HIBSAGO
(bepirovirsen)

Subcutaneous Use 150 mg/mL



DISCUSSING HIBSAGO WITH YOUR PATIENTS

This guide is meant to supplement and support conversations with your patients. It is designed to make complex information easier to explain in clear, patient-friendly terms, while supporting shared decision-making.

INDICATION

HIBSAGO is indicated in combination with nucleos(t)ide analog reverse transcriptase inhibitor (NrtI) therapy to treat chronic hepatitis B virus (HBV) infection in adults without cirrhosis who have been on NrtI therapy for ≥6 months with suppressed HBV DNA and who have HBV surface antigen (HBsAg) levels ≤3,000 IU/mL as determined by an FDA-authorized test.

IMPORTANT SAFETY INFORMATION

WARNING: ON-TREATMENT HEPATIC FLARES AND THROMBOCYTOPENIA

On-Treatment Hepatic Flares

HIBSAGO may cause on-treatment hepatic flares with increases in alanine aminotransferase (ALT) of >20-40x upper limit of normal (ULN) associated with decline in HBsAg. Some cases were associated with hyperbilirubinemia. Most occurred within the first 12 weeks and resolved when treatment was interrupted or discontinued. Do not initiate HIBSAGO in patients with evidence of acute hepatic impairment or cirrhosis. ALT and total bilirubin must be measured prior to treatment and frequently monitored during treatment. Treatment interruption, followed by dose reduction or discontinuation, may be necessary based on liver laboratory results.

Thrombocytopenia

HIBSAGO may cause reductions in platelet counts that may result in sudden and unpredictable thrombocytopenia, which can be life-threatening. Obtain platelet count prior to treatment; HIBSAGO is contraindicated in patients with platelet count <100 x 10^9/L. Monitor platelet counts weekly during treatment and more frequently if platelet count falls <75 x 10^9/L. Do not re-dose unless platelet count returns to ≥100 x 10^9/L. Permanently discontinue HIBSAGO if platelet count falls <50 x 10^9/L.

Please see additional Important Safety Information for HIBSAGO throughout. Please see full Prescribing Information, including Boxed Warning, for HIBSAGO.

EXPLAINING FUNCTIONAL CURE

With functional cure now part of the treatment conversation in chronic hepatitis B, a clear explanation can help patients understand what it can mean for them.

FUNCTIONAL CURE MEANS[1-3]:

- **HBV is controlled**
- **No daily HBV treatment**
- **Blood tests no longer detect hepatitis B surface antigen (HBsAg) and viral load (HBV DNA) after stopping treatments**
- **Functional cure does not completely eliminate the virus from the body, but it is inactive**

Some patients may already be familiar with HBV DNA, while others may be less familiar with HBsAg. Patients should understand that these biomarker tests are just two complementary ways we keep track of their chronic hepatitis B.[4-6]

- HBV DNA, also known as viral load, is one of the main signs we use to track chronic hepatitis B and how well treatment is working[4-6]
- While hepatitis B surface antigen (HBsAg) is one of the signs we use to track chronic hepatitis B in the body, a quantitative HBsAg (qHBsAg) test is how we measure those levels[4-6]
- If HBV DNA and HBsAg remain undetectable for at least 6 months after stopping treatment, it means you've reached functional cure[1-3]

DNA=deoxyribonucleic acid; HBV=hepatitis B virus.

IMPORTANT SAFETY INFORMATION (CONT'D)

CONTRAINDICATIONS

HIBSAGO is contraindicated in patients:

- with acute hepatic impairment or cirrhosis who have mild, moderate, or severe hepatic impairment (Child-Pugh Class A, B, or C).
- with a platelet count <100 x 10^9/L prior to initiation of treatment.

WARNINGS AND PRECAUTIONS

On-Treatment Hepatic Flares

Increases in ALT ≥3x ULN to 69x ULN were observed during treatment with HIBSAGO, most within the first 12 weeks. Isolated cases of ALT increases associated with an increase in total bilirubin resolved when treatment was permanently discontinued.

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THE POTENTIAL FOR ACHIEVING FUNCTIONAL CURE WITH HIBSAGO

SETTING EXPECTATIONS[1,2]

When discussing HIBSAGO, it's important to set expectations. Not all patients may achieve functional cure, but the potential for functional cure is now possible for patients with chronic hepatitis B.

DETERMINING HIBSAGO ELIGIBILITY[1]

Patients should understand that qHBsAg testing helps show whether they may be eligible for HIBSAGO. If they've been on nucleos(t)ide analog (NA)* therapy for at least 6 months with suppressed HBV DNA, have HBsAg levels at or below 3,000 IU/mL, and are noncirrhotic, they may be eligible for treatment.

