REDEFINE WHAT'S POSSIBLE FOR YOUR PATIENTS

FUNCTIONAL CURE. FINITE THERAPY.

IN CHRONIC HEPATITIS B, ENTER THE ERA OF HIBSAGO[1-3]

- 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[1,2,4]
- In patients with baseline HBsAg ≤3,000 IU/mL: in B-Well 1, HIBSAGO + nucleos(t)ide analog (NA)* was 20% (n=127/650) vs 0% (n=0/328) with placebo + NA (p<0.0001), and in B-Well 2, HIBSAGO + NA was 19% (n=106/570) vs 0% (n=0/286) with placebo + NA (p<0.0001), at Week 72, respectively[1,2]
- Functional cure is evaluated at 18 months: after 6 months of HIBSAGO + NA, 6 months of NA alone, and 6 months without treatment for eligible patients who discontinue NA therapy[1]

*NA=nucleos(t)ide analog for treatment of chronic hepatitis B, herewith used interchangeably with NrtI.
DNA=deoxyribonucleic acid; HBsAg=hepatitis B surface antigen; HBV=hepatitis B virus; LLOQ=lower limit of quantification; LOD=limit of detection; NrtI=nucleos(t)ide analog reverse transcriptase inhibitor.



Not an actual patient.

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.

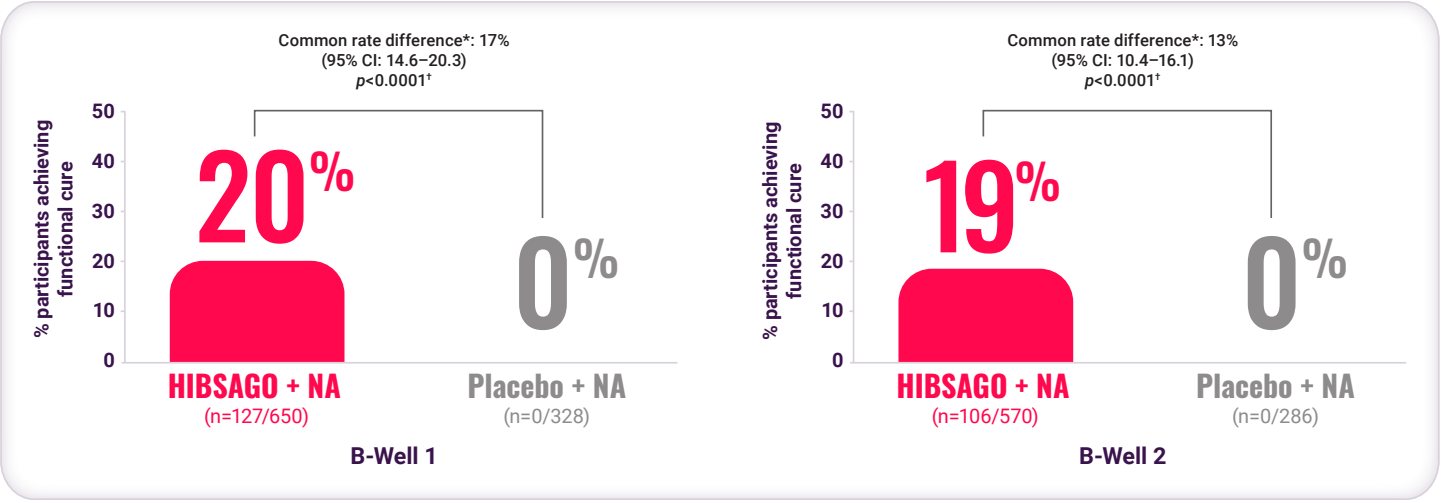
HIBSAGO (bepirovirsen)

Subcutaneous Use 150 mg/mL

HIBSAGO (bepirovirsen) + NA DEMONSTRATED A SUPERIOR FUNCTIONAL CURE RATE VS NA[1,2]

PRIMARY ENDPOINT: Baseline HBsAg ≤3,000 IU/mL

Functional cure rate at Week 72 achieved with HIBSAGO + NA in participants with baseline HBsAg ≤3,000 IU/mL*



In a pooled analysis, the functional cure rate with HIBSAGO + NA was 19% compared to 0% with placebo + NA at Week 72‡

Results are descriptive.

