Many patients with chronic hepatitis B (CHB) are not receiving adequate monitoring or treatment, putting them at increased risk for serious liver disease.[1]

Choose VEMLIDY as your first-line CHB therapy for your appropriate treatment-naïve patients with CHB

With the guidance of the Simplified Approach Hepatitis B Algorithm (SABA), consider VEMLIDY as a treatment option for your adult patients with CHB and compensated liver disease.

Actor portrayals.

Learn about expert panel recommendations for a simplified approach to treating CHB

INDICATION

VEMLIDY is indicated for the treatment of chronic hepatitis B virus (HBV) infection in adults with compensated liver disease.

IMPORTANT SAFETY INFORMATION

BOXED WARNING: POSTTREATMENT SEVERE ACUTE EXACERBATION OF HEPATITIS B

- **Discontinuation of anti-hepatitis B therapy, including VEMLIDY, may result in severe acute exacerbations of hepatitis B. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who discontinue anti-hepatitis B therapy, including VEMLIDY. If appropriate, resumption of anti-hepatitis B therapy may be warranted.**

Click here for full Prescribing Information for VEMLIDY, including **BOXED WARNING** on posttreatment severe acute exacerbation of hepatitis B.

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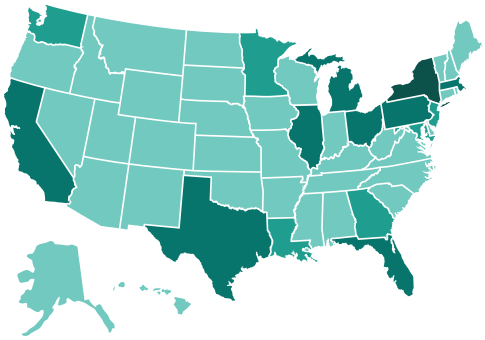
Recognizing important gaps in the management of CHB

In the United States, CHB is undermanaged and undertreated



The map depicts US 2021 CHB diagnosis estimates indicated by teal shading; darker shade indicates higher estimated diagnosis rates.[4]

>600,000
people diagnosed with CHB in the US[2,3,a]

Data show that there are significant gaps in:

CHB treatment

~70%
of patients who are diagnosed with CHB are **not receiving antiviral treatment[5,b]**

Moreover, ***~65%***
of patients who have **CHB and cirrhosis are not receiving antiviral treatment[5,b]**

Understanding CHB outcomes

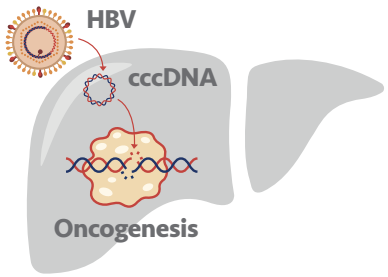
28%
of patients have **significant fibrosis despite normal ALT levels[6,c]**

20%-30%
of adults with chronic hepatitis B will **develop complications such as cirrhosis, and potentially, HCC[7]**

CHB monitoring

>60%
of patients with CHB are **not receiving regular monitoring of their CHB or screening for HCC[8,9,d]**

HBV increases the risk of HCC through direct and indirect mechanisms, which may occur at early stages of tumor development and during any phase of HBV infection[10-12]



- Direct mechanisms revolve around the ability of HBV to integrate into the host's genome, leading to potentially carcinogenic chromosomal aberrations and protein expression[10-12]
- Indirect mechanisms center on the ability of HBV to induce continuous, recurring liver necroinflammation, which may culminate in the development of cirrhosis[11,12]
- Persons with CHB are at a 25- to 37-fold increased risk of HCC compared to non-infected people[1]

Real-world data indicate that using **HBV DNA level >2000 IU/mL alone** for patients without cirrhosis and removing ALT and HBeAg treatment eligibility criteria **would help avoid many cases of HCC and early deaths[1,13]**

ALT, alanine aminotransferase; cccDNA, covalently closed circular DNA; HBeAg, hepatitis B envelope antigen; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; ULN, upper limit of normal.