EXPLAINING THE DATA[1,2]

For patients who are eligible, the data can help set patient expectations for the possibility of reaching functional cure. You might explain that in the 2 clinical trials† for patients with chronic hepatitis B with HBsAg ≤3,000 IU/mL, 20% and 19% of patients, respectively, achieved functional cure with HIBSAGO + NA, while noting that lower HBsAg levels (at or below 1,000 IU/mL) may mean a better chance of reaching functional cure.†‡§

SAFETY[1,2]

Patients may experience side effects with HIBSAGO. Among more than 1,200 participants with chronic hepatitis B who received HIBSAGO + NA in the 2 clinical trials†:

- The most common adverse reactions (≥10%), excluding laboratory abnormalities, reported with HIBSAGO included injection site reactions, pyrexia, fatigue, and headache
- Selected lab abnormalities reported with HIBSAGO included increased ALT ≥3x ULN (24%), AST ≥3x ULN (12%), total bilirubin ≥ULN (10%), platelets <140 x 10^9/L (47%), ANC cells/mm^3 <1,000 (10%), eGFR ≥15% decline from baseline (69%), and uACR ≥0.3 mg/mg (2%).[7] Please see Prescribing Information for additional details

MAKING IT EASIER TO SPEAK UP

Encourage patients to report all side effects or concerns they experience, even if they are unsure whether they are related to treatment or seem important.

*NA=nucleos(t)ide analog for treatment of chronic hepatitis B, herewith used interchangeably with NrtI.

†The efficacy and safety of HIBSAGO in the treatment of chronic HBV infection have been evaluated across two Phase 3, placebo-controlled, randomized studies, B-Well 1 and B-Well 2. Functional cure was defined as HBsAg loss (LOD=0.05 IU/mL) and undetectable HBV DNA (<LLOQ), sustained for ≥24 weeks off all HBV treatment, with or without hepatitis B surface antibodies present.[1-3]

‡Functional cure rates in participants with baseline HBsAg ≤3,000 IU/mL with HIBSAGO + NA were 20% (127/650) vs 0% (0/328) with placebo + NA in B-Well 1 and 19% (106/570) vs 0% (0/286) in B-Well 2. Among participants with baseline HBsAg ≤1,000 IU/mL, rates were 25% (105/426) with HIBSAGO + NA vs 0% (0/214) with placebo + NA and 28% (95/342) with HIBSAGO + NA vs 0% (0/179) with placebo + NA, in B-Well 1 and B-Well 2, respectively. Across both trials, 1,220 participants with baseline HBsAg ≤3,000 IU/mL received HIBSAGO + NA and 614 received placebo + NA.[1,2]

§To be eligible for NA cessation in B-Well 1 and B-Well 2, participants had to have no evidence of cirrhosis at Week 36, have HBV DNA <LLOQ and HBsAg not detected from Week 24 to 46, be HBeAg negative with ALT values ≤2x ULN at Week 46, and have remained on stable NA therapy for the preceding 48 weeks. HIBSAGO must be stopped upon completion of 24 weeks of treatment, and patients must remain on their NA therapy for an additional 24 weeks.[1,2]

ALT=alanine aminotransferase; ANC=absolute neutrophil count; AST=aspartate aminotransferase; eGFR=estimated glomerular filtration rate; HBeAg=hepatitis B e-antigen; LLOQ=lower limit of quantification; LOD=limit of detection; NrtI=nucleos(t)ide analog reverse transcriptase inhibitor; uACR=urine albumin-to-creatine ratio; ULN=upper limit of normal.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

Thrombocytopenia

In addition to sudden and unpredictable thrombocytopenia, a gradual, dose-dependent decline in platelet count was observed in most patients that continued to worsen while on HIBSAGO. If a patient develops signs or symptoms of thrombocytopenia, pause HIBSAGO and obtain a platelet count as soon as possible. Instruct patients to report any symptoms of thrombocytopenia to their healthcare provider immediately. Consider the risks and benefits of treatment with HIBSAGO when treating patients who may be particularly susceptible to platelet count decreases.

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DOSING SCHEDULE

Sharing what to expect when adding HIBSAGO to their treatment regimen will help patients understand what treatment involves, what monitoring to expect, and that they will need to stay on their daily antiviral treatment throughout treatment.

WALKING PATIENTS THROUGH TREATMENT

In the First Phase[1]:

HIBSAGO must be used in combination with NA therapy. Refer to the NA Prescribing Information for additional information.