*Common rate difference, calculated as a weighted average of the stratum-specific rate differences, with the associated 95% confidence interval (CI) from stratified Miettinen-Nurminen method.[1,2]
†Based on 2-sided p value (exact Cochran-Mantel Haenszel).[1]
‡In this analysis, 233 of 1,220 participants achieved functional cure with HIBSAGO + NA compared with 0 of 614 participants with placebo + NA.[1]

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.

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

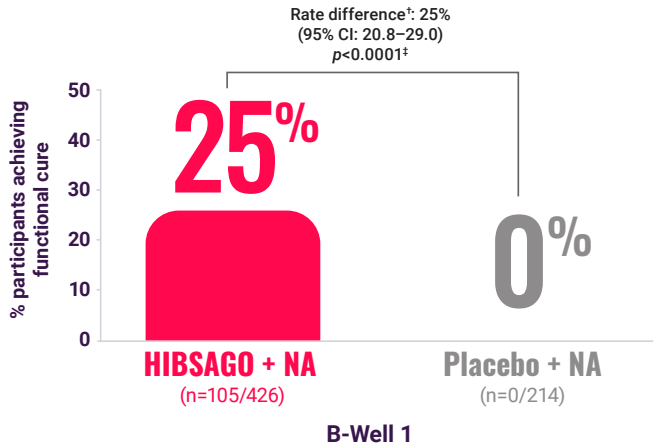
HIBSAGO (bepirovirsen)
Subcutaneous Use 150 mg/mL

IN A POOLED ANALYSIS

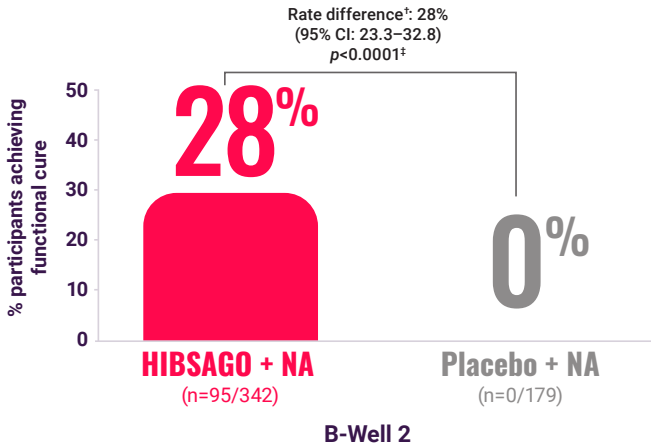
26% OF PARTICIPANTS WITH BASELINE HBsAg ≤1,000 IU/mL ACHIEVED FUNCTIONAL CURE WITH HIBSAGO[1,2]

KEY SECONDARY ENDPOINT: Baseline HBsAg ≤1,000 IU/mL

Functional cure rate at Week 72 achieved with HIBSAGO + NA in participants with baseline HBsAg ≤1,000 IU/mL*



B-Well 1



B-Well 2

In a pooled analysis, the functional cure rate with **HIBSAGO + NA was 26%** compared to 0% with placebo + NA at Week 72§

Results are descriptive.

*In the B-Well 1 and B-Well 2 trials, the primary endpoint of participants with baseline HBsAg ≤3,000 IU/mL achieving functional cure was met.[1,2]
†95% Miettinen-Nurminen confidence interval (CI).[1]
‡Based on 2-sided p value (Boschloo's test).[1]
§In this analysis, 200 of 768 participants achieved functional cure with HIBSAGO + NA compared with 0 of 393 participants with placebo + NA.[1,2]

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.

