HIBSAGO
(bepirovirsen)

Subcutaneous Use 150 mg/mL

DOSING AND MONITORING GUIDE

A resource for healthcare professionals

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

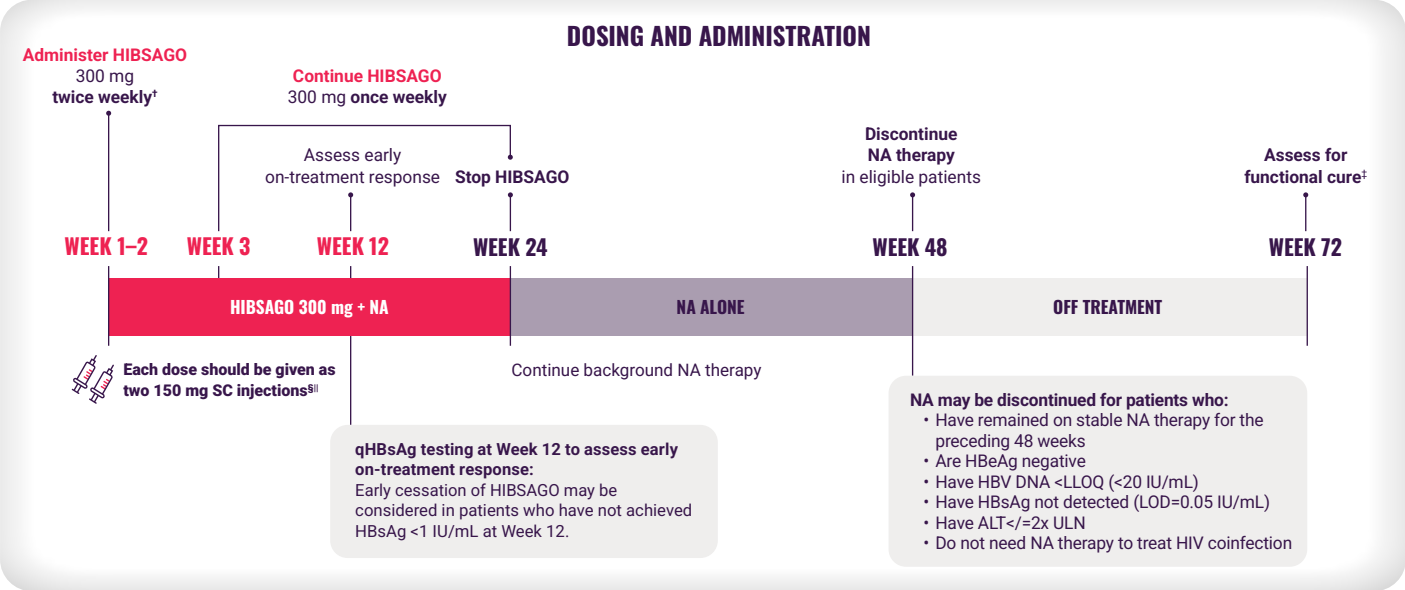
HIBSAGO may cause reductions in platelet counts that may result in sudden and unpredictable thrombocytopenia, which can be life-threatening. Obtain platelet count prior to treatment; HIBSAGO is contraindicated in patients with platelet count <100 x 10^9/L. Monitor platelet counts weekly during treatment 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.

DOSING SCHEDULE

HIBSAGO is administered weekly by subcutaneous injection alongside a nucleos(t)ide analog (NA)* for 6 months, followed by 6 months of NA alone. Eligible patients may then discontinue NA therapy.[1]

HIBSAGO must be administered under the guidance and supervision of a healthcare provider for the initial dose to ensure proper injection technique.[1]



*NA=nucleos(t)ide analog for treatment of chronic hepatitis B, herewith used interchangeably with NrtI.
†In Weeks 1–2 when dosing is twice weekly, there should be 3 to 4 days between doses.[1]
‡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]
§Each 300-mg dose is administered as two 150-mg SC injections into the abdomen, thigh, or, if administered by a caregiver or HCP, the upper arm. Patients or caregivers may administer HIBSAGO only after their healthcare provider determines that it is appropriate and provides injection training, with continued medical follow-up, including laboratory testing. Rotate injection sites each week and separate the two injections by at least 2 inches (5 cm). Never inject into skin that is tender, bruised, red, or hard.[1]
‖For dose adjustments where the 150-mg dose should be given, one syringe must be administered.[1]
ALT=alanine aminotransferase; DNA=deoxyribonucleic acid; HBeAg=hepatitis B e-antigen; HBsAg=hepatitis B surface antigen; HBV=hepatitis B virus; HCP=healthcare professional; HIV=human immunodeficiency virus; LLOQ=lower limit of quantification; LOD=limit of detection; NrtI=nucleos(t)ide analog reverse transcriptase inhibitor; qHBsAg=quantitative hepatitis B surface antigen; SC=subcutaneous; ULN=upper limit of normal.