- For the first 2 weeks, you'll receive 2 HIBSAGO doses of 300 mg each week. Each dose is given as two 150-mg subcutaneous injections
- Then you'll receive 1 HIBSAGO dose of 300 mg each week for the next 22 weeks (Weeks 3–24)
- Consider early cessation of HIBSAGO in patients who have not achieved HBsAg <1 IU/mL by Treatment Week 12

In the Second Phase[1]:

After 6 months, you'll stop HIBSAGO. For the next 6 months, you'll continue taking your daily NA. This gives us a chance to see how you've responded to treatment.

- At Week 48 (Month 12), if HBsAg and HBV DNA are no longer detected in the blood, we can talk about whether it may be appropriate to stop your daily antiviral treatment*

*In addition to having undetectable HBsAg and HBV DNA levels, other considerations for stopping daily NA treatment are that the patient should be HBeAg negative, have ALT values ≤2x ULN, and not need NA therapy to treat human immunodeficiency virus (HIV) coinfection.

In the Third Phase[1]:

Finally, daily antivirals can be discontinued if the hepatitis B virus remains under control for another 6 months.

- At the end of this phase, at Week 72 (Month 18), we'll check to see whether you've achieved functional cure

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

Worsening Renal Function

Mean estimated glomerular filtration rate (eGFR) declined within 4 weeks of initiation and continued to decline during treatment. These changes were generally reversible after treatment discontinuation.

Obtain eGFR and urine albumin-creatinine ratio (uACR) in all patients prior to initiation of treatment. Monitor eGFR frequently during and after treatment; treatment interruption or discontinuation may be necessary. Although no cases of glomerulonephritis were observed with HIBSAGO, glomerulonephritis has been observed with other antisense oligonucleotides; if suspected or confirmed, permanently discontinue HIBSAGO.

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ROUTINE MONITORING

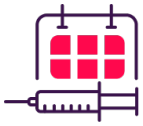
YOU MIGHT EXPLAIN:



Monitoring involves more than office visits. You'll need[1]:

- Blood draws and urine samples before treatment begins so we know where you're starting
- You'll continue having blood draws on a regular basis throughout treatment
- Blood and urine samples help us keep track of:
  - Your liver function
  - Your kidney function
  - Your platelet count

Depending on laboratory results, adjustments to the HIBSAGO dosage, treatment interruption, and increased frequency of laboratory test monitoring may be required.[1]



After HIBSAGO treatment[1]

- You will continue to be monitored while only taking your daily antivirals for the next 6 months
- Depending on your treatment response, we'll discuss whether it may be appropriate to discontinue antiviral therapy
- Additional blood work or monitoring may be needed based on your test results

If NA therapy is stopped, frequent monitoring of HBsAg, HBV DNA, and hepatic function is recommended for at least one year following NA therapy cessation, with routine monitoring as clinically indicated afterwards.[1]

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

Inflammatory and Immune Effects

Influenza-like symptoms, laboratory test changes (eg, decreases in complement factors C3 and C4), purpuric leg rashes, cutaneous leukocytoclastic vasculitis, dermatitis, pruritus/erythematous plaque, and polyarthralgia were observed. In addition, serious inflammatory and immune adverse reactions were reported, including immune thrombocytopenia, autoimmune hemolytic anemia, systemic inflammatory response syndrome, and a cryoglobulinemic flare.

Consider the risks and benefits of HIBSAGO in patients who may be susceptible to inflammatory and immune effects, including solid organ transplant recipients, patients with autoimmune hepatitis, patients with a history of or conditions associated with vasculitis, or extrahepatic disorders related to HBV immune-mediated effects. If signs and symptoms suggestive of vasculitis/immune-associated events occur, and no alternative cause is identified, permanently discontinue treatment with HIBSAGO.

Serious Adverse Reaction with Improper Administration

Improper HIBSAGO administration, including not rotating injection sites, has been associated with the serious adverse reaction of omental infarction in one participant. Ensure injection sites are rotated from one week to the next and that the two injections making up each dose are separated by at least 2 inches (5 cm). Never inject into areas where the skin is tender, bruised, red, or hard.

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CLOSING THE CONVERSATION

MOVING FORWARD TOGETHER

While it may not be the right option for every patient, discussing the possibility together can help patients better understand their treatment choices, what to expect, and what they hope to achieve.
Shared decision-making ensures every treatment plan reflects both the clinical evidence and what matters most to the patient.

CONVERSATION REMINDERS



Ask what matters most to your patient and what they hope treatment could mean for their future.