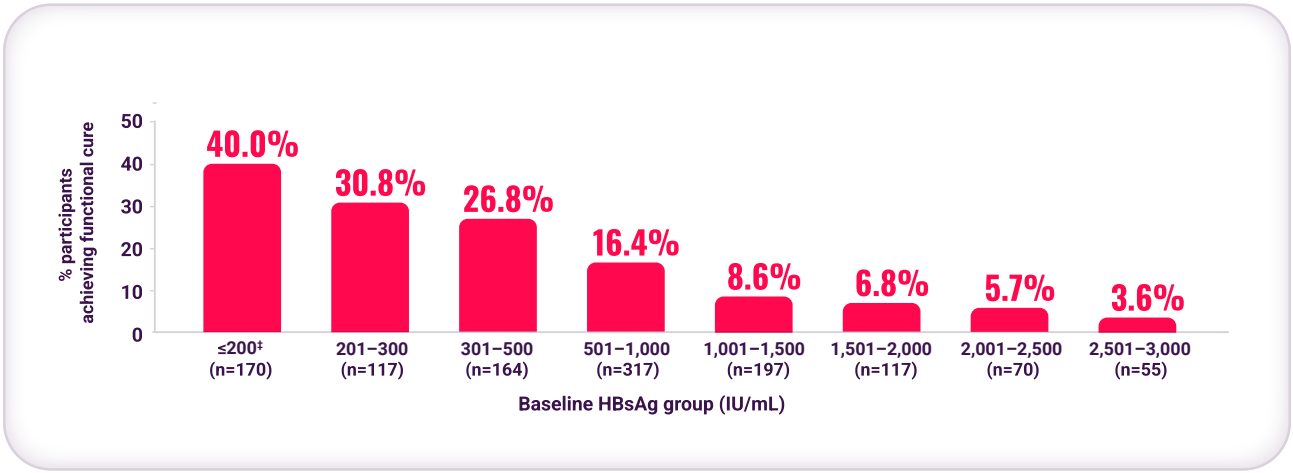
Please see additional Important Safety Information for HIBSAGO throughout.
Please see full Prescribing Information, including Boxed Warning, for HIBSAGO.

HIBSAGO (bepirovirsen)
Subcutaneous Use 150 mg/mL

LOWER BASELINE HBsAg WAS ASSOCIATED WITH HIGHER FUNCTIONAL CURE RATES[5]*

POST HOC EXPLORATORY: Baseline HBsAg ≤3,000 IU/mL

Rates of functional cure relative to baseline HBsAg pooled from B-Well 1 and B-Well 2†



Results are descriptive.

*Unless otherwise specified, baseline was the last value/assessment before the first dose of study treatment (Day 1 pre-dose). If there were multiple assessments collected at the same scheduled time, the average of these assessments was used as the baseline.[6]
†Functional cure rates are derived for mutually exclusive baseline HBsAg intervals from a cumulative threshold pooled subgroup analysis.[5]
‡The B-Well 1 and B-Well 2 clinical trials enrolled participants with HBsAg >100 to ≤3,000 IU/mL at screening.[1,2]

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.

Please see additional Important Safety Information for HIBSAGO throughout.
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HIBSAGO (bepirovirsen)
Subcutaneous Use 150 mg/mL

DURABILITY OF FUNCTIONAL CURE WAS ASSESSED AT WEEK 96 IN A POOLED ANALYSIS[1]

EXPLORATORY: Baseline HBsAg ≤3,000 IU/mL

91% **of participants achieving functional cure at Week 72 maintained it through 96 weeks** (n=211/233)

Among participants who met the criteria and discontinued NA therapy at Week 48 (295/1,220 across both trials), long-term durability of response at Week 96 was evaluated in participants who achieved functional cure at Week 72 (233/295).

Results are descriptive.

Long-term follow-up **to evaluate durability of treatment response is ongoing[2]**

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.

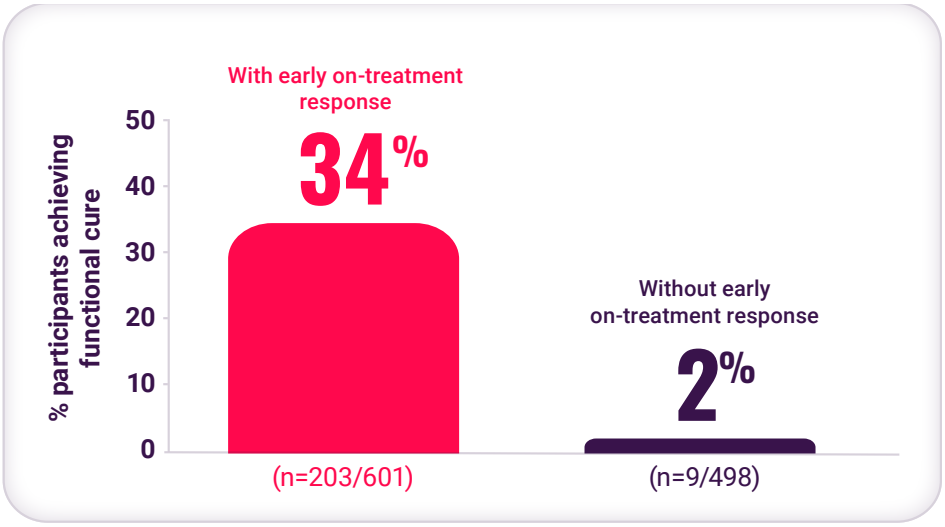
Please see additional Important Safety Information for HIBSAGO throughout.
Please see full Prescribing Information, including Boxed Warning, for HIBSAGO.

