) dose	
	Nucleoside naïve patients	Lamivudine-refractory or decompensated liver disease
≥ 50	0.5 mg once daily	1 mg once daily
30 - 49	0.25 mg once daily* OR 0.5 mg every 48 hours	0.5 mg once daily
10 - 29	0.15 mg once daily* OR 0.5 mg every 72 hours	0.3 mg once daily* OR 0.5 mg every 48 hours
< 10	0.05 mg once daily* OR 0.5 mg every 5-7 days	0.1 mg once daily* OR 0.5 mg every 72 hours

**Tenofovir disoproxil:**

Creatinine clearance ml/min	Tenofovir disoproxil dose
≥ 50	245 mg daily
30 to 49	245 mg alternate days
< 30	245 mg twice weekly

Duration of therapy in HBV+ve patients:

- Patients with chronic HBV infection who require treatment irrespective of their immunosuppression should have ongoing management by a hepatitis specialist, with stopping rules as per any other chronically infected patient.
- In patients with chronic infection but who only require prophylaxis due to their immunosuppression, or any patient started on prophylaxis for a past HBV infection, should continue anti-HBV medication during immunosuppressive therapy and
  - for additional 18 months after completion of immunosuppressive therapy for rituximab-based regimens and allogeneic stem cell transplant patients, or
  - for additional 12 months after completion of immunosuppressive therapy<sup>1</sup> for patients receiving moderate and other high risk drugs/interventions<sup>1</sup>
- Monitoring of patients on anti-hepatitis B drugs should be managed by the viral hepatitis specialist clinic.

**Section 6: Monitoring patients**

- HBsAg +ve patients on anti-HBV drugs should be monitored with HBV DNA, HBsAg, HBeAg, HBeAb and LFTs as per existing clinic protocols. Expected frequency for viral markers is no more than every three months.
- HBsAg –ve patients on anti-HBV drugs should also be monitored every three months with HBsAg and HBV DNA.
- Patients not on anti-HBV drugs but followed up with pre-emptive strategy (also referred to as on-demand therapy) should be monitored with liver function tests, HBV DNA and HBsAg every
  - 1 month for moderate risk immunosuppression
- Large proportion of HBV reactivations develop after anti-HBV drug discontinuation<sup>6</sup>. Monitoring should be done for the duration of immunosuppression and for additional:
  - 18 months after withdrawal of anti-HBV drugs for high risk immunosuppressants (every month for first three months, then every three months)

- STH guidelines on management of HBV in immunocompromised patients (V3) July 2019
- 12 months after withdrawal of anti-HBV drugs for moderate risk immunosuppressants (every three months)
  - Investigations for any new abnormality noted in liver function tests should include HBsAg and HBV DNA.

### **Auditable standards**

1. 100% of patients in whom potentially moderate or high risk immunosuppressive treatment (defined in Table 1) is being planned are screened prior starting treatment for HBsAg and HBcTotal Ab
2. 100% of patients with baseline detectable HBsAg are commenced on a nucleos(t)ide analogue before commencing potentially moderate or high risk immunosuppressive treatment (defined in Table 1)
3. 100% of patients with baseline undetectable HBsAg but detectable HBcTotal Ab are commenced on a nucleos(t)ide analogue before commencing potentially moderate or high risk immunosuppressive treatment (defined in Table 1)

All major specialties within STH NHS FT administering potentially moderate and/or high risk immunosuppressive treatments will audited against these standards on an annual basis (April), for patients commencing potentially moderate and/or high risk immunosuppressive treatments in the preceding financial year.

### **Section 7: References**

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