Review whether HIBSAGO may be an appropriate option based on their clinical profile.



Discuss what treatment involves, including expectations for monitoring and follow-up.



Encourage questions and make decisions together, based on the patient's goals and the available evidence. Lab work will be done before treatment begins, then regularly throughout the treatment journey.[1]

Several resources are available at **HIBSAGO.com** to give patients more information on understanding treatment and finding financial assistance for those who qualify.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

Post-Treatment Exacerbations of HBV Infection After NrtI Discontinuation
Severe acute exacerbations of HBV infection may occur after discontinuation of anti-HBV therapy. If NrtI therapy is discontinued after completing HIBSAGO treatment, frequent monitoring is recommended for at least one year to detect acute exacerbations of HBV infection and the possible need for resumption of HBV treatment.

Risk of Human Immunodeficiency Virus-1 (HIV-1) Virologic Failure in Patients with HBV/HIV-1 Coinfection Who Discontinue NrtI Therapy
Patients who are taking NrtI for HIV-1 and HBV coinfection must not stop taking their NrtI unless an HIV healthcare provider has directed them to do so.

Risk of Hepatitis Flare in Patients with HBV/Hepatitis D Virus (HDV) Coinfection
HIBSAGO is not recommended in patients with HDV coinfection due to the potential for an exacerbated risk of clinically significant ALT increases.

Unknown Effect on Preventing Transmission of HBV
There are no data on the effect of HIBSAGO in preventing transmission of HBV. Patients must be advised to use appropriate precautions to prevent transmission of HBV.

ADVERSE REACTIONS

The most common adverse reactions (≥10%), excluding laboratory abnormalities, reported with HIBSAGO included injection site reactions, pyrexia, fatigue, and headache.

Selected laboratory abnormalities worsened from baseline, including but not limited to, increases in ALT and total bilirubin, decreases in platelets and eGFR.

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IMPORTANT SAFETY INFORMATION (CONT'D)

DRUG INTERACTIONS

- Monitor patients for signs of bleeding and thrombocytopenia if HIBSAGO is taken concomitantly with anticoagulants, antiplatelets, or drugs that decrease platelet count.
- Monitor patients for signs of worsening renal function during concomitant administration of HIBSAGO with drugs that may impair renal function.
- Concomitant administration of HIBSAGO and peginterferon alfa-2a is not recommended due to the potential for an exacerbated risk of increased ALT, decreased platelet count, and immune-mediated effects.

USE IN SPECIFIC POPULATIONS

Pregnancy and Lactation

There are insufficient data on HIBSAGO use in pregnancy or during breastfeeding. Consider the benefits of breastfeeding together with the mother's clinical need for HIBSAGO.

Pediatric Use

HIBSAGO's safety and effectiveness have not been established in patients under 18 years of age.

Renal Impairment

HIBSAGO can cause worsening renal function. No dosage adjustment is recommended for mild renal impairment. Data are insufficient for moderate or severe renal impairment or end-stage renal disease (ESRD).

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To report SUSPECTED ADVERSE REACTIONS, contact GSK at gsk.public.reportum.com or 1-888-825-5249, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Intended for US healthcare professionals only.

References: 1. HIBSAGO. Prescribing Information. GSK; 2026. **2.** Hou J, Lim SG, Buti M, et al; B-Well Study Group. Phase 3 results of bepirovirsen treatment for chronic hepatitis B virus infection. *N Engl J Med.* 2026;394(24):2395-2406. **3.** Ghany MG, Buti M, Lampertico P, Lee HM; 2022 AASLD-EASL HBV-HDV Treatment Endpoints Conference Faculty. Guidance on treatment endpoints and study design for clinical trials to achieve cure in chronic hepatitis B and D: report from the 2022 AASLD-EASL HBV-HDV Treatment Endpoints Conference. *J Hepatol*. 2023;79(5):1254-1269. **4.** Screening and testing for hepatitis B virus infection: CDC recommendations – United States, 2023. Centers for Disease Control and Prevention. March 10, 2023. Accessed August 20, 2026. https://www.cdc.gov/mmwr/volumes/72/rr/rr7201a1.htm **5.** Clinical testing and diagnosis for hepatitis B. Centers for Disease Control and Prevention. August 14, 2026. Accessed August 20, 2026. https://www.cdc.gov/hepatitis-b/hcp/diagnosis-testing/index.html **6.** European Association for the Study of the Liver. EASL Clinical Practice Guidelines on the management of hepatitis B virus infection. *J Hepatol*. 2025;83(2):502-583. **7.** Data on file, GSK.

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