HIBSAGO (bepirovirsen)
Subcutaneous Use 150 mg/mL

USE OF QUANTITATIVE HBsAg AT WEEK 12 TO PREDICT FUNCTIONAL CURE AT WEEK 72[1]

POST HOC EXPLORATORY: Baseline HBsAg ≤3,000 IU/mL

Functional cure rates in participants with or without early on-treatment response



Definition of early on-treatment response:

- HBsAg <1 IU/mL at Week 12

Results are descriptive.

Pooled post hoc analysis of B-Well 1 and B-Well 2

n values for participants with and without treatment response are derived from participants with available data at Week 12 of the studies.

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.

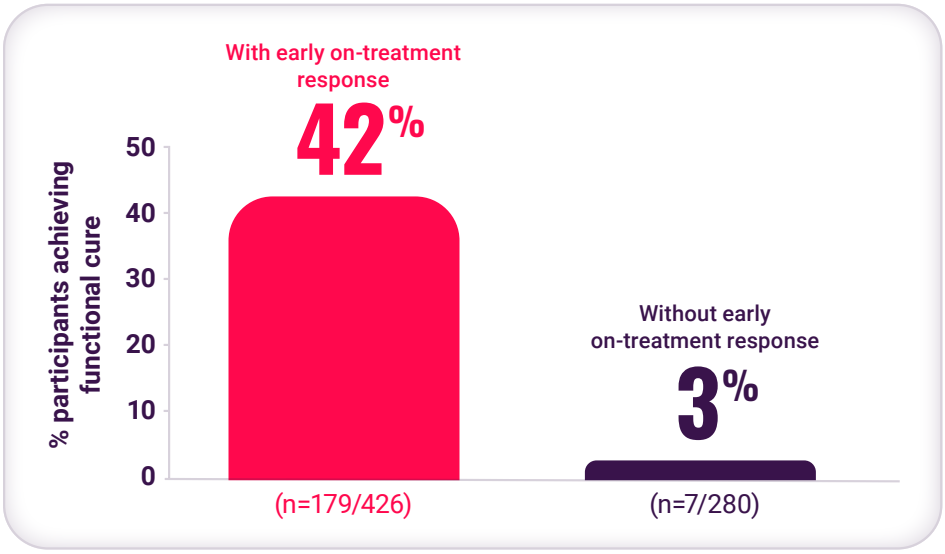
Please see additional Important Safety Information for HIBSAGO throughout.
Please see full Prescribing Information, including Boxed Warning, for HIBSAGO.

HIBSAGO (bepirovirsen)
Subcutaneous Use 150 mg/mL

USE OF QUANTITATIVE HBsAg AT WEEK 12 TO PREDICT FUNCTIONAL CURE AT WEEK 72[1]

POST HOC EXPLORATORY: Baseline HBsAg ≤1,000 IU/mL

Functional cure rates in participants with or without early on-treatment response



Definition of early on-treatment response:

- HBsAg <1 IU/mL at Week 12

Results are descriptive.

Pooled post hoc analysis of B-Well 1 and B-Well 2

n values for participants with and without early on-treatment response are derived from participants with available data at Week 12 of the studies.

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.

