EPIC EHR CHRONIC HBV INFECTION
Toolkit for End Users

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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.

EHR = electronic health record.

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

Toolkit Overview and Limitations

This toolkit is intended to help Epic users configure and use selected EHR functionality relevant to HIBSAGO, including patient identification workflows, a non-oncology therapy plan, after-visit summary content, and specialty pharmacy–related workflow support. These instructions are suggestions only and are not meant to replace institutional expertise, guidance, or independent clinical judgment. These instructions support the following and are not appropriate for other conditions, treatments, therapeutic areas, or for other EHR systems:

- Identifying potential patient candidates for treatment
  - Use Epic end-user reporting tools, including Reporting Workbench and SlicerDicer, to help identify patients who may be appropriate for review based on selected clinical criteria and organizational workflows
- Ordering of HIBSAGO within the EHR
  - Adding orders and therapy plans to a provider's preference list
- Providing After-Visit Summary content for patients
  - Use easily copied sample After-Visit Summary content to reinforce patient education and other follow-up information as part of the ongoing treatment workflow. Specific content needs may vary by user and organization
- Specialty pharmacy–related workflow support
  - Use specialty pharmacy–related workflow support in Epic to help guide prescription routing and related specialty pharmacy considerations

The customer shall be solely responsible for implementing, testing, monitoring, and maintaining any EHR tools to ensure proper function in its own EHR environment. Capabilities, functionality, and set-up vary across institutions and Epic configurations. While EHRs may assist providers in identifying appropriate patients for consideration of assessment and treatment, the decision and action should ultimately be decided by a provider in consultation with the patient after review of the patient's records to determine eligibility.

Rather than prescribing a single-build approach, the toolkit provides modular, step-by-step guidance; clinical decision support (CDS) examples; and workflows that organizations can adapt based on their Epic maturity, governance structure, and local practice patterns. Each section is described in detail in this document.

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.

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HIBSAGO (bepirovirsen)
Subcutaneous Use 150 mg/mL

Why This Matters

HIBSAGO is a hepatitis B virus (HBV) mRNA-directed antisense oligonucleotide (ASO) indicated in combination with nucleos(t)ide analog reverse transcriptase inhibitor (NrtI) therapy for treatment of chronic HBV infection in adult patients without cirrhosis[1]:

- who have been on NrtI therapy for at least 6 months and have suppressed HBV deoxyribonucleic acid (DNA), and
- who have HBV surface antigen (HBsAg) levels less than or equal to 3,000 IU/mL as determined by an FDA-authorized test

Quantitative HBsAg testing measures the amount of HBV surface protein circulating in the blood (IU/mL), providing a more precise and clinically meaningful measure than qualitative testing alone.[2,3] Quantitative HBsAg levels inform prognosis, support treatment eligibility assessments, and allow clinicians to monitor therapy response and help track a patient's progress toward functional cure.[3]

Because HIBSAGO treatment is tied to specific clinical, laboratory, and safety considerations, successful implementation may require coordinated EHR support.[1] Patient identification logic, therapy plan content, clinical decision support, quantitative HBsAg testing, specialty pharmacy coordination, and patient-facing education can each support a different part of the care process.

HBsAg = hepatitis B surface antigen.

Patient Identification and Reporting

End-user reporting solutions in Epic are generally available to most end users and allow the user to find patients who meet a set of inclusion/exclusion criteria. The end-user reporting solutions in Epic are **Reporting Workbench** and **SlicerDicer** and **SlicerDicer Sidekick**.

Additional reporting solutions are available, but the operation of these tools requires analyst/reporting privileges and is beyond the scope of most users.

The provided steps will assist an end user to create the following patient queries.

Suggested clinical content

Consider the following scenario when creating the patient query: identifying adult patients receiving nucleos(t)ide analog (NA) therapy for treatment of chronic HBV infection (without cirrhosis) with HBsAg levels ≤3,000 IU/mL. Here are the selected inclusion and exclusion criteria for your consideration:

These criteria are intended to help identify potentially appropriate patients. Providers should always apply their independent clinical judgment and consider each patient's individual circumstances when making treatment decisions.