[a]Based on a prevalence estimate of ~2 million people with CHB in the US in 2018[2] and a rate of awareness of CHB infection of ~34% among people with CHB, from a National Health Nutrition and Examination Survey analysis from 2013-2016.[3]

[b]Based on an analysis of 57,847 patients diagnosed with CHB from the commercial US Truven Health MarketScan Database (2007-2014). In this analysis, treatment rates were 30.7% in the overall population of patients diagnosed with CHB and 34.8% in patients diagnosed with CHB and cirrhosis.[5]

[c]Based on a meta-analysis of 3 clinical studies that used ULN of 30 IU/L for men and 19 IU/L for women, comprising a total of 81 patients with CHB.[6]

[d]Based on a study of 2338 CHB patients followed during 2006–2013 in the Chronic Hepatitis Cohort Study, in which 62% received less than annual HBV DNA assessment,[8] and a study of 55,317 patients with CHB from the US Truven MarketScan Databases of commercially insured and Medicare patients with private insurance supplement (2007-2014), in which <40% received annual HCC surveillance.[9]

The importance of earlier antiviral treatment for appropriate CHB patients

The Simplified Approach Hepatitis B Algorithm[1]

A group of expert liver and infectious disease specialists developed a streamlined algorithm of HBV intervention,[1] which encourages earlier treatment

Expert Panel

Douglas Dieterich, MD • Camilla Graham, MD, MPH • Su Wang, MD, MPH • Paul Kwo, MD • Young-Suk Lim, MD, PhD • Chun-Jen Liu, MD, PhD • Kosh Agarwal, MD • Mark Sulkowski, MD

Gastro Hep Advances; October 13, 2022

Click here to learn more about the **SABA recommendations** for the management of CHB.

Gilead is not responsible for the content of the site that is referred to by this link.

Background and objectives[1]

"Hepatitis B virus (HBV) infection continues to threaten millions of lives across the globe, despite universal vaccination efforts…[T]he complexity of existing guidelines can make it difficult to identify which patients to target for treatment, and recommendations that are difficult to implement in real-world settings pose a barrier to eligible patients to receive therapy and contribute to health disparities in HBV care.

The goal of this global expert panel was to gain consensus on a streamlined approach to HBV care to facilitate implementation of HBV intervention and treatment, especially in the primary care setting."[1]

The expert panel believes that current CHB management guidelines are complex and **may leave many people inadequately managed**[1]

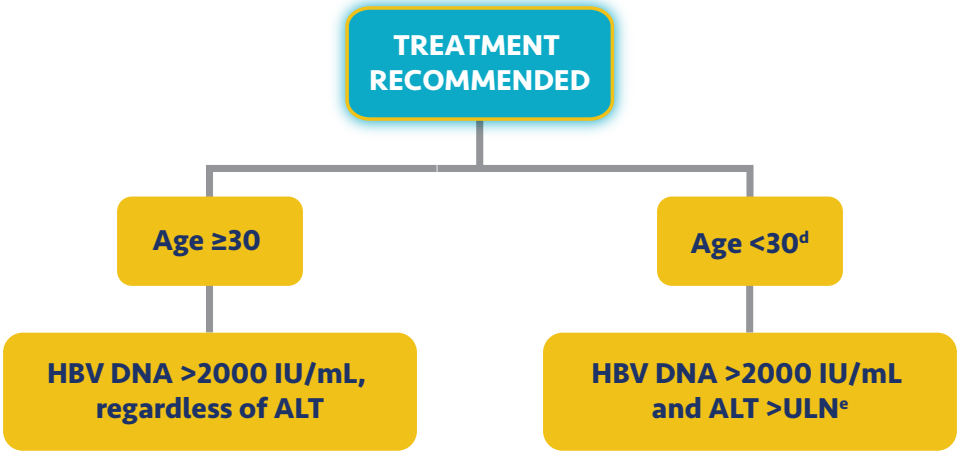
The 2022 SABA guideline was funded by Gilead Sciences, Inc., and developed independently by the SABA panel.