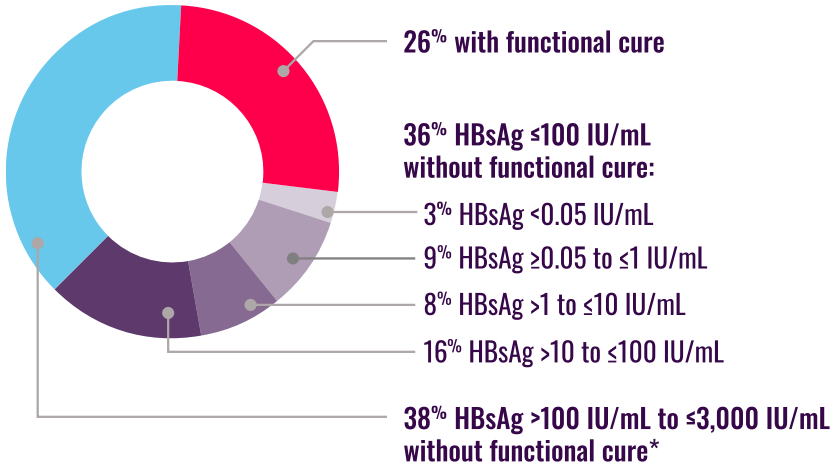
Please see additional Important Safety Information for HIBSAGO throughout.
Please see full Prescribing Information, including Boxed Warning, for HIBSAGO.

HIBSAGO (bepirovirsen)
Subcutaneous Use 150 mg/mL

HBsAg LEVELS AT WEEK 72 FOR PARTICIPANTS WITH BASELINE HBsAg ≤1,000 IU/mL[5]

POST HOC EXPLORATORY: Baseline HBsAg ≤1,000 IU/mL

HBsAg levels in participants with baseline HBsAg ≤1,000 IU/mL at Week 72 (N=768)



62% of patients with baseline HBsAg ≤1,000 IU/mL reached HBsAg ≤100 IU/mL at Week 72: 26% achieved functional cure and 36% had HBsAg ≤100 IU/mL

Results are descriptive.

*Includes participants with missing data (n=53/768).

Pooled post hoc analysis of B-Well 1 and B-Well 2

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)
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.

Please see additional Important Safety Information for HIBSAGO throughout.
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HIBSAGO (bepirovirsen)
Subcutaneous Use 150 mg/mL

SAFETY PROFILE[1]

ASSESSED IN B-WELL 1 AND B-WELL 2 PHASE 3 STUDIES WITH OVER 1,200 HIBSAGO-TREATED PATIENTS

The most common adverse reactions (≥10%), excluding laboratory abnormalities, reported with HIBSAGO + NA vs placebo + NA, respectively, included injection site reactions (57% vs 15%), pyrexia (20% vs 4%), fatigue (16% vs 8%), and headache (14% vs 12%).[1]

Summary of selected laboratory abnormalities reported in the B-Well 1 and B-Well 2 trials (Weeks 1-36)[1,5]*

Lab categories	HIBSAGO + NA (N=1,223)	Placebo + NA (N=611)
ALT ≥3x ULN	294 (24%)	3 (<1%)
AST ≥3x ULN	142 (12%)	6 (1%)
Total bilirubin ≥ULN	118 (10%)	82 (13%)
Platelets (x10^9/L) <140	575 (47%)	43 (7%)
ANC cells/mm^3 <1,000	121 (10%)	24 (4%)
eGFR ≥15% decline from baseline	841 (69%)	225 (37%)
uACR ≥0.3 mg/mg	22 (2%)	9 (1%)

In the pooled safety population,† any on-treatment AEs during Weeks 1–24 were reported in 89% of patients receiving HIBSAGO + NA (1,087/1,223) and 65% receiving placebo + NA (399/611). These included AEs leading to permanent discontinuation (3% vs <1%), dose reduction (2% vs 0%), dose interruption/delay (16% vs 2%), Grade ≥3 severity AEs (16% vs 3%), treatment-related AEs (80% vs 35%), and SAEs related to study treatment (2% v 0%), respectively.[2]

See the full safety profile at HIBSAGOhcp.com

HIBSAGO also has a Boxed Warning for on-treatment hepatic flares and thrombocytopenia.[1]

*Laboratory abnormalities (worsening from baseline) were summarized cumulatively; within each laboratory category, patients within the specified threshold were only counted once.[5]

†All the patients in the 2 trials received HIBSAGO or placebo through Weeks 1 to 24 (treatment period). Categories of adverse events were not mutually exclusive, so patients may have been counted in more than one category.[1,2]

AE=adverse event; ALT=alanine aminotransferase; ANC=absolute neutrophil count; AR=adverse reaction; AST=aspartate aminotransferase; eGFR=estimated glomerular filtration rate; SAE=serious adverse event; uACR=urine albumin-to-creatinine ratio; ULN=upper limit of normal.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

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.