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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LABORATORY MONITORING

Quantitative HBsAg testing is required to identify patients who may benefit from treatment with HIBSAGO.[1]
Patients should also be tested for HBV DNA, ALT, AST, bilirubin, platelet count, uACR, and eGFR at baseline and as directed while on treatment and following treatment completion.

Close laboratory monitoring is required to assess for toxicities that may necessitate dose modification, treatment interruption, or permanent discontinuation of HIBSAGO.[1]

Monitoring is required at prespecified time points during treatment with HIBSAGO for ALT and total bilirubin, platelet count, and eGFR.[1]

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]

AST=aspartate aminotransferase; eGFR=estimated glomerular filtration rate; uACR=urine albumin-to-creatinine ratio.

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.

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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DOSING AND MONITORING MODIFICATIONS

Based on laboratory test values, adjustments to HIBSAGO dosage, treatment interruption, and laboratory test monitoring frequency may be required.[1]

For ALT and/or total bilirubin[1,*]

IF LABORATORY VALUE IS:	MAKE THIS DOSAGE ADJUSTMENT:	AND CHANGE MONITORING FREQUENCY TO[†]:
ALT <3x ULN	**Continue treatment** No dosage adjustment required	Weekly through Week 12 and every other week from Weeks 12 through 24[‡]
ALT <10x ULN **AND** Total bilirubin <1.5x ULN		
ALT ≥10x to <12x ULN **AND** Total bilirubin <1.5x ULN	**Continue treatment** No dosage adjustment required	Increase monitoring to **twice weekly** until ALT is on a downward trajectory
ALT ≥12x ULN **AND** Total bilirubin <1.5x ULN	**Pause treatment** • When ALT is **<10x ULN**, resume at **150 mg weekly** • If **ALT continues to decline**, increase dosage to **300 mg weekly**	
ALT ≥3x ULN **AND** Total bilirubin ≥1.5x to <2x ULN	**Pause treatment** • When ALT is **<10x ULN** and total bilirubin is **<1.5x ULN**, resume at **150 mg weekly** • If **ALT is on a downward trajectory**, increase dosage to **300 mg weekly**	
ALT ≥10x ULN for ≥4 weeks **AND** Total bilirubin <1.5x ULN	**Permanently discontinue treatment**	**Twice weekly** until ALT is on a downward trajectory and then as clinically indicated
ALT ≥3x ULN **AND** Total bilirubin ≥2x ULN		

*If ALT or total bilirubin has increased markedly from the previous assessment, repeat laboratory testing and review the results before giving the next dose of HIBSAGO, even if the values have not yet reached the thresholds that require treatment interruption or discontinuation.
[†]In all patients with abnormal values at the time of HIBSAGO discontinuation, obtain ALT and total bilirubin values at 4, 12, and 24 weeks post-treatment to assess recovery of ALT values to within the normal range, as appropriate.
[‡]The minimum recommended on-treatment monitoring of ALT and total bilirubin in all patients.

