CCHCS Care Guide: Hepatitis B

**Summary**

**Goals**
- Screen for chronic Hepatitis B Virus (HBV) infection
- Vaccinate non-immune patients
- Evaluate patients with active HBV for treatment
- Monitor patients for hepatocellular carcinoma (HCC) as appropriate
- Screen for substance use disorder

**Diagnostic Criteria**

Chronic HBV is a deoxyribonucleic acid (DNA) virus infection defined by Hepatitis B surface antigen (HBsAg) present for > 6 months. Disease presentation can vary:
1. Serum HBV DNA varies from undetectable to several billion IU/mL
2. Subdivided into Hepatitis B e-antigen (HBeAg) positive and negative. The “e” antigen represents replicating virus and infectivity.
   - **HBeAg positive patients** have HBV DNA levels that are typically > 20,000 IU/mL and they have an increased risk of progressive liver disease, but they can respond better to treatment
   - **HBeAg negative patients** typically have lower HBV DNA values (2,000-20,000 IU/mL) but can have elevated alanine aminotransferase (ALT) levels, necroinflammation in their liver, a more fluctuating and less predictable course to cirrhosis, and less response to treatment
3. Normal or elevated ALT and/or aspartate aminotransferase (AST) levels
4. Biopsy results show chronic hepatitis with variable necroinflammation and/or fibrosis (see page 5).

**Evaluation**

Indication for screening for chronic HBV is based on several risk factors, most of our patients have indications (see page 3). Screening is based on HBsAg and Hepatitis B surface antibody (HBsAb) in addition to total hepatitis B core antibody (anti-HBc) (see page 4 for interpretation). Treatment is not indicated in all patients, but for those being considered for additional evaluation, testing is done which can include:
- History and Physical (H&P): mode of transmission, family history of liver disease and/or HCC cancer, and Hepatitis A Virus (HAV) vaccine status
- Sexual risk assessment and substance use disorder screening
- Labs: complete blood count (CBC), comprehensive metabolic panel (CMP), INR, HBeAg, HBe antibody (anti-HBe), and HBV DNA
- Identify viral co-infections: Hepatitis C, Human Immunodeficiency Virus (HIV), and Hepatitis D (anti-HDV)
- In some patients liver fibrosis staging with Fibroscan or FibroSure, or in some rare cases liver biopsy

**Prevention**

Vaccinate non-immune patients for HAV and/or HBV (for those who screen negative and are still susceptible). For HBV, use current 2-dose formula product (e.g., Heplisav-B® which is only 2 doses separated by 1 month). Note that the HBV/HAV combination vaccine is no longer favored and for those patients with both HAV and HBV non-immune status, use the 2 dose HBV vaccine and the 2 dose Hepatitis A series (1440 units/mL, Havrix®) for 4 shots total. Certain populations need a test of immunity 1 month after completing the HBV vaccine series, including chronic dialysis patients, people with HIV and other immunocompromised people (disease state or immunosuppressant medications), and patients with an isolated core antibody positive (cleared HBV, but reactivation risk). See Attachment A.

Patients with chronic HBV should be vaccinated for HAV if not immune. Offer COVID-19 (see CDC COVID-19 Guidelines), annual influenza and pneumococcal vaccines (Note: Pneumococcal vaccination recommendations have changed in 2022. Please see the new CDC Pneumococcal Guidelines). HBV vaccination is not needed in patients with chronic HBV, but it will not harm the patient if they do receive the vaccine.

**Treatment**

- Refer to the HBV Central Team for assistance with treatment and consultant decisions
- Treatment with antiviral agents (interferon alpha and nucleoside/nucleotide analogues [NAs]) is unlikely to eradicate HBV infection, but is used to suppress viral replication and hopefully, induce seroconversion to HBeAg negative status and potentially reduce progression to cirrhosis or HCC.
- The decision to treat is based on multiple factors including:
  - Severity of liver disease/risk of progression (patients with cirrhosis generally treated)
  - Co-infection with HIV, HDV, HCV (patients generally treated)
  - Higher ALT and HBV DNA levels
  - HBeAg status (HBeAg negative patients less responsive to treatment)
  - Age of patients/duration of infection (Patients > 40 more likely to be treated)
- Typically patients should be referred to a specialist for consideration of HBV treatment (see page 7)

**Monitoring (see pages 7-8)**

- Follow-up visit
  - On treatment: every 3 months or as indicated
  - Not on treatment: every 6 months or as indicated

- Labs
  - On treatment: follow specialist direction
  - Not on treatment: frequency of ALT and HBV DNA level monitoring varies depending on HBeAg status
    (See algorithm page 6)

- Ultrasound
  - HCC is a lifetime risk. Optimal screening is not known but is in higher risk group screen for HCC with ultrasound every 6 months (see page 4).

**Alerts**

- Acute flare of HBV may occur with treatment discontinuation, monitor patient for several months after discontinuation
- If patient has a co-infection with Hepatitis C Virus (HCV), consult with the HCV Central Team. Treatment for HBV should be initiated concurrently or prior to HCV treatment. Order “Consult to HBV Central Team” in the electronic health record system (EHRS)

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</tbody>
</table>

*Information contained in the Care Guide is not a substitute for a health care professional’s clinical judgment. Evaluation and treatment should be tailored to the individual patient and the clinical circumstances. Furthermore, using this information will not guarantee a specific outcome for each patient. Refer to “Disclaimer Regarding Care Guides” for further clarification.*
Screen for chronic HBV infection with:
- HBsAg
- Anti-HBs
- Anti-HBc (Total or IgG*)

*Do not include anti-HBc IgM in HBV screening panel unless suspect acute HBV.

HBsAg Positive
- See HBV Evaluation, Counseling, Monitoring, Treatment and HCC Surveillance (page 4)
- If treatment indicated, see Treatment pages 5-7

HBsAg Negative
- See HBV Serology Interpretation and Monitoring (page 4)
- If susceptible to HBV, (anti-HBc negative and anti-HBs negative) then vaccinate
- If prior HBV infection (anti-HBc positive), counsel on HBV reactivation risk
HBV is a DNA virus that replicates in the liver with hematologic dissemination systemically. It is a blood borne and sexually transmitted pathogen that is spread through percutaneous mucosal exposures to infected blood and body fluids.

- The majority of adults acutely infected with HBV eventually clear HBsAg from the blood and develop antibodies to HBsAg (anti-HBs) that confer long-term protection from re-infection.
- Only a small subset of adults acutely infected with HBV develop chronic HBV infection (HBsAg-positive for > 6 months).
- Risk of chronic HBV is much greater in persons from parts of the world where HBV is endemic and acquired perinatally.
- Immunosuppressed individuals also are more likely to develop chronic HBV infection.
- Ten genotypes of HBV, labeled A through J, have been identified. Prevalence varies geographically. HBV genotypes A through H have been found in the U.S., with A, B, and C being most prevalent.
- HBV genotypes may play an important role in the progression of HBV-related liver disease as well as response to interferon (IFN) therapy.
- HBV genotyping is NOT typically done in the primary care setting and should ONLY be ordered if requested by a specialist.

**Course of Infection:**
The course of chronic HBV infection is varied and unpredictable and may result in one of three main presentations:
- **Chronic active HBV**: associated with active hepatic necroinflammation and progressive fibrosis and is accompanied by a persistently positive HBsAg, serum HBV DNA > 20,000 IU/ml, and persistent or intermittent elevations in ALT levels.
- **Inactive carrier state**: persistently positive HBsAg, but relatively quiescent disease activity, a negative HBeAg and positive or negative anti-HBe, HBV DNA level < 2,000 IU/ ml, and normal ALT levels, but may be accompanied by intermittent exacerbations or flares.
- **Resolved infection**: once established, chronic HBV can resolve spontaneously with clearance of HBsAg and development of anti-HBs, but does so in less than 1–2% of patients per year.

**Complications of Chronic HBV:**
- Individuals with chronic HBV infection are at increased risk of developing decompensated cirrhosis and HCC.
- Rates of progression to cirrhosis or HCC are increased by a variety of factors, including:
  - HBeAg positivity; higher HBV DNA or ALT levels; HBV genotype C; co-infections with HCV, HDV, or HIV; immunosuppression; advanced age; duration of infection; alcohol ingestion; male gender; and family history of HCC.