Inclusion Criteria for the Patient List

- Adult patients with chronic HBV infection[1] (ICD-10-CM code: B18.1–chronic viral hepatitis B without delta-agent)[4]
- Patients currently receiving NA therapy for at least 6 months and have suppressed HBV deoxyribonucleic acid (DNA)[1]
- Patients with HBsAg ≤3,000 IU/mL[1]
- Patients with platelet count ≥100 × 10^9/L prior to treatment initiation, since HIBSAGO is contraindicated in patients with platelet count <100 × 10^9/L prior to initiation of treatment[1]

Exclusion Criteria for the Patient List

- 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)[1] (ICD-10-CM codes: K70.30–alcoholic cirrhosis of liver without ascites, K70.31–alcoholic cirrhosis of liver with ascites, K72.00–acute and subacute hepatic failure without coma, K72.01–acute and subacute failure with coma, K74.3–primary biliary cirrhosis, K74.4–secondary biliary cirrhosis, K74.5–biliary cirrhosis unspecified, K74.60–unspecified cirrhosis of liver, K74.69–other cirrhosis of liver)[4]

IMPORTANT SAFETY INFORMATION (CONT'D)

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.

ICD-10-CM = International Classification of Diseases, Tenth Revision, Clinical Modification.

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

Patient Identification and Reporting (cont'd)

Instructions for Reporting Workbench

1. Access **Reporting Workbench** (click the **Epic logo > Reports > My Reports**)
2. Navigate to the **Library tab** from the **Reports menu**
3. Enter **"generic criteria"** or **"find patients"** in the search field and click **Search**
4. Select the **Find My Patients – Generic Criteria report** and click the starburst/asterisk icon to create a **new report**
5. The **Report Settings field** will display and default to the **Criteria tab**
6. In the **Find Criteria** search field, enter "living" and select **Patient: Living Status**
7. Set the status to **Alive**
8. In the **Find Criteria** search field, enter "age" and select the **Age in Years** criterion
9. Set the age range to **greater than or equal to 18 years**
10. In the **Find Criteria** search field, enter "diagnosis"
11. Select the **Diagnosis by Code** criterion
    Note: Alternatively, **Diagnosis by Grouper** or **Problems by Grouper** can be leveraged if using a CHRONIC HEPATITIS B VIRUS INFECTION grouper. Ensure that the diagnoses in the grouper are the ones of interest for the query. If using a grouper, skip to step 14
12. Set the **Code Set** to **ICD-10-CM**
13. Enter the ICD-10 code **B18.1**
14. In the **Find Criteria** search field, enter "diagnosis"
15. Select the **Diagnosis by Code** criterion
    Note: Alternatively, **Diagnosis by Grouper** or **Problems by Grouper** can be leveraged if using a cirrhosis grouper. Ensure that the diagnoses in the grouper are the ones of interest for the query. If using a grouper, skip to step 18.
16. Set the **Code Set** to **ICD-10-CM**
17. Enter the ICD-10 codes for acute hepatic impairment or cirrhosis (K70.30, K70.31, K72.00, K72.01, K74.3, K74.4, K74.5, K74.60, K74.69)[4] that should be excluded and update the **Report Logic** to **AND NOT** for this criterion

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.

Patient Identification and Reporting (cont'd)

Instructions for Reporting Workbench (cont'd)

18. In the **Find Criteria** search field, enter "Meds"
19. **Select the Meds: Current, by exact medication criterion**
20. **Enter the nucleos(t)ide analog therapy medications [eg, entecavir (Baraclude), tenofovir DF (Viread), tenofovir AF (Vemlidyl)].** Alternatively, select the **Meds: Current, by pharm. Class/Subclass criterion and** select the pharmaceutical class/subclass for **NA therapy** (this name may vary depending on the compendium and naming conventions)
21. In the **Find Criteria** search field, enter "result"
22. Multiple lab results criteria are available. Select the **"Results: Last numeric val, base name"** criterion
23. Many individual lab components are mapped to a single base name. Search for the base name for **HBsAg** used at your organization (this field may vary depending on the lab catalog). Typically, these names will be variations of "hepatitis B surface antigen," "HBsAg," "Hep B surface antigen," "absHBsAg," or similar. Alternatively, the "Results: Component" criterion can be used if your organization only uses a single lab record for HBsAg that will not change. Include **HBV DNA** results in the reporting output, along with quantitative HBsAg and other relevant laboratory results, to support review of patient-selection criteria and the clinical workflow
24. In the **comparison** field for each base name, enter "Less than or equal to." In the **value** field for each base name, enter 3,000 (ensure that this value appropriately represents the units from the prescribing information of "IU/mL" or is converted according to the units used by the site's lab)
25. Search for the base name for **platelet count** used at your organization (this field may vary depending on the lab catalog). Typically, these names will be variations of "platelets," "plts," "platelet count," "absplatelets," or similar
26. In the **comparison** field for each base name, enter ≥. In the **value** field for each base name, enter 100×10^9 (ensure that this value appropriately represents the units from the prescribing information of "/L" or is converted according to the units used by the site's lab)

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.