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

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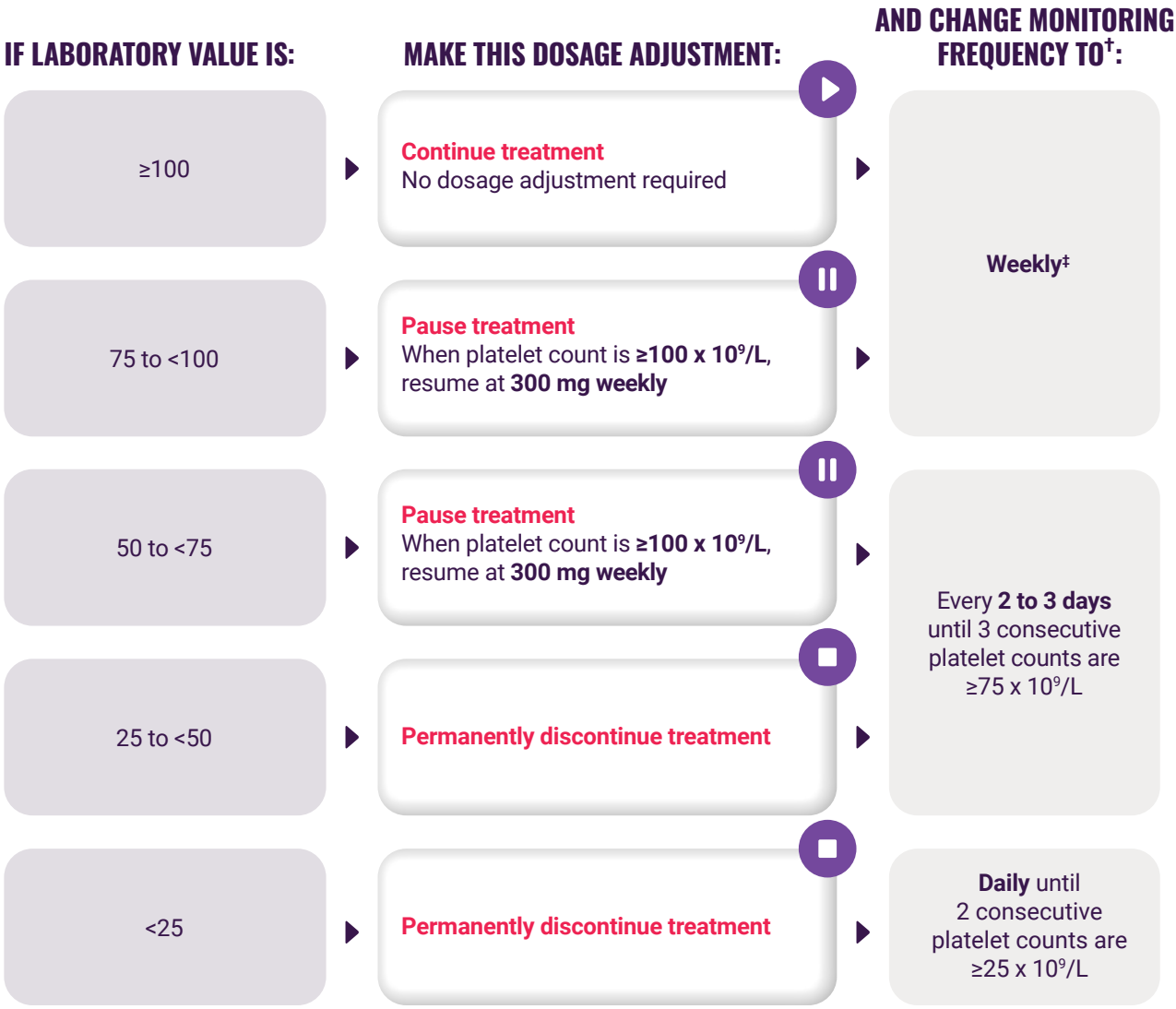
DOSING AND MONITORING MODIFICATIONS (CONT'D)

For platelet count (x 10^9/L)[1,*]



*If platelet count decreases by ≥30% between consecutive readings, repeat and review platelet count before administering further doses of HIBSAGO, even if platelet count is ≥100 x 10^9/L.

†In all patients with abnormal values at the time of HIBSAGO discontinuation, obtain repeat platelet counts 4 and 12 weeks post-treatment to assess for platelet count recovery, as appropriate.

‡The minimum recommended on-treatment monitoring of platelet counts in all patients.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

Inflammatory and Immune Effects (cont'd)

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.

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DOSING AND MONITORING MODIFICATIONS (CONT'D)

For eGFR[1]

IF LABORATORY VALUE IS:	MAKE THIS DOSAGE ADJUSTMENT:	AND CHANGE MONITORING FREQUENCY TO*:
No significant change from baseline	**Continue treatment** No dosage adjustment required	**Every other week through Week 24†**
Reduced by ≥30% from pretreatment levels for ≥2 consecutive readings	**Pause treatment** When eGFR increases to within 15% of pretreatment levels, resume at **300 mg weekly**	**Weekly** until eGFR stabilizes or returns to pretreatment levels

*In all patients with abnormal values at the time of HIBSAGO discontinuation, obtain eGFR at 4 weeks and 12 weeks post-treatment to monitor for renal function recovery, as appropriate.
†The minimum recommended on-treatment monitoring of eGFR in all patients.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

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.

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

STORAGE AND HANDLING



Prior to dispensing[1]

Store in a refrigerator at 36°F to 46°F (2°C to 8°C)

- **Do not** freeze or shake
- **Store** in the original carton to protect from light



Following dispensing[1]

HIBSAGO may be stored at room temperature up to 86°F (30°C) for 12 weeks

- **HIBSAGO injection must be administered within 6 hours once removed from the carton.** Discard if not administered within 6 hours
- **Do not** freeze or shake
- **Store** in the original carton to protect from light
- **Discard** if the expiry date has passed, or it has been 12 weeks since carton was received, whichever comes first
- **Dispose of unused medicine in an FDA-cleared sharps disposal container,** in accordance with local requirements

Ensure syringes have been kept at room temperature for a minimum of 30 minutes before use.[1]

IMPORTANT SAFETY INFORMATION (CONT'D)

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.

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.

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IMPORTANT SAFETY INFORMATION (CONT'D)

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.

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.

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PMUS-BPRLBND260002 October 2026
Produced in USA. 0002-0050-97

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