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

HIBSAGO (bepirovirsen)
Subcutaneous Use 150 mg/mL

KEY CONSIDERATIONS FOR LABORATORY ABNORMALITIES & ARs OF SPECIAL INTEREST[1,2]

ALT increases	Platelet decreases
• During treatment with HIBSAGO, increases in ALT ≥3x ULN to 69x ULN were observed in clinical trials • Most ALT increases occurred in the first 12 weeks of treatment (typically between Weeks 5 to 10), started to resolve within 2 weeks, and were not associated with any clinical signs or symptoms of liver dysfunction • The ALT increases were temporally associated with a preceding or concurrent decline in HBsAg, suggesting host immune response • 2% of participants receiving HIBSAGO had ALT increases ≥20x ULN that resolved when treatment was interrupted or permanently discontinued. There have been isolated cases of ALT increases associated with an increase in total bilirubin up to 4x ULN that resolved when treatment was permanently discontinued • Do not initiate HIBSAGO in patients with evidence of acute hepatic impairment or cirrhosis • Please see the full Prescribing Information for HIBSAGO for additional information on testing and monitoring	• HIBSAGO may cause reductions in platelet count at any time during treatment that may result in sudden and unpredictable thrombocytopenia that can be life-threatening • Do not initiate HIBSAGO in patients with a platelet count below 100 x 10^9/L. In patients with platelet count below the normal range but ≥100 x 10^9/L, rule out cirrhosis before initiating HIBSAGO • If platelet count falls below 50 x 10^9/L, permanently discontinue treatment with HIBSAGO and consider corticosteroid treatment in consultation with an expert • Symptoms of thrombocytopenia can include unusual or prolonged bleeding, neck stiffness, or atypical severe headache. If a patient develops signs or symptoms of thrombocytopenia, treatment with HIBSAGO must be paused and a platelet count obtained as soon as possible • Consider the risks and benefits of treatment with HIBSAGO when treating patients who may be particularly susceptible to platelet count decreases, eg, elderly patients, or patients with bleeding diathesis/coagulopathy, history of major bleeding events, or patients taking antiplatelets, anticoagulants, or drugs that lower platelet count • Please see the full Prescribing Information for HIBSAGO for additional information on testing and monitoring

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

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.

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

KEY CONSIDERATIONS FOR LABORATORY ABNORMALITIES & ARs OF SPECIAL INTEREST[1,2] (CONT'D)

Worsening renal function	Inflammatory and immune effects
• In the HIBSAGO clinical trials, mean eGFR declined within 4 weeks of initiation of HIBSAGO and continued to decline during treatment. These changes were generally reversible after treatment discontinuation. The mechanism of the decrease in eGFR is not clear • Consider the risks and benefits of HIBSAGO when treating patients who may be more susceptible to renal injury • Glomerulonephritis has been observed after administration of other antisense oligonucleotides. Consider assessing for proteinuria periodically during treatment, as appropriate. If a diagnosis of glomerulonephritis is suspected or confirmed, permanently discontinue HIBSAGO and consider early initiation of immunosuppressive therapy in consultation with an expert • Please see the full Prescribing Information for HIBSAGO for additional information on testing and monitoring	• In trials with HIBSAGO, influenza-like symptoms, laboratory test changes (eg, decreases in complement factor 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 when treating patients who may be more susceptible to inflammatory and/or immune effects, eg, solid organ transplant recipients, patients with autoimmune hepatitis, or patients with a history of vasculitis or conditions associated with vasculitis. The risks and benefits of HIBSAGO must also be considered in patients with a history of, or suspected, 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 • Please see the full Prescribing Information for HIBSAGO for additional information on testing and monitoring



Regular monitoring of ALT, platelet counts, and renal function is required to manage any potential safety events with HIBSAGO.[1,2]

IMPORTANT SAFETY INFORMATION (CONT'D)

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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HIBSAGO (bepirovirsen)
Subcutaneous Use 150 mg/mL

ROUTINE SAFETY LAB MONITORING SCHEDULE[1]

Laboratory monitoring is required during treatment at the following time points. Based on laboratory test values, adjustments to HIBSAGO dosage, treatment interruption, and increased frequency of laboratory monitoring may be required.