Patient Identification and Reporting (cont'd)

Instructions for Reporting Workbench (cont'd)

27. Using the **Report Logic field**, set the logic operator to:

- Patient: Living status: Alive
  AND
  Age in years: ≥18 years
  AND
- Diagnosis of chronic hepatitis B virus infection[4]:
  - B18.1—chronic viral hepatitis B without delta-agent
  AND
- Medications: NA therapy[1]
  AND
- HBsAg ≤3,000 IU/mL[1]
  AND
  Platelets ≥100 × 10^9/L[1]
  AND NOT
- Diagnosis of acute hepatic impairment or cirrhosis[4]:
  - K70.30–alcoholic cirrhosis of liver without ascites
  - K70.31–alcoholic cirrhosis of liver with ascites
  - K72.00–acute and subacute hepatic failure without coma
  - K72.01–acute and subacute failure with coma
  - K74.3–primary biliary cirrhosis
  - K74.4–secondary biliary cirrhosis
  - K74.5–biliary cirrhosis unspecified
  - K74.60–unspecified cirrhosis of liver
  - K74.69–other cirrhosis of liver

28. Click the **Display tab** to select all display columns to be included in the report (search in the available columns or click **+ Add** to manually add a display column). In the **Available Columns window,** select **Current Medications** and **Other Desired Patient Information** to display in the report. Once an Available Column has been selected, click the **arrow** to move it to the **Selected Column window**

- In the **General tab,** enter the desired **Report Name** and a **Description: "Adult patients with chronic HBV without cirrhosis on NA therapy with HBsAg ≤3,000 IU/mL and platelets ≥100 × 10^9/L"**
- Include **HBV DNA** results in the reporting output, along with quantitative HBsAg and other relevant laboratory results, to support review of patient-selection criteria and the clinical workflow

29. Click **Save and Run** to create the patient list. The list will display all patients matching the search criteria. The results may be further manipulated if desired or exported to Excel. Identified patients can be contacted and invited to schedule an appointment with their provider

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.

Patient Identification and Reporting (cont'd)

Instructions for SlicerDicer

1. Access **SlicerDicer** (click the **Epic logo > Reports > SlicerDicer**)
2. Select the **Patients** data model (the numbers in the data model box represent the base population and number of records in the data model)
3. In the right-hand column, select the desired patient base (eg, "All Patients")
   Note: First-time users of SlicerDicer may see a tutorial prompted during initial use. Complete the tutorial and continue with the steps below
4. In the **Search for Criteria** field, enter "status"
5. Select the **Patient: Living Status** criterion and set to **Alive**
6. In the **Search for Criteria** field, enter "age"
7. Set the age range to **greater than or equal to 18 years**
8. In the **Search for Criteria** field, enter "diagnosis." Alternatively, the **+ Browse** button can be used. When using the **+ Browse** button, a new screen will display where the filter criterion and inclusion/exclusion status can be selected
9. Select the **Diagnosis criterion**
10. Set the mode to ICD/Grouper and enter and select this ICD-10 code for CHRONIC HEPATITIS B VIRUS INFECTION: **B18.1**[4]
    Note: If using a grouper, enter the HBV grouper instead of the individual ICD-10 code
11. In the **Search for Criteria** field, enter "medications"
12. Enter and select the desired **pharmaceutical class/subclass and/or medications** (eg, **NA therapy**)
    Note: Individual medications or medication groupers can be used in place of pharmaceutical classes/subclasses if they are not an available option
13. In the **Search for Criteria** field, enter "result"
14. Many individual lab components are mapped to a single base name. Search for the base name for **HBsAg** used at your organization (this field may vary depending on the lab catalog). Typically, these names will be variations of "hepatitis B surface antigen," "HBsAg," "Hep B surface antigen," "absHBsAg," or similar. Include **HBV DNA** results in the reporting output, along with quantitative HBsAg and other relevant laboratory results, to support review of patient-selection criteria and the clinical workflow
15. In the **comparison** field for each base name, enter ≤. In the **value** field for each base name, enter **3,000**
16. Many individual lab components are mapped to a single base name. Search for the base name for **platelet count** used at your organization (this field may vary depending on the lab catalog). Typically, these names will be variations of "platelets," "plts," "platelet count," "absplatelets," or similar
17. In the **comparison** field for each base name, enter ≥. In the **value** field for each base name, enter **100×10^9** (ensure that this value appropriately represents the units from the prescribing information of "/L" or is converted according to the units used by the site's lab)
18. In the **Search for Criteria** field, enter "diagnosis." Alternatively, the **+ Browse** button can be used. When using the **+ Browse** button, a new screen will display where the filter criterion and inclusion/exclusion status can be selected
19. Select the **Diagnosis criterion**
20