Simplified Approach Hepatitis B Algorithm (SABA)

To reduce the number of patients who are not receiving appropriate treatment, the expert panel's approach was ***"to assume that all patients with chronic HBV infection need to be treated, and then to exclude those who do not 'qualify' for treatment,"*** rather than the currently prevailing, reverse perspective.[1]

Treatment Criteria Recommendations[a-c]

CHB patients with compensated cirrhosis and detectable HBV DNA, regardless of ALT levels, should be treated



- **Refer to a specialist if HIV coinfection exists**
- **VEMLIDY is not indicated for patients with decompensated (Child-Pugh B or C) hepatic impairment and has not been tested in this population**

VEMLIDY is a recommended FIRST-LINE HBV therapy for CHB patients[1,f]

- VEMLIDY can be considered in patients with, or at risk for, renal dysfunction and bone disease[1,b]
- VEMLIDY has demonstrated antiviral efficacy with a low risk of drug resistance[1,f]

IMPORTANT SAFETY INFORMATION (continued)

Warnings and Precautions

- **Risk of Development of HIV-1 Resistance in HBV/HIV-1 Coinfected Patients:** Due to this risk, VEMLIDY alone should not be used for the treatment of HIV-1 infection. Safety and efficacy of VEMLIDY have not been established in HBV/HIV-1 coinfected patients. HIV antibody testing should be offered to all HBV-infected patients before initiating therapy with VEMLIDY, and, if positive, an appropriate antiretroviral combination regimen that is recommended for HBV/HIV-1 coinfected patients should be used.
- **New Onset or Worsening Renal Impairment:** Postmarketing cases of renal impairment, including acute renal failure, proximal renal tubulopathy (PRT), and Fanconi syndrome have been reported with TAF-containing products. Patients with impaired renal function and/or taking nephrotoxic agents (including NSAIDs) are at increased risk of renal-related adverse reactions. Discontinue VEMLIDY in patients who develop clinically significant decreases in renal function or evidence of Fanconi syndrome. Monitor renal function in all patients – See Dosage and Administration.

Click here for full Prescribing Information for VEMLIDY, including **BOXED WARNING** on posttreatment severe acute exacerbation of hepatitis B.

HIV, human immunodeficiency virus; NSAID, non-steroidal anti-inflammatory drug; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate.
[a]If HBV DNA <2000 IU/mL OR if less than age 30[d] and HBV DNA >2000 IU/mL and ALT ≤ULN, then re-evaluate for treatment eligibility in 6 months. Use clinical judgment and shared decision-making to determine if patient would benefit from or prefer treatment.
[b]**VEMLIDY is not recommended in patients with end stage renal disease (ESRD; estimated creatinine clearance [eCrCl] <15 mL/min) who are not receiving chronic hemodialysis; in patients on chronic hemodialysis, on hemodialysis days, administer VEMLIDY after completion of hemodialysis treatment.**
[c]**VEMLIDY has not been tested for use during pregnancy.**
[d]VEMLIDY is indicated for the treatment of chronic hepatitis B virus infection in adults with compensated liver disease.
[e]ALT ULN is defined as 30 U/L for men and 19 U/L for women.[1]
[f]Other recommended first-line nucleos(t)ide analogs are entecavir and TDF.