Before initiating HIBSAGO, obtain qHBsAg, HBV DNA, ALT, AST, bilirubin, platelet count, uACR, and eGFR.

Laboratory parameter	Weeks 2–12	Weeks >12–24
ALT and total bilirubin*	Weekly	Every other week
Platelet count†	Weekly	
eGFR‡	Every other week	
	6 MONTHS OF HIBSAGO + NA	

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

*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.
†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.
‡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.

qHBsAg=quantitative hepatitis B surface antigen.

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.

Please see additional Important Safety Information for HIBSAGO throughout.
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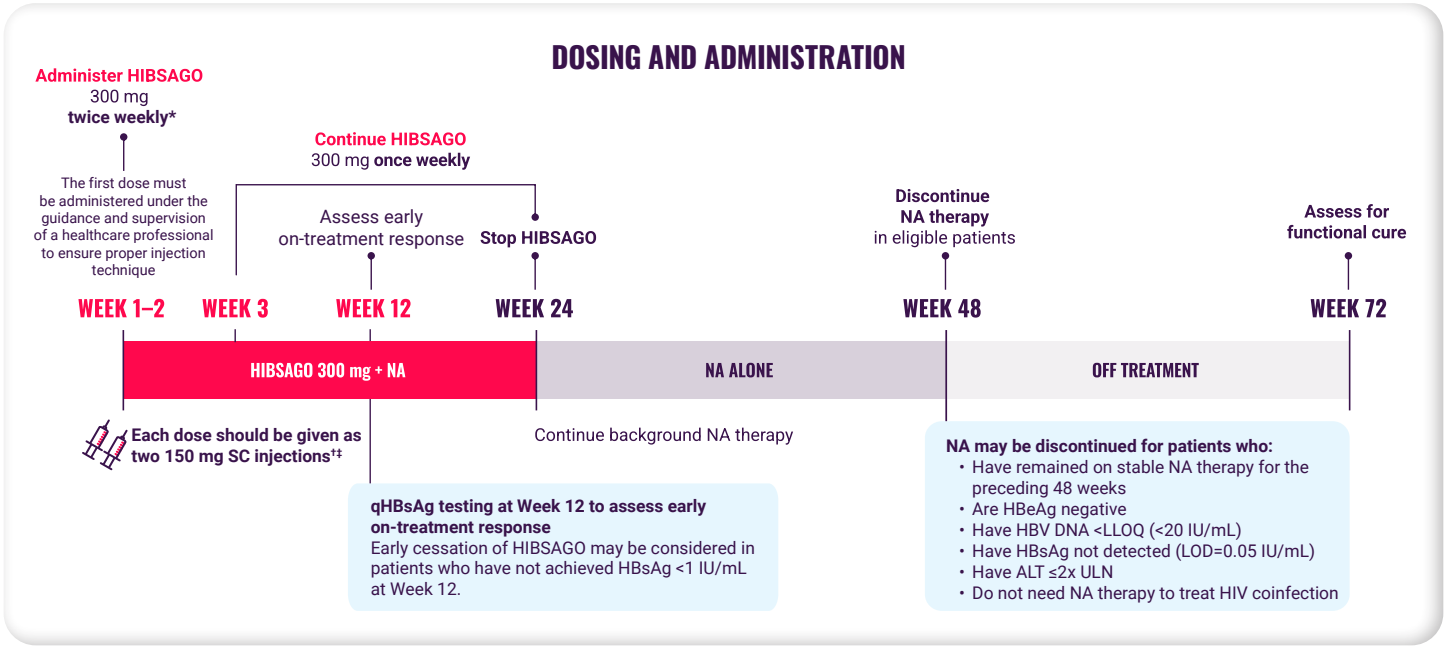
HIBSAGO (bepirovirsen)
Subcutaneous Use 150 mg/mL

HIBSAGO IS THE FIRST AND ONLY 6-MONTH FINITE TREATMENT, USED WITH NA, FOR CHRONIC HEPATITIS B[1-3]

HIBSAGO is administered weekly by subcutaneous injection alongside NA for 6 months, followed by 6 months of NA alone and 6 months without treatment for eligible patients who discontinue NA therapy. Functional cure is evaluated at 18 months.



*In Weeks 1–2 when dosing is twice weekly, there should be 3 to 4 days between doses.
†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.
‡For dose adjustments where the 150-mg dose should be given, one syringe must be administered.