**Treatment:**
- Treatment with antiviral medications is unlikely to completely eradicate HBV, the goal is to suppress viral replication and induce seroconversion to HBeAg-negative status, and thereby potentially prevent or reduce progression to cirrhosis or HCC.
- Medications approved for treatment of HBV infection may require many years of treatment (NAs). Therefore, the decision to recommend antiviral treatment should be based on a variety of factors. In California Correctional Health Care Services (CCHCS), specialty referral is required. (See page 7)

**Screening for Chronic HBV infection**
Screening for chronic HBV is done by looking at results of HBsAg and anti-HBs, and anti-HBc for further specificity.

All incarcerated patients are considered high risk and will be offered screening within CCHCS (opt out).

In the community, people at higher risk should be screened based on the following factors:
- Born in countries where the HBV prevalence is ≥ 2%.
- Born in the US, and not vaccinated, and parents were from areas with HBV prevalence > 8%.
- High risk sexual activities or history of sexually transmitted infections (Men who have sex with men).
- Household contacts of persons with chronic HBV.
- Ever injected drugs.
- Inmate in correctional facility.
- Co-infected with HIV or HCV.
- Undergoing dialysis.
- Pregnant patients (routine screening imperative, due to the risk of perinatal transmission).
- Asymptomatic patients with elevated ALT levels of unknown etiology.
- As clinically indicated (e.g., patients with signs or symptoms of acute or chronic hepatitis, percutaneous blood exposure or planned or current treatment with immune suppressants including chemotherapy or anti-tumor necrosis factor alpha medications).

For interpretation see next page
**INTERPRETATION OF SCREENING FOR CHRONIC HBV INFECTION**

Note the results of the screening tests.
- Persistence of HBsAg for > 6 months implies chronic infection.
- Presence of anti-HBs typically indicates patient is immune from prior infection, or has received vaccination.
- HBV vaccination is indicated for patients who are not infected and not immune.
- Consider HAV vaccination for all HAV non-immune patients with priority given to patients with underlying liver disease. (Prescreening for immunity to HAV, by detecting IgG [or total] anti-HAV, should also be considered prior to vaccination for Native American populations and foreign-born patients from Latin America, Africa, Southeast Asia, and China where HAV infection is endemic, patients with HCV, patients living with HIV, and for inmates ≥ 50 years old).

### Interpretation of Screening Tests for HBV Infection

<table>
<thead>
<tr>
<th>HBsAg</th>
<th>Anti-HBc (Total or IgG)</th>
<th>Anti-HBs</th>
<th>Interpretation</th>
<th>Management</th>
<th>Vaccinate?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>Positive/ (IgM Neg)</td>
<td>Negative</td>
<td>Chronic Hepatitis B</td>
<td>Additional testing and management needed— see evaluation section</td>
<td>No</td>
</tr>
<tr>
<td>Positive</td>
<td>Positive/ (IgM Pos)</td>
<td>Negative</td>
<td>Acute infection</td>
<td>Monitor to determine clearance or development of Chronic Hepatitis B</td>
<td>No</td>
</tr>
<tr>
<td>Negative</td>
<td>Positive</td>
<td>Positive</td>
<td>Past HBV infection, resolved</td>
<td>No transmission risk, HBV dormant in the liver. No further management, unless immunocompromised or undergoing chemotherapy or immunosuppressive therapy</td>
<td>No</td>
</tr>
<tr>
<td>Negative</td>
<td>Positive</td>
<td>Negative</td>
<td>Resolved HBV infection without immunity or with waning immunity, false positive, occult HBV infection</td>
<td>If immunocompetent counsel reactivation risk if on immunosuppressant medication, HBV DNA testing if immunocompromised</td>
<td>Yes</td>
</tr>
<tr>
<td>Negative</td>
<td>Negative</td>
<td>Positive</td>
<td>Immune from prior vaccination</td>
<td>No further testing</td>
<td>No</td>
</tr>
<tr>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Susceptible, uninfected and not immune</td>
<td>No further testing</td>
<td>Yes</td>
</tr>
</tbody>
</table>

### MANAGEMENT OF HBsAg POSITIVE PATIENTS

**Patient Counseling**

Patients diagnosed with chronic HBV infection should be counseled by a health care provider about the natural history of the infection, potential treatment options, and specific measures for preventing transmission of HBV infection to others (during incarceration and upon release). Provide the information and recommendations on Patient Education pages PE-1 and PE-2. These include:
- Most persons with HBV infection will remain healthy, but a small number of persons will develop serious liver disease.
- Drug treatment options for chronic HBV are developing. Medications may or may not be appropriate for you.
- Most people need blood tests at least every 6 months and many need liver ultrasound to look for development of liver cancer (see below).
- Make sure every new healthcare provider knows that you have chronic HBV, especially if you need treatment with immunosuppressant medications.
- Annual sexual risk assessment (EHRS banner bar AdHoc sexually transmitted Infection Screening Form).
- Substance use disorder discussions, screening and referral as appropriate.

**Hepatocellular Carcinoma (HCC) Screening**

- HCC occurs in persons with chronic HBV infection with or without cirrhosis.
- The goal of screening is to improve survival through early detection and treatment of HCC. Screening at baseline and every 6 months with a liver ultrasound is recommended for patients who meet the indications below:
  - All persons with cirrhosis, including persons who become HBsAg negative
  - The following populations, even in the absence of cirrhosis:
    - Asian or black/African males > 40 years old
    - Asian females > 50 years old
    - Persons with a family history of HCC
    - Persons with HDV co-infection
A baseline evaluation is indicated for patients who have chronic HBV infection to help determine if referral for anti-viral therapy is indicated. Evaluation should include the following:

**History/Examination**
- Age and mode of initial infection
- Symptoms/signs of cirrhosis
- Alcohol history and metabolic risk factors
- Family history of HCC
- HAV vaccination status
- Targeted physical examination (assess for evidence of decompensated cirrhosis such as jaundice, ascites, encephalopathy, asterixis, and peripheral edema).

**Routine Laboratory Tests**
- CBC with differential and platelet count
- Comprehensive metabolic panel including:
  - AST/ALT+
  - Total bilirubin
  - Alkaline phosphatase
  - Albumin
  - Creatinine/BUN
- INR
- Consider evaluation for other causes of liver disease including hemochromatosis, Wilsons disease or autoimmune hepatitis, if indicated

**Serology/Virology**
- HBeAg/anti-HBe
- HBV DNA (PCR)
- Anti-HCV
- Anti-HDV
- Anti-HIV
- Although there are multiple HBV genotypes identified, genotype testing is NOT yet a routine part of the primary care diagnostic evaluation and treatment strategy for chronic HBV
- Anti-HAV (total or IgG) to determine need for vaccination if none documented

**Imaging/Staging Studies**
- Abdominal ultrasound if HCC risk
- Elastography (e.g., FibroScan) or Serum fibrosis assessment.

**Determining severity of liver fibrosis to guide therapy**
Some groups of patients including those who are HBeAg positive with HBV DNA levels > 20,000 IU/mL and ALT levels less than 2 X upper limit of normal (ULN) should undergo testing to evaluate degree of liver fibrosis, especially those > 40 years old and who were infected at a young age (i.e., long duration of infection).

- Liver biopsy offers the best means of assessing both fibrosis and inflammation. If the biopsy specimen shows moderate or severe inflammation (A2 or A3) or significant fibrosis (F2), treatment is recommended.

  **Liver biopsies are invasive and present significant potential risk for the patient. Consultation with specialist is strongly recommended if liver biopsy is being considered, especially in light of non-invasive testing being available.**

- Alternative methods to assess fibrosis are elastography (preferred) and liver fibrosis biomarkers (FibroTest). If these noninvasive tests indicate significant fibrosis (≥ F2), treatment is recommended.

**Which patients require treatment:**
Whether to initiate treatment should be generally determined by a specialist for the following reasons:

- The risks and benefits of long-term treatment are unknown.
- The potential for drug resistance is of concern with some treatments.
- Discontinuing therapy in some persons who are responding to treatment may result in relapse.
- A subset of infected persons spontaneously clear HBV infection without therapy or have inactive disease that may not progress.
- Future treatment options may be more effective, better tolerated, and more easily administered.

The decision to recommend antiviral treatment should be based on the severity of liver disease, the likelihood of response, existing co-morbid conditions, the potential for adverse reactions, and other relevant patient-specific factors.