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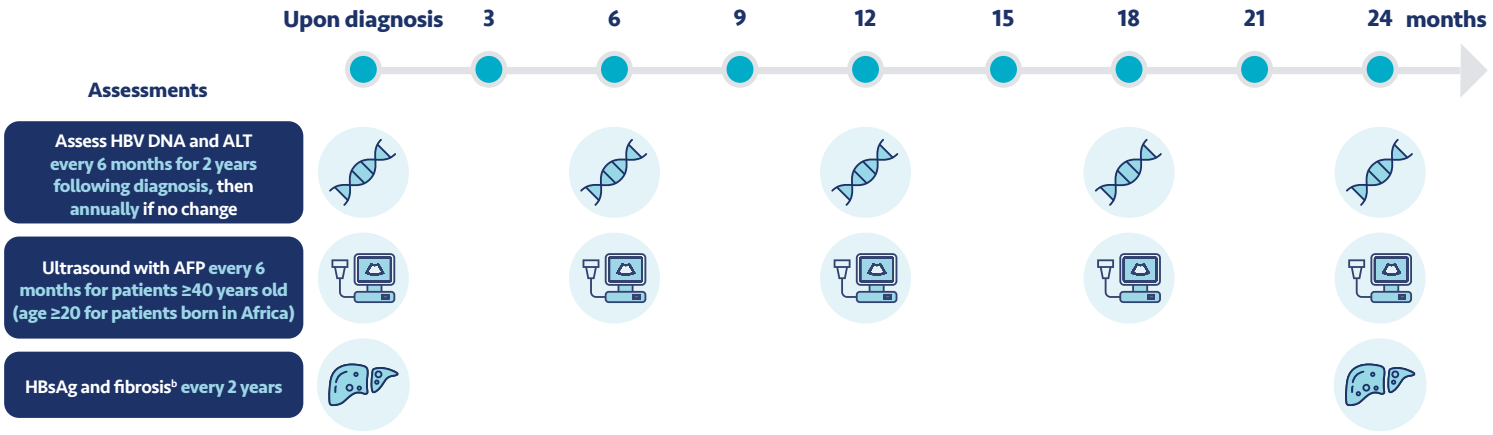
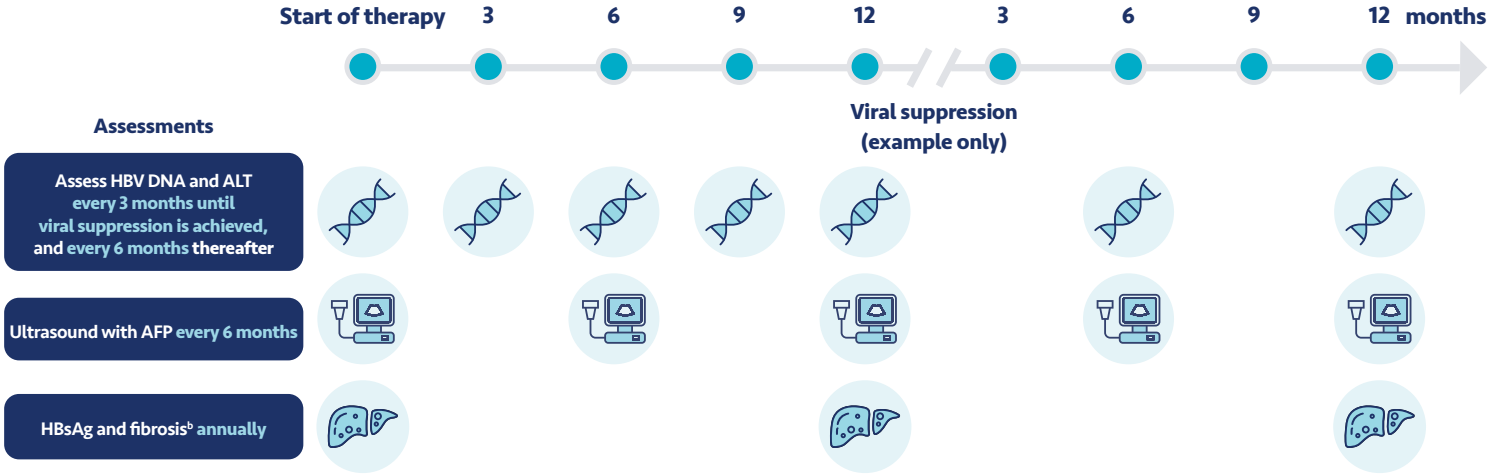
Expert panel recommendations for monitoring patients with CHB

Newly diagnosed patients not eligible for treatment[a]



Patients starting treatment



AFP, alpha-fetoprotein; HBsAg, hepatitis B surface antigen.
[a]If HBV DNA <2000 IU/mL OR if less than age 30[c] and HBV DNA >2000 IU/mL and ALT ≤ULN, then re-evaluate for treatment eligibility in 6 months. Use clinical judgment and shared decision-making to determine if patient would benefit from or prefer treatment.
[b]To help assess fibrosis, the SABA recommends the use of the aspartate aminotransferase-to-platelet ratio index (APRI), the Fibrosis-4 index (FIB-4), or transient elastography.
[c]VEMLIDY is indicated for the treatment of chronic hepatitis B virus infection in adults with compensated liver disease.

IMPORTANT SAFETY INFORMATION (continued)

Warnings and Precautions (continued)

- **Lactic Acidosis and Severe Hepatomegaly with Steatosis:** Fatal cases have been reported with the use of nucleoside analogs, including tenofovir disoproxil fumarate (TDF). Discontinue VEMLIDY if clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity develop, including hepatomegaly and steatosis in the absence of marked transaminase elevations.

Adverse Reactions

Most common adverse reactions (incidence ≥5%; all grades) in clinical studies through week 144 were headache, upper respiratory tract infection, abdominal pain, cough, back pain, arthralgia, fatigue, nausea, diarrhea, dyspepsia, and pyrexia.