HCP=healthcare provider; HBeAg=hepatitis B e-antigen; HIV=human immunodeficiency virus; SC=subcutaneous.

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.

Please see additional Important Safety Information for HIBSAGO throughout.
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HIBSAGO (bepirovirsen)
Subcutaneous Use 150 mg/mL

HIBSAGO MAY BE APPROPRIATE FOR YOUR ELIGIBLE PATIENTS

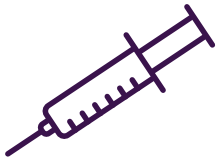
HIBSAGO may be appropriate across a range of patients. HIBSAGO should be prescribed only when appropriate lab monitoring can be performed.[1] Initiating treatment begins with these 3 steps:



1. IDENTIFY PATIENTS*

HIBSAGO may be appropriate for adult patients with chronic hepatitis B who have been on NA therapy for at least 6 months and who have suppressed HBV DNA, have HBsAg ≤3,000 IU/mL, and are noncirrhotic.[1]

Quantitative HBsAg testing is needed to identify those with HBsAg levels ≤3,000 IU/mL. Testing may be available through your institution's laboratory or a third-party commercial lab.[1,4]



2. KNOW DOSING AND MONITORING

Review dosing, administration, routine monitoring, and treatment management considerations for HIBSAGO.



3. SUPPORT FOR YOUR PATIENTS

Together with HIBSAGO, a patient support program, can help eligible patients throughout treatment.

Copay assistance is for eligible, commercially insured patients.

E-prescribe or enroll in Together with HIBSAGO to get started.

*Additional label-specific contraindications and precautions can be found in the Prescribing Information.

IMPORTANT SAFETY INFORMATION (CONT'D)

USE IN SPECIFIC POPULATIONS (CONT'D)

Pediatric Use

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

Please see additional Important Safety Information for HIBSAGO throughout.
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HIBSAGO (bepirovirsen)
Subcutaneous Use 150 mg/mL

THE HIBSAGO ERA IN CHRONIC HEPATITIS B BEGINS WITH THE POTENTIAL FOR FUNCTIONAL CURE AND FINITE THERAPY[1-3]*

ENTER THE ERA OF HIBSAGO

HIBSAGO is the first and only 6-month finite treatment, used with NA, with the potential for functional cure[1-3]*†

- Functional cure is evaluated at 18 months: after 6 months of HIBSAGO + NA, 6 months of NA alone, and 6 months without treatment for eligible patients who discontinue NA therapy‡

Higher functional cure rates at Week 72 were achieved with lower baseline HBsAg[1,2]*

- In a pooled analysis, 26% of participants with baseline HBsAg ≤1,000 IU/mL achieved functional cure with HIBSAGO + NA versus 0% with placebo + NA (19% and 0%, respectively, in participants with baseline HBsAg ≤3,000 IU/mL).† Results are descriptive

Safety was assessed in >1,200 HIBSAGO-treated participants[1,2]

- The most common adverse reactions (≥10%), excluding laboratory abnormalities, are injection site reactions, pyrexia, fatigue, and headache
- 3% of treated patients discontinued treatment due to adverse reactions

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*The primary endpoint at Week 72 in participants with baseline HBsAg ≤3,000 IU/mL was functional cure, 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. In B-Well 1 and B-Well 2, the primary endpoint was met.[1,2,4]

†In a pooled analysis of B-Well 1 and B-Well 2, functional cure (primary endpoint) was achieved in 19% (n=233/1,220) with HIBSAGO + NA vs 0% (n=0/614) with placebo + NA in participants with baseline HBsAg ≤3,000 IU/mL at Week 72. Results are descriptive.[1]

‡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 detectable 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]

IMPORTANT SAFETY INFORMATION (CONT'D)

USE IN SPECIFIC POPULATIONS (CONT'D)

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).)

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

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. Figures and tables copyright © (2026) Massachusetts Medical Society. Adapted with permission from Massachusetts Medical Society. **3.** Yuen MF, Chen DS, Dusheiko GM, et al. Hepatitis B virus infection. *Nat Rev Dis Primers.* 2018;4:18035. **4.** 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. **5.** Data on file, GSK. **6.** 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 [protocol].

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HIBSAGO (bepirovirsen) GSK

Subcutaneous Use 150 mg/mL