See next page for algorithm on who to treat, and how to monitor patients not receiving treatment.

- In general treatment is usually indicated for patients with cirrhosis, co-infected with HIV, HBeAg positive with ALT ≥ 2X ULN, patients with F2 fibrosis, and those patients with persistent ALT elevation especially those patients > 40 years old
- Monitoring of ALT and HBV DNA are more typical for patients with HBeAg negative with HBV DNA < 2000; HBeAg positive with HBV DNA < 20,000, HBeAg with HBV DNA ≥ 20,000 with ALT < 2X ULN and age < 40 years old; patients with F0-F1 fibrosis
Patients who are HBsAg positive

Does patient have cirrhosis?

Yes

Is patient co-infected with HIV?

Yes

Refer to CCHCS HIV provider for probable lifelong HBV treatment

HBeAg positive:

What is the ALT level? (^See below)

Is patient co-infected with HCV?

Yes

Refer to CCHCS HCV Central Team for evaluation BEFORE treating HCV or HBV. HBV must be treated during HCV treatment

ALT < ULN:

HBV DNA < 2000

Do NOT Treat - monitor ALT and HBV DNA every 3-6 months and HBeAg every 12 months

HBV DNA ≥ 2000

Monitor ALT and HBV every 3 months for a year then every 6 months. STRONG RECOMMENDATION to refer for evaluation

ALT > 2X ULN:

HBV DNA ≥ 2000 REFER for Treatment

HBV DNA < 2000

Need further evaluation for other causes ↑ ALT, and assess disease severity with noninvasive test or liver biopsy. STRONG RECOMMENDATION to refer for evaluation, especially if fibrosis ≥ F2

ALT > ULN but < 2XULN

HBV DNA ≥ 2000 or < 2000

Need further evaluation for other causes ↑ ALT, and assess disease severity with noninvasive test or liver biopsy. STRONG RECOMMENDATION to refer for evaluation, especially if fibrosis ≥ F2 or persistent ALT > ULN and HBV DNA ≥ 2000, especially if age > 40

NOTE: American Association for the Study of Liver Disease (AASLD) HBV Guidelines consider normal ALT as < 35 for males, < 25 for females, which is different from the Electronic Health Record System (EHRS) that has normal < 46 males/females

ALT > ULN but < 2XULN

HBV DNA > 20,000

Refer to outside specialist for possible HBV treatment (Loma Linda University Hepatology econsult preferred)

HBeAg negative: What is the ALT level? (^See below)

HBeAg positive: What is the ALT level? (^See below)

ALT < ULN:

HBV DNA > 20,000

Do NOT Treat - monitor ALT and HBV DNA every 3-6 months and HBeAg every 6-12 months

ALT > 2X ULN:

HBV DNA > 20,000 REFER for Treatment

[HBV DNA 2000-20,000IU/ml may represent seroconversion - monitor every 1-3 months and if persists > 6 months then REFER for Treatment]

ALT > ULN but < 2XULN

HBV DNA > 20,000

Need further evaluation for other causes ↑ ALT, and assess disease severity with noninvasive test or liver biopsy. REFER to consider treatment especially if fibrosis ≥ F2 and/or age > 40.

[HBV DNA 2000-20,000IU/ml may represent seroconversion - monitor every 1-3 months and if persists > 6 months then REFER for Treatment]
## Referral for Treatment

The CCHCS HBV Central Care Team is the first line referral option in newly identified patients not already established with an outside specialist. Use the EHRS order “Consult to HBV.” Once it is determined that patient meets the criteria for consideration of antiviral treatment for chronic HBV, they should be referred to a specialist. Loma Linda University (LLU) Hepatology is the preferred specialist. The econsult drop down choice is “Hepatology, (LLU Hepatitis B Only)”. Note: the Central HBV Team will place econsults, but primary care providers can also. Please make sure that the lab evaluation as outlined in page 5 is complete. Patients who are co-infected can be referred to the appropriate CCHCS providers as noted below. If the patient needs to be seen “in person,” an eRFS to LLU Hepatology Team via Telemedicine can be placed.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Refer to</th>
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<tbody>
<tr>
<td>HCV co-infection</td>
<td>CCHCS HCV Central Team + outside specialist*</td>
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<tr>
<td></td>
<td>(LLU hepatology econsult preferred)</td>
</tr>
<tr>
<td>HIV co-infection (generally lifelong suppressive treatment is given)</td>
<td>CCHCS HIV provider + outside specialist*</td>
</tr>
<tr>
<td></td>
<td>(LLU hepatology econsult preferred)</td>
</tr>
<tr>
<td>Cirrhosis-compensated or decompensated</td>
<td>CCHCS HBV Central Team + outside specialist*</td>
</tr>
<tr>
<td></td>
<td>(LLU hepatology econsult preferred)</td>
</tr>
<tr>
<td>Hepatocellular carcinoma (HCC) with HBV</td>
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<tr>
<td>HBV DNA ≥ 20,000 IU/ml and ALT ≥ 2x ULN</td>
<td></td>
</tr>
<tr>
<td>Liver biopsy with ≥ stage 2/4 (more than portal) fibrosis or moderate/severe inflammation</td>
<td>CCHCS HBV Central Team + outside specialist*</td>
</tr>
<tr>
<td></td>
<td>(LLU hepatology econsult preferred)</td>
</tr>
<tr>
<td>Planned treatment with immunosuppressant therapy, including chemotherapy or anti-tumor necrosis factor alpha agents, and organ transplant recipients</td>
<td></td>
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</tbody>
</table>

*Outside Specialty Consultation: In CCHCS, HBV has typically been managed by either Infectious Disease or Hepatology specialists. CCHCS is trying to standardize chronic HBV management in consultation with LLU’s Hepatology Team. Econsult is preferred as the first step with the appropriate baseline workup on page 5 and then via Telemedicine if indicated. Note that if an RFS is needed, the current InterQual Criteria for HBV is relatively narrow:

- 300 Chronic hepatitis B infection **[Both]**
  - 310 Transaminase > 150% of upper limit of normal range **[Both]**
    - ≥ 6 months duration and Confirmed x3, ≥ 4 weeks apart
  - 320 Evidence of viral infection **[≥ One]**
    - HBsAg positive ≥ 6 months
    - Hepatitis B DNA positive
  - 323 HBeAg positive

If the patient appears to need consultation for treatment but does not fit current InterQual criteria, discuss with HBV Central Team (warmline under pools in EHRS) and institution medical leadership.

**Note:** If not referred for treatment, lifelong periodic monitoring is required (see page 8).

## Monitoring While Patient on Treatment

Once antiviral medication is initiated, ongoing monitoring of ALT, HBV DNA, and, in some patients, HBsAg and HBeAg is required to assess response to therapy, and the development of side effects or adverse events.

- **Treatment goal** is HBV DNA decrease by 2 log within 6 months, and eventually undetectable.
- After initiation of HBV antiviral, recheck HBV DNA every 3 months until undetectable, then every 6 months once undetectable.
- If the patient does not achieve undetectable HBV DNA after 1 year of antiviral therapy and the HBV DNA levels are not down-trending, discuss with the specialist managing the treatment.
- If viral breakthrough or rebound occurs, check medication compliance/adherence and discuss with specialist.
- Other considerations:
  - **Persons with cirrhosis:** Do not stop antiviral treatment, unless guided by expert consultation.
  - **Persons without cirrhosis and HBeAg positive at baseline:** Patients with persistent undetectable HBV DNA, normal ALT, and persistent HBeAg negative and anti-HBe positive 1 year after HBeAg seroconversion may have trial off antiviral treatment.
  - **Persons without cirrhosis and HBeAg negative at baseline:** Continue antiviral treatment until HBsAg clearance.
### Monitoring Patients Not on Treatment

**Guidance Statements for Monitoring Patients With Chronic HBV Infection Who Are Not Currently on Treatment**

- Although the risk for disease progression is low in these cases, it is not non-existent, chronic HBV can follow a variable and unpredictable course. Therefore, periodic monitoring is indicated through routine follow-up in a chronic care clinic as follows:

<table>
<thead>
<tr>
<th>Patient Factors</th>
<th>Monitoring Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HBeAg positive</strong></td>
<td></td>
</tr>
</tbody>
</table>
| Persistently normal ALT | ALT at 3-6 month intervals.  
  - If ALT levels increase above ULN, ALT along with HBV DNA should be tested more frequently (every 1-3 months).  
  - HBeAg status should be checked every 6-12 months. | |
| ALT > ULN but < 2 x ULN  
HBV DNA 2000-20,000 | | |
| **HBeAg positive** | Should undergo testing to evaluate degree of liver fibrosis especially those > 40 years old and who were infected at a young age (i.e., long duration of infection).  
  - Exclude other causes of ALT elevation and assess disease severity with non-invasive test. If staging indicates ≥ F2, treat. If other causes of ALT > ULN excluded and elevation persists, treat, especially if age > 40. | |
| ALT levels < 2 x ULN  
HBV DNA levels > 20,000 IU/mL | | |
| **HBeAg negative** | ALT and HBV DNA every 3 months during the first year to confirm they have inactive CHB.  
  - Thereafter, ALT and HBV DNA should be tested every 6 months.  
  - If costs are a concern ALT monitoring alone can be used and if above normal limit, ALT and HBV DNA tested every 3-6 months. | |
| Normal ALT (25 U/L women, 35 U/L men)  
HBV DNA ≥ 2,000 IU/ml | | |
| Normal ALT (25 U/L women, 35 U/L men)  
HBV DNA < 2,000 IU/ml | ALT at 3-6 month intervals.  
  - If ALT levels increase above ULN, ALT along with HBV DNA should be tested more frequently (every 1-3 months).  
  - HBsAg status should be checked annually. | |
| Elevated ALT levels less than 2 x ULN  
HBV DNA levels at all levels | | |
| Elevated ALT levels  
HBV DNA < 2,000 IU/mL | Should undergo testing to evaluate degree of liver fibrosis especially those > 40 years old and who were infected at a young age (i.e., long duration of infection).  
  - If staging indicates > F2, refer for treatment.  
  - If persistent ALT > ULN with HBV DNA > 2,000, refer for treatment especially those > 40 years old. | |
| Inactive CHB | Evaluate for loss of HBsAg annually. | |
| In persons who achieve sustained HBsAg sero-clearance | Routine ALT and HBV DNA monitoring are no longer required.  
  - HCC surveillance should continue if the person has cirrhosis, including persons who become HBsAg negative, Asian or black/African males > 40 years old, Asian females > 50 years old, persons with a family history of HCC, persons with HDV co-infection. | |
<table>
<thead>
<tr>
<th>MEDICATION</th>
<th>DOSING</th>
<th>ADVERSE EFFECTS/INTERACTIONS*</th>
<th>COMMENTS*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pegylated Interferon Alfa-2a Pegasys® Injection: 180 mcg/ml, 1ml vial</td>
<td>$$$$$</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Dosing:**
- **180 mcg SC once weekly for 48 weeks.**
  - There are no safety and efficacy data on treatment longer than 48 weeks.
- **Renal dosing:**
  - CrCl < 30 ml/min or hemodialysis (HD): 135 mcg SC once weekly

  If severe adverse reactions or laboratory abnormalities develop, the dose may be further reduced to 90 mcg SC once weekly until the adverse reactions abate. If intolerance persists after dose adjustment, discontinue therapy.

**Hepatic dosing:**
- Child-Pugh class B or C: contraindicated
- Autoimmune hepatitis: contraindicated

**ALT Elevations in Chronic Hepatitis B Patients:**
- ALT values more than 5 times the upper limit of normal, consider dose reduction to 135 mcg SC once weekly or temporary drug discontinuation and perform more frequent liver function monitoring. Treatment may be resumed after ALT flares subside. Therapy discontinuation may be appropriate for patients with persistent ALT elevations more than 10 times the upper limit of normal.

**Hematological Dosing:**
- **ANC < 750 cells/mm³:** Reduce dose to 135 mcg
- **ANC < 500 cells/mm³:** Discontinue treatment until ANC values return to more than 1000 cells/mm³. Reinstates at 90 mcg and monitor ANC.
- **Platelet < 50,000 cells/mm³:** Reduce dose to 90 mcg
- **Platelet < 25,000 cells/mm³:** If the platelets are <25,000, the drug should be discontinued.

**Adverse effects:**
- Flu-like symptoms, depression and related symptoms, anemia, cytopenia, neutropenia, thrombocytopenia, colitis, hair loss, dermatitis, dry skin, pruritus, rash, increased serum triglycerides, weight loss, abdominal pain, diarrhea, loss of appetite, nausea, vomiting, elevated hepatic enzymes, arthralgia, myalgia, dizziness, insomnia, headache, anxiety, reduced concentration, cough, fever, dyspnea, fatigue, rigor, pancreatitis, vision problems, injection site reactions, graft rejection, hypersensitivity reactions,

**Drug interactions:**
- live vaccines, methadone, theophylline, zidovudine, telbivudine

**Black Box Warning:**
- Alpha interferons, including peginterferon alfa-2a, may cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders. Patients should be monitored closely with periodic clinical and laboratory evaluations. Therapy should be withdrawn in patients with persistently severe or worsening signs or symptoms of these conditions. In many, but not all cases, these disorders resolve after stopping peginterferon alfa-2a therapy

**Contraindications:**
- Hypersensitivity reactions, including, angioedema, urticaria, bronchoconstriction, anaphylaxis, or Stevens-Johnson syndrome to alfa interferons or any component of the product, E. coli protein hypersensitivity, autoimmune hepatitis, Child-Pugh class B or C, cirrhotic chronic hepatitis C and HIV coinfection and Child-Pugh score ≥ 6 before treatment

**Caution in the following:**
- autoimmune disease, diabetes, cardiovascular disease, infectious disorders, thyroid disorders, seizure disorders, renal impairment, ischemic disorders, hepatic impairment, liver or other organ transplant, history of substance abuse, encephalopathy, depression or severe psychiatric disorder, pregnancy, breast-feeding, the elderly

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**Bold = Formulary**

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The cost scale $-$$$$ represents the relative cost of acquisition of medication only. Frequency and complexity of medication administration (institution workload, effect on adherence) should be considered when determining overall cost-effectiveness of treatment.

May 2022
# CCHCS Care Guide: Hepatitis B

## MEDICATIONS CONTINUED

### Oral Antiviral Agents

Black Box Warnings associated with oral HBV antiviral agents:
- Hepatitis B Exacerbation: Acute HBV exacerbations following abrupt discontinuation have been reported. Closely monitor hepatic function for several months after discontinued.
- HIV Resistance (not telbivudine): Use in patients with untreated or unrecognized HIV can result in HIV resistance; baseline HIV testing recommended.
- Lactic Acidosis/Severe Hepatomegaly: nucleoside analogue use alone or in combination has been associated with lactic acidosis and severe hepatomegaly with steatosis, including fatal cases. Stop treatment if clinical or laboratory findings suggest lactic acidosis.

### Entecavir Baraclude®

#### Tablet: 0.5 mg, 1mg

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<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosing</th>
<th>Adverse Effects/Interactions*</th>
<th>Comments*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entecavir Baraclude®</td>
<td>All: take on an empty stomach (2 hours before or after a meal)</td>
<td>Adverse Effects: nausea, dizziness, headache, fatigue, lactic acidosis, ascites, fever, rash, elevated hepatic enzymes, hepatic encephalopathy, infection, peripheral edema, hypergycmia, diarrhea, hematuria, abdominal pain, dyspepsia, alopecia, insomnia, somnolence</td>
<td>Black Box Warnings: Severe acute exacerbations of hepatitis B have been reported in patients who have discontinued anti-HBV therapy, including entecavir. Hepatic function should be monitored closely for at least several months after discontinuation. Initiation of anti-HBV therapy may be warranted</td>
</tr>
<tr>
<td>Entecavir Baraclude®</td>
<td>Compensated Liver Disease: - Nucleoside naïve: 0.5 mg orally once daily</td>
<td>Drug interactions: orlistat, cladribine, acyclovir, metformin, nucleoside reverse transcriptase inhibitors (NRTIs), amiloride, Angiotensin-converting enzyme (ACE) inhibitors, cisplatin, methylprednisolone, digoxin, aminoglycosides, Nonsteroidal anti-inflammatory drugs (NSAIDs), cyclosporine, amphotericin B, quinidine, memantine, triamterene, midodrine, ketoconazole, quinine, morphine, megestrol, quinidine, procainamide, prochlorperazine, trimethoprim, trosporium, vancomycin</td>
<td></td>
</tr>
<tr>
<td>Entecavir Baraclude®</td>
<td>Compensated Liver Disease: - Nucleoside naïve: - CrCl 30-49 ml/min: 0.5 mg orally dose every 48 hours</td>
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<tr>
<td>Entecavir Baraclude®</td>
<td>Compensated Liver Disease: - Nucleoside naïve: - CrCl 10-29 ml/min: 0.5 mg orally every 72 hours</td>
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<tr>
<td>Entecavir Baraclude®</td>
<td>Compensated Liver Disease: - Nucleoside naïve: - CrCl &lt; 10 ml/min: 0.5 mg orally once weekly</td>
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<tr>
<td>Entecavir Baraclude®</td>
<td>Hemodialysis/peritoneal dialysis (HD/ PD): 0.5 mg orally once weekly after HD</td>
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<tr>
<td>Entecavir Baraclude®</td>
<td>Compensated Liver Disease, Nucleoside resistant or Decompensated Liver Disease: - CrCl 30-49 mL/min: 1 mg orally every 48 hours</td>
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<tr>
<td>Entecavir Baraclude®</td>
<td>Compensated Liver Disease, Nucleoside resistant or Decompensated Liver Disease: - CrCl 10-29 mL/min: 1 mg orally every 72 hours</td>
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<tr>
<td>Entecavir Baraclude®</td>
<td>Compensated Liver Disease, Nucleoside resistant or Decompensated Liver Disease: - CrCl &lt; 10 mL/min: 1 mg orally once weekly</td>
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<tr>
<td>Entecavir Baraclude®</td>
<td>HD/PD: 1 mg orally once weekly after HD</td>
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<tr>
<td>Entecavir Baraclude®</td>
<td>Hepatic dosing: No dose adjustment needed</td>
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</tbody>
</table>

NOTE: Entecavir should not be used for patients with lamivudine-resistant HBV, since resistance has been observed in up to 50% of lamivudine-refractory patients after 5 years of treatment

*See prescribing information for complete description of contraindications/precautions, adverse effects and drug interactions. Hypersensitivity to the medication, medication class or any component of the formulation is a contraindication to use of the drug.

The cost scale $$$$$$ represents the relative cost of acquisition of medication only. Frequency and complexity of medication administration (institution workload, effect on adherence) should be considered when determining overall cost-effectiveness of treatment.
## MEDICATIONS CONTINUED

### ORAL ANTIVIRAL AGENTS

**Black Box Warnings associated with oral HBV antiviral agents**

- **Hepatitis B Exacerbation**: Acute HBV exacerbations following abrupt discontinuation have been reported. Closely monitor hepatic function for several months if discontinued.
- **HIV Resistance** (not telbivudine): Use in patients with untreated or unrecognized HIV can result in HIV resistance; baseline HIV testing recommended.
- **Lactic Acidosis/Severe Hepatomegaly**: Nucleoside analogue use alone or in combination has been associated with lactic acidosis and severe hepatomegaly with steatosis, including fatal cases. Stop treatment if clinical or laboratory findings suggest lactic acidosis or hepatotoxicity.

### Medication

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosing</th>
<th>Adverse Effects/Interactions*</th>
<th>Comments*</th>
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</thead>
<tbody>
<tr>
<td>Lamivudine</td>
<td>100 mg orally once daily Coinfected with HIV: 150 mg orally twice daily or 300 mg orally once daily as part of a fully suppressive antiretroviral regimen</td>
<td>Adverse Effects: diarrhea, dizziness, cough, fever, fatigue, malaise, lactic acidosis, headache, nausea, pancreatitis, stomatitis, insomnia, peripheral neuropathy, abdominal cramps, hyperglycemia, rash, fat maldistribution, dyslipidemia, abdominal pain, neutropenia, anemia, hepatotoxicity, myalgia, hepatomegaly, musculoskeletal pain, rhinorrhea, vomiting</td>
<td>Black Box Warnings: Non-Interchangeable Forms: lamivudine dosage forms used to treat HIV infection contain higher doses compared to lamivudine dosage forms used to treat chronic HBV infection; ensure patients receive correct dosage form for indicated use</td>
</tr>
<tr>
<td>Epivir-HBV®</td>
<td>Solution: 10 mg/ml Tablet: 100 mg</td>
<td>Drug interactions: amiloride, metformin, adefovir, dolutiilide, emtricitabine, orlistat, cabozantinib, sorbitol, memantine, cladrinbe, trimethoprim, trosiapm, procainamide</td>
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<td>Note: formulary dosage of lamivudine (150 mg, 300 mg) is not approved for use in HBV</td>
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<td>Note: this medication carries a high risk of viral resistance</td>
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**Renal dosing:**
- CrCl 30-49 ml/min: 100 mg orally once, then 50 mg orally once daily
- CrCl 15-29 ml/min: 100 mg orally once, then 25 mg orally once daily
- CrCl 5-14 ml/min: 35 mg orally once, then 15 mg orally once daily
- CrCl < 5 ml/min: 35 mg orally once, then 10 mg orally once daily
- HD/PD: after corrections for renal impairment, no additional dose modifications are required. Give dose after dialysis, no supplement

**Hepatic dosing:**
- Compensated liver disease: No dose adjustment needed
- Decompensated liver disease: Not defined

**Adverse Effects:**
- Hypersensitivity to the medication, medication class or a component of the formulation is a contraindication to use of the drug.
- See prescribing information for complete description of contraindications/precautions, adverse effects and drug interactions.

**Drug interactions:**
- procainamide
- trimethoprim, trospium
- memantine, cladribine, tenofovir
- amiloride, metformin, adefovir, dolutiilide, emtricitabine, orlistat, cabozantinib, sorbitol, memantine, cladrinbe, trimethoprim, trosiapm, procainamide

**Contraindications:**
- Hypersensitivity to lamivudine or any component of the formulation

**Caution in the following:**
- renal impairment, co-infection with HBV and HIV, females, obesity, untreated HIV
- tyrosine-methionine-aspartate-aspartate (YMDD)-mutant hepatitis B, hepatic disease, patients with known risk factors for liver disease, peripheral neuropathy, organ transplant, pregnancy, breastfeeding, the elderly

*See prescribing information for complete description of contraindications/precautions, adverse effects and drug interactions. Hypersensitivity to the medication, medication class or a component of the formulation is a contraindication to use of the drug.

The cost scale 3-$$$$$ represents the relative cost of acquisition of medication only. Frequency and complexity of medication administration (institution workload, effect on adherence) should be considered when determining overall cost-effectiveness of treatment.

### SUMMARY

**MEDICATIONS**

- Lamivudine
- Epivir-HBV®

### DECISION SUPPORT

**COMMENTS**

- Non-Interchangeable Forms: lamivudine dosage forms used to treat HIV infection contain higher doses compared to lamivudine dosage forms used to treat chronic HBV infection; ensure patients receive correct dosage form for indicated use

- Lamivudine-HBV is not approved for the treatment of HIV-1 infection because the lamivudine dosage in lamivudine-HBV is subtherapeutic and monotherapy is inappropriate for the treatment of HIV-1 infection. HIV-1 resistance may emerge in chronic hepatitis B-infected patients with unrecognized or untreated HIV-1 infection. HIV counseling and testing should be offered to all patients before beginning treatment with lamivudine-HBV and periodically during treatment

- Severe acute exacerbations of hepatitis B have been reported in patients who are coinfected with HBV and HIV-1 and have discontinued lamivudine or discontinued anti-hepatitis B therapy (including lamivudine-HBV). Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who discontinue lamivudine and are coinfected with HIV-1 and HBV or who discontinue anti-hepatitis B therapy. If appropriate, initiation of anti-HBV therapy may be warranted

**Contraindications:**
- Hypersensitivity to lamivudine or any component of the formulation

**Caution in the following:**
- renal impairment, co-infection with HBV and HIV, females, obesity, untreated HIV
- tyrosine-methionine-aspartate-aspartate (YMDD)-mutant hepatitis B, hepatic disease, patients with known risk factors for liver disease, peripheral neuropathy, organ transplant, pregnancy, breastfeeding, the elderly

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## MEDICATIONS CONTINUED

### ORAL ANTIVIRAL AGENTS

Black Box Warnings associated with oral HBV antiviral agents

- **Hepatitis B Exacerbation:** Acute HBV exacerbations following abrupt discontinuation have been reported. Closely monitor hepatic function for several months if discontinued.
- **HIV Resistance (not telbivudine):** Use in patients with untreated or unrecognized HIV can result in HIV resistance; baseline HIV testing recommended.
- **Lactic Acidosis/Severe Hepatomegaly:** Nucleoside analogue use alone or in combination has been associated with lactic acidosis and severe hepatomegaly w/ steatosis, including fatal cases. Stop treatment if clinical or laboratory findings suggest lactic acidosis or hepatotoxicity.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage</th>
<th>Adverse Effects/Interactions*</th>
<th>Comments*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tenofovir disoproxil fumarate (Viread®)</td>
<td>300 mg orally once daily</td>
<td>Adverse Effects: asthenia, diarrhea, fatigue, abdominal pain, depression, dizziness, fever, elevated hepatic enzymes, headache, insomnia, vomiting, hypercholesterolemia, pruritis, hypertriglyceridemia, bone pain, factures, increased serum creatinine, myopathy, nausea, sinusitis, neutropenia, nephrotoxicity, osteomalacia, pancreatitis, rhabdomyolysis.</td>
<td>Black Box Warning: Severe acute exacerbations of hepatitis B have been reported in patients who have discontinued anti-hepatitis B therapy, including tenofovir disoproxil fumarate. Closely monitor hepatic function in these patients for several months following discontinuation and resume anti-HBV therapy if warranted.</td>
</tr>
<tr>
<td>Tablet: 300 mg</td>
<td>Renal dosing: CrCl 30-49 ml/min: 300 mg orally every 48 hours CrCl 10-29 ml/min: 300 mg orally every 72-96 hours CrCl &lt; 10 ml/min: not recommended unless on HD HD: 300 mg orally every 7 days; give dose after HD</td>
<td>Drug interactions: didanosine, atazanavir, lopinavir, ritonavir, darunavir, adefovir, nephrotoxic agents (e.g., acyclovir, high-dose NSAIDS, aminoglycosides, salicylates), clarithromycin, colchicine, metformin, quinidine, erythromycin, ketoconazole, orlistat, posaconazole, rifaximin, verapamil.</td>
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<tr>
<td>Oral powder: 40 mg/1 g</td>
<td>Hepatic dosing: No dose adjustment needed. However, use caution due to the risk of hepatotoxicity</td>
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<tr>
<td>Tablet: 150 mg, 200 mg, 250 mg</td>
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</table>

| Tenofovir alafenamide (Vemlidy®) | 25 mg orally once daily with food | Adverse Effects: headache, abdominal pain, arthralgia, back pain, cough, diarrhea, fatigue, glycosuria, nausea, vomiting, hepatic failure, rash, bone pain, bone fractures, myalgia, urticaria, hypercholesterolemia, osteopenia, osteoporosis, | Black Box Warning: Severe acute exacerbations of hepatitis B have been reported in patients who have discontinued anti-hepatitis B therapy, including tenofovir alafenamide. Closely monitor hepatic function in these patients for several months following discontinuation and resume anti-HBV therapy if warranted. |
| Tablet: 25 mg | Renal dosing: CrCl ≥ 15 ml/min: no dose adjustments needed CrCl < 15 ml/min: not recommended unless on HD; administer after completion of HD on dialysis days | Drug interactions: phenytoin, carbamazepine, rifampin, phenobarbital, and St. John’s wort are all contraindicated; rifabutin, oxcarbazepine, rifapentine, atazanavir, lopinavir, ritonavir, darunavir, adefovir, nephrotoxic agents (e.g., high-dose NSAIDS, acyclovir, salicylates, aminoglycosides), erythromycin, fefolidine, verapamil, norgestimate, orlistat. |  |
| $$$ | Hepatic dosing: Child-Pugh A: No dose adjustment needed Child-Pugh B and C: Use not recommended |  |  |

**Bold = Formulary**

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## CCHCS Care Guide: Hepatitis B

### MEDICATIONS CONTINUED

#### Oral Antiviral Agents

Black Box Warnings associated with oral HBV antiviral agents

- Hepatitis B Exacerbation: Acute HBV exacerbations following abrupt discontinuation have been reported. Closely monitor hepatic function for several months if discontinued.
- HIV Resistance (not telbivudine): Use in patients with untreated or unrecognized HIV can result in HIV resistance; baseline HIV testing recommended.
- Lactic Acidosis/Severe Hepatomegaly: nucleoside analogue use alone or in combination has been associated with lactic acidosis and severe hepatomegaly w/ steatosis, including fatal cases. Stop treatment if clinical or laboratory findings suggest lactic acidosis or hepatotoxicity.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosing</th>
<th>Adverse Effects/ Interactions*</th>
<th>Comments*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tenofovir alafenamide/emtricitabine Descovy*</td>
<td>25 mg/200 mg orally once daily</td>
<td>Adverse Effects: headache, abdominal pain, arthralgia, back pain, cough, diarrhea, fatigue, glycosuria, nausea, vomiting, hepatic failure, rash, hypercholesterolemia, hypertriglyceridemia, bone pain, bone fractures, urticaria, myalgia, osteopenia, osteoporosis, angioedema</td>
<td>Black Box Warning: Severe acute exacerbations of hepatitis B (HBV) have been reported in HBV-infected individuals who have discontinued products containing emtricitabine (FTC) and/or tenofovir disoproxil fumarate (TDF) and may occur with discontinuation of emtricitabine/tenofovir alafenamide. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in individuals who are infected with HBV and discontinue emtricitabine/tenofovir alafenamide. If appropriate, initiation of antiviral therapy may be warranted. Emtricitabine/tenofovir alafenamide used for HIV-1 pre-exposure prophylaxis must only be prescribed to individuals confirmed to be HIV-negative immediately prior to initiating and at least every 3 months during use. Drug-resistant HIV-1 variants have been identified with use of FTC during use. Drug-resistant HIV-1 variants have been identified with use of FTC/TDF for HIV-1 pre-exposure prophylaxis (PrEP) following undetected acute HIV-1 infection. Do not initiate emtricitabine/tenofovir alafenamide for HIV-1 pre-exposure prophylaxis if signs or symptoms of acute HIV-1 infection are present unless negative infection status is confirmed.</td>
</tr>
<tr>
<td>Coformulated tablet: 25 mg/200 mg</td>
<td>Renal dosing:</td>
<td>Drug interactions: phenytoin, carbamazepine, rifampin, phenobarbital, and St. John’s wort are all contraindicated; didanosine, atazanavir, lopinavir, ritonavir, darunavir, adefovir, nephrotoxic agents (e.g., ayclovir, aminoglycosides, high-dose NSAIDS), erythromycin, felodipine, verapamil, norgestimate, orlistat, oxcarbazepine, rifabutin, rifampetine</td>
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<tr>
<td>Note: Not FDA approved for use in HBV (off label use)</td>
<td>Hepatic dosing:</td>
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<td>$$$$$$$</td>
<td>Mild to moderate (Child-Pugh A and B): No dose adjustment needed</td>
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<td>Severe (Child-Pugh C): Safety and efficacy have not been established</td>
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</table>

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**Bold = Formulary**

May 2022
### Oral Antiviral Agents

Black Box Warnings associated with oral HBV antiviral agents

- Hepatitis B Exacerbation: Acute HBV exacerbations following abrupt discontinuation have been reported. Closely monitor hepatic function for several months if discontinued.
- HIV Resistance (not telbivudine): Use in patients with untreated or unrecognized HIV can result in HIV resistance; baseline HIV testing recommended.
- Lactic Acidosis/Severe Hepatomegaly: nucleoside analogue use alone or in combination has been associated with lactic acidosis and severe hepatomegaly with steatosis, including fatal cases. Stop treatment if clinical or laboratory findings suggest lactic acidosis or hepatotoxicity.

<table>
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<tr>
<th>Medication</th>
<th>Dosing</th>
<th>Adverse Effects/Interactions*</th>
<th>Comments*</th>
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</thead>
<tbody>
<tr>
<td>Tenofovir disoproxil fumarate/emtricitabine Truvada®</td>
<td>300 mg/200 mg orally once daily</td>
<td>Adverse Effects: headache, dizziness, abdominal pain, arthralgia, back pain, cough, diarrhea, fatigue, glycosuria, nausea, vomiting, hepatic failure, pruritus, insomnia, peripheral neuropathy, rash, depression, dream disorder, pneumonia, hyperglycemia, elevated hepatic enzymes, hypercholesterolemia, hypertriglyceridemia, bone pain, bone fractures, fatigue, neutropenia, myalgia, myopathy, osteopenia, osteoporosis, osteomalacia, angioedema, pancreatitis, increased serum creatinine, rhabdomyolysis</td>
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<tr>
<td>Coformulated tablet: 300 mg/200 mg</td>
<td>Renal dosing:</td>
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<td>CrCl 30-49: 1 tablet every 48 hours</td>
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<td>CrCl &lt; 30: Not recommended</td>
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<td>HD: Not recommended</td>
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<td>Hepatic dosing:</td>
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<td>Safety and efficacy have not</td>
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<td>Drug interactions:</td>
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<td>rifaxamin, didanosine, atazanavir,</td>
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<td>lopinavir, ritonavir, darunavir,</td>
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<td>adeovir, nephrotoxic agents (e.g.,</td>
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<td>acyclovir, aminoglycosides, high-dose NSAIDS), erythromycin, verapamil, orlistat, ledipasvir</td>
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<td>Black Box Warning:</td>
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<td>Emtricitabine/tenofovir disoproxil</td>
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<td>fumarate is not approved for the</td>
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<td>treatment of chronic HBV infection,</td>
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<td>and the safety and efficacy of</td>
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<td>emtricitabine/tenofovir disoproxil</td>
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<td>fumarate have not been</td>
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<td>established in patients coinfected</td>
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<td>with HBV and HIV-1. Severe acute</td>
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<td>exacerbations of hepatitis B have</td>
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<td>been reported in patients who are</td>
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<td>coinfected with HBV and discontinue</td>
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<td>emtricitabine/tenofovir disoproxil</td>
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<td>fumarate. Therefore, hepatic</td>
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<td>function should be monitored closely</td>
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<td>with both clinical and laboratory</td>
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<td>follow-up for at least several</td>
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<td>months in patients who are</td>
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<td>infected with HBV and discontinue</td>
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<td>emtricitabine/tenofovir disoproxil</td>
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<td>fumarate. If appropriate, initiation</td>
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<td>Emtricitabine/tenofovir disoproxil</td>
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<td>individuals confirmed to be HIV-</td>
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<td>initiating and periodically (at least</td>
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<td>every 3 months) during use. Drug-</td>
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<td>following undetected acute HIV-1</td>
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<td>acute HIV-1 infection are</td>
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<td>present unless negative infection</td>
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<td>Contraindications: Hypersensitivity</td>
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<td>to emtricitabine/tenofovir disoproxil fumarate or any component of the formulation</td>
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<td>Caution in the following: concomitant use with atazanavir, lamivudine, or adeovir, renal impairment, hepatic disease, females, obesity, untreated HIV, coinfection with HIV, concurrent use or recent use of nephrotoxic agents, history of pathologic bone fractures or substantial risk for osteopenia, osteoporosis or osteomalacia, pregnancy, breastfeeding, the elderly</td>
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*Bold = Formulary

*See prescribing information for complete description of contraindications/precautions, adverse effects and drug interactions. Hypersensitivity to the medication, medication class or a component of the formulation is a contraindication to use of the drug.

The cost scale $$$$$ represents the relative cost of acquisition of medication only. Frequency and complexity of medication administration (institution workload, effect on adherence) should be considered when determining overall cost-effectiveness of treatment.
REFERENCES


**ATTACHMENT A: IMMUNIZATIONS IN HBV PATIENTS TABLE**

### HBV (For nonimmune)

Dosage: 2 doses only 1 month apart
- In EHRs: Use Heplisav-B® (more potent) for all patients
- CDC states: For ESRD/dialysis, solid organ transplant, other immunocompromised and for those with isolated core AB+ (difficulty mounting a vigorous response to HBV vaccination), testing should be performed 1-2 months after administration of the last dose of the vaccine series to ensure anti-HBs is 10 mIU/mL. ESRD/dialysis, solid organ transplant, other immunocompromised and for those with isolated core AB+ (difficulty mounting a vigorous response to HBV vaccination). If < 10, re-vaccinate with Heplisav® brand. If still not > 10, test for HBV Sag.
- Test annually for HBV Sab in ESRD/dialysis and in solid organ transplant recipients.

### Pneumococcal Pneumonia

#### Age ≥19 (Ages 19-64 and >65 years now have the same guidelines*)

For those who have not previously received any pneumococcal vaccine, CDC recommends:
- Give 1 dose of PCV15 or PCV20.
  - If PCV15 is used, this should be followed by a dose of PPSV23 at least 12 months later. (Note: for ESRD is considered an immunocompromising conditions, the minimum interval is 8 weeks instead of the 1 year minimum interval for non-immunocompromised adults.)
  ```
  PCV15 12 months PPSV23
  ```
  - If PCV20 is used, a dose of PPSV23 is NOT indicated.
  ```
  PCV20 No follow up dose needed
  ```

For those who have only received PPSV23, CDC recommends:
- Give 1 dose of PCV15 or PCV20 administered at least one year after the most recent PPSV23 vaccination.
- Regardless of if PCV15 or PCV20 is given, an additional dose of PPSV23 is not recommended since they already received it.
  ```
  PPSV23 1 year PCV15 OR PCV20 No follow up dose needed
  ```

For those who have received PCV13 with or without PPSV23, CDC recommends:
- Give dose of PPSV23 at least 8 weeks after PCV13 and at least 5 years after the previous dose of PPSV23 (Note: A second dose is not indicated for those with cerebrospinal fluid leaks or cochlear implants).
- Administer 1 final dose of PPSV23 at 65 years or older. This dose should be given at least 5 years after the most recent dose of PPSV23.
  ```
  PPSV23 (at <65 years) At least 1 year apart PCV13 (at ≥19 years) At least 12 months apart PPSV23 (at <65 years) every 5 years At least 5 years apart PPSV23* (one final dose at ≥65 years)
  ```
  *For adults who have received PCV13 but have not completed their recommended pneumococcal vaccine series with PPSV23, one dose of PCV20 may be used if PPSV23 is not available. If PCV20 is used, their pneumococcal vaccinations are complete.

### SARS-CoV-2 (COVID-19)

Dosage: Per the latest Advisory Committee on Immunization Practices (ACIP) recommendations* and CDC Interim Clinical Considerations†

**General population:**
2 dose series for Pfizer-BioNTech or Moderna and then booster (3rd dose) 5 months after completion of initial series. Mix and match boosters allowed and mRNA vaccine recommended as 2nd dose if Jansen’s was 1st dose– at least 2 months after first and no further doses.

**Immunocompromised‡:**
- Pfizer-BioNTech: 3 doses with the first 2 doses separated by at least 21 days, the third dose 28 days after the second dose, then 4th dose (booster) 3 months after initial series.
- Moderna: 3 dose series separated by at least 28 days, then 4th dose (booster) 3 months after initial series.
- Jansen: do not give as initial series for the immunocompromised. If already received 1st dose, mix and match 2nd dose preferred with Pfizer-BioNTech or Moderna, then third dose (booster) 2 months after.

Please check current CDC recommendations.‡

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* [https://www.cdc.gov/vaccines/vpd/pneumo/hcp/recommendations.html](https://www.cdc.gov/vaccines/vpd/pneumo/hcp/recommendations.html)
† [https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/covid-19.html](https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/covid-19.html)
WHAT YOU SHOULD KNOW: HEPATITIS B VIRUS

WHAT IS HEPATITIS B?
- Hepatitis B is a virus that causes swelling and irritation of the liver.
- The liver helps with digestion and filters waste products out of the blood. Hepatitis B can cause serious damage to the liver.

HOW DO YOU GET HEPATITIS B?
You can get hepatitis B from:
- Dirty needles (tattoos or piercing) or injecting drugs
- Snorting drugs with infected equipment
- Sharing needles to inject drugs
- Unprotected sex (rarely)
- A blood transfusion if you got one in the United States before 1992.
   (All blood is now tested for hepatitis B before it is used for transfusion)

HOW DO YOU KNOW IF YOU HAVE HEPATITIS B?
- Most people who have hepatitis B look and feel fine.
- You can have hepatitis B for a long time and not know it.
- Usually hepatitis B is found by doing blood tests.
- If hepatitis B damages the liver, it can cause scarring. This is called cirrhosis (sir-oh-sis).
- Your health care provider may order more tests to see how much liver damage you have.

WHAT CAN YOU DO TO TAKE CARE OF YOURSELF?
- Get vaccinated for hepatitis A. Get yearly vaccinations for pneumonia and the flu.
- Do not drink alcohol or use illegal drugs - these will damage your liver more.
- Do not take a lot of medications like acetaminophen (Tylenol®) and ibuprofen (Motrin®). Talk to your health care provider about all medications, including over-the-counter medications, vitamins, and herbs to be sure they will not damage your liver. Ask your health care provider before you take any pain medicine.
- Do not get tattoos in prison to avoid blood borne infections.
- Do not share your toothbrush, razor, or other personal items.
- Try to lose weight if you are overweight.
- Eat a healthy diet.
- Drink plenty of water.
- Get plenty of rest and regular exercise.
- Quit smoking cigarettes.
- Follow your health care provider’s instructions about medications for hepatitis B treatment.
- See your health care provider regularly.

DOES EVERYONE WITH HEPATITIS B NEED TREATMENT?
- Many people with hepatitis B do not need treatment.
- A few people may develop severe liver damage and can die from problems with hepatitis B.
- Who needs treatment depends on many things and these are different for each person. You should discuss your case with your health care provider.
# Patient Education/Self Management

## For Patients Infected with Hepatitis B Virus (HBV)

### What Do I Need to Know About My Hepatitis B Infection?

- Most persons with HBV infection will remain healthy, but a small number of persons will develop serious liver disease.
- Drug treatment options for chronic hepatitis B are developing. Medications may or may not be appropriate for you.
  - Talk with your doctor about the natural history of the infection, potential treatment options, and specific things you can do to prevent transmission of HBV infection to others (during incarceration and upon release).

### What Can I Do to Take Care of Myself?

- Do not shoot drugs, have sex with other incarcerated persons, or get a tattoo or body piercing while in prison.
- Do not share personal items such as toothbrushes, dental appliances, nail-grooming equipment, or razors.
- Cover your cuts and skin sores to keep your blood from contacting other persons.
- Do not drink alcohol (or at least really limit use) and speak to a physician before taking any new medications, including over-the-counter meds such as nonsteroidal anti-inflammatory agents and herbal remedies that may damage your liver.

### If You Are Being Released

- Upon release, do not donate blood, body organs, other tissue, or semen.
- Upon release, seek medical attention so that your condition is appropriately monitored and treated.
  - Most people need blood tests at least every 6 months and many need liver ultrasound to look for development of liver cancer.
  - Make sure every new health care provider knows that you have chronic HBV, especially if you need treatment with immunosuppressant medications.
- Try to be at normal range body weight and control diabetes and dyslipidemia (to prevent concurrent development of metabolic syndrome and fatty liver).
# Educación para el Paciente/Control Personal del Caso

## Lo Qué Debe Saber: El Virus de la Hepatitis B

### ¿Qué Es La Hepatitis B?

- La hepatitis B es un virus que causa la inflamación e irritación del hígado.
- El hígado ayuda con la digestión y filtra las toxinas para expulsarlas de la sangre. La hepatitis B puede causar graves daños al hígado.

### ¿Cómo Se Puede Contraer La Hepatitis B?

Puede contraer la hepatitis B a través de lo siguiente:

- Agujas sucias (tatuajes o perforaciones) o drogas inyectables.
- Inhalar drogas con un equipo infectado.
- Compartir agujas para inyectarse drogas.
- Sexo sin protección (pocas veces).
- Una transfusión de sangre, si la recibió en los Estados Unidos antes de 1992 (actualmente se analiza toda la sangre para detectar la hepatitis B antes de usarse para transfusiones).

### ¿Cómo Saber Si Sufre de la Hepatitis B?

- La mayoría de las personas que tienen la hepatitis B se ven y se sienten bien.
- Puede tener la hepatitis B por mucho tiempo y no saberlo.
- Por lo general, la hepatitis B se detecta al hacer análisis de sangre.
- Si la hepatitis B daña el hígado, puede causar cicatrices. A esto se le llama cirrosis (sí-rrro-sis).
- Su proveedor de atención a la salud puede ordenar más pruebas para ver cuánto daño hepático tiene.
- Algunas personas que sufren de la hepatitis B presentan:
  - Fatiga.
  - Dolor estomacal.
  - Dolor en las articulaciones.
  - Sudoración nocturna.
  - Pérdida del apetito o náuseas.

### ¿Qué Puede Hacer para Cuidarse?

- Vacúñese contra la hepatitis A. Vacúñese anualmente contra la neumonía y la gripe.
- No beba alcohol ni consuma drogas ilegales; esto dañará más su hígado.
- No tome muchos medicamentos como el paracetamol (Tylenol®) y el ibuprofeno (Motrin®). Hable con su proveedor de atención a la salud sobre todos los medicamentos, incluidos los de venta libre, vitaminas e hierbas para asegurarse de que no dañarán su hígado. Pregúntele antes de tomar cualquier medicamento para el dolor.
- No se tatúe en la cárcel para evitar infecciones que se transmiten por la sangre.
- No comparta su cepillo de dientes, rasuradora u otros artículos personales.
- Si tiene sobrepeso, trate de perderlo.
- Coma una dieta saludable.
- Beba mucha agua.
- Descanse mucho y haga ejercicio regularmente.
- Deje de fumar cigarrillos.
- Siga las instrucciones de su proveedor de atención a la salud sobre los medicamentos para el tratamiento de la hepatitis B.
- Visite a su proveedor de atención a la salud con regularidad.

### ¿Toda Persona Que Sufre de la Hepatitis B Necesita Tratamiento?

- Muchas personas con hepatitis B no necesitan tratamiento.
- Algunas personas pueden desarrollar un daño hepático severo y morir por problemas relacionados con la hepatitis B.
- La necesidad de tratamiento dependerá de muchas cosas, las cuales serán diferentes para cada persona. Debe conversar sobre su caso con su proveedor de atención a la salud.
¿QUÉ NECESITO SABER SOBRE MI INFECCIÓN DE HEPATITIS B?

- La mayoría de las personas infectadas con el virus de la hepatitis B (VHB) permanecerán sanas, pero un pequeño número desarrollará una enfermedad hepática grave.
- Se están desarrollando opciones de tratamiento con medicamentos para la hepatitis B crónica. Los medicamentos pueden o no ser apropiados para usted.
  - Hable con su médico sobre el antecedente natural de la infección, las posibles opciones de tratamiento y las medidas específicas que puede tomar para evitar la transmisión del VHB a otras personas (durante el encarcelamiento y al salir de la cárcel)

¿QUÉ PUEDO HACER PARA CUIDARME?

- No se inyecte drogas, no tenga relaciones sexuales con otras personas encarceladas ni se haga tatuajes o perforaciones corporales mientras esté en prisión.
- No compartire artículos personales como cepillos de dientes, aparatos dentales, equipos para arreglarse las uñas o rasuradoras.
- Cubra los cortes y las llagas en la piel para evitar que su sangre entre en contacto con otras personas.
- No beba alcohol (o al menos limite su consumo) y hable con un médico antes de tomar cualquier medicamento nuevo, incluidos los de venta libre, como agentes antiinflamatorios no esteroideos y remedios a base de hierbas que puedan dañar su hígado.

SI ES PUESTO EN LIBERTAD

- Tras la liberación, no done sangre, órganos corporales, otros tejidos o semen.
- Tras la liberación, busque atención médica para que su condición sea revisada y tratada adecuadamente.
  - La mayoría de las personas necesitan análisis de sangre al menos cada 6 meses, y muchos necesitan un ultrasonido hepático para detectar si se ha desarrollado cáncer de hígado.
  - Asegúrese de que cada nuevo proveedor de atención a la salud sepa que tiene el VHB crónico; especialmente si necesita tratamiento con medicamentos inmunosupresores.
- Intente tener un peso corporal normal y controlar la diabetes y la dislipidemia (para evitar el desarrollo simultáneo del síndrome metabólico y del hígado graso).