Drug Interactions

- Coadministration of VEMLIDY with drugs that reduce renal function or compete for active tubular secretion may increase concentrations of tenofovir and the risk of adverse reactions.
- Coadministration of VEMLIDY is not recommended with the following: oxcarbazepine, phenobarbital, phenytoin, rifabutin, rifampin, rifapentine, or St. John's wort. Such coadministration is expected to decrease the concentration of tenofovir alafenamide, reducing the therapeutic effect of VEMLIDY. Drugs that strongly affect P-glycoprotein (P-gp) and breast cancer resistance protein (BCRP) activity may lead to changes in VEMLIDY absorption.

Consult the full prescribing information for VEMLIDY for more information on potentially significant drug interactions, including clinical comments.

Click here for full Prescribing Information for VEMLIDY, including **BOXED WARNING** on posttreatment severe acute exacerbation of hepatitis B.

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Initiate treatment earlier for appropriate CHB patients by leveraging the Simplified Approach algorithm

Consensus from the SABA expert panel[1]

- Many patients with CHB are not receiving adequate monitoring or treatment, putting them at increased risk for serious liver disease
- The Simplified Approach Hepatitis B Algorithm (SABA) suggests the importance of treatment early in CHB disease progression

Choose VEMLIDY as your first-line CHB therapy for your appropriate treatment-naïve patients

Click here or visit www.VemlidyHCP.com to learn more about VEMLIDY pivotal and 5-year efficacy and safety data.

VEMLIDY is indicated for the treatment of chronic hepatitis B virus (HBV) infection in adults with compensated liver disease

IMPORTANT SAFETY INFORMATION (continued)

Dosage and Administration

- **Testing Prior to Initiation:** HIV infection.
- **Prior to or When Initiating, and During Treatment:** On a clinically appropriate schedule, assess serum creatinine, estimated creatinine clearance, urine glucose, and urine protein in all patients. In patients with chronic kidney disease, also assess serum phosphorus.
- **Dosage in Adults:** 1 tablet taken once daily with food.
- **Renal Impairment:** Not recommended in patients with end stage renal disease (ESRD; eCrCl <15 mL/min) who are not receiving chronic hemodialysis; in patients on chronic hemodialysis, on hemodialysis days, administer VEMLIDY after completion of hemodialysis treatment.
- **Hepatic Impairment:** Not recommended in patients with decompensated (Child-Pugh B or C) hepatic impairment.

Click here for full Prescribing Information for VEMLIDY, including **BOXED WARNING** on posttreatment severe acute exacerbation of hepatitis B.

References: 1. Dieterich D, Graham C, Wang S, et al. It Is Time for a Simplified Approach to Hepatitis B Elimination. *Gastro Hep Advances*. 2023;2(2):209-218. This is an open-access article under the CC BY-NC-ND license (https://creativecommons.org/licenses/by-nc-nd/4.0/). https://doi.org/10.1016/j.gastha.2022.10.004 **2.** Wong RJ, et al. *Hepatology*. 2021;74(2):607-626. **3.** Kim HS, et al. *J Viral Hepat*. 2019;26(5):596-602. **4.** Data on file. Gilead Sciences, Inc. **5.** Ogawa E, et al. *JAMA Netw Open*. 2020;3(4):e201844. **6.** Chao DT, et al. *Aliment Pharmacol Ther*. 2014;39(4):349-358. **7.** *Guidelines for the Prevention, Care and Treatment of Persons with Chronic Hepatitis B Infection*. Geneva: World Health Organization; March 2015. **8.** Spradling PR, et al. *Clin Infect Dis*. 2016;63(9):1205-1208. **9.** Tran S, et al. *Am J Gastroenterol*. 2021;116(9):1885-1895. **10.** Lupberger J, Hildt E. *World J Gastroenterol*. 2007;13(1):74-81. **11.** Levrero M, Zucman-Rossi J. *J Hepatol*. 2016;64(1 Suppl):S84-S101. **12.** Di Bisceglie AM. *Hepatology*. 2009;49(5 Suppl):S56-S60. **13.** Lim YS, et al. *Aliment Pharmacol Ther*. 2022;56(3):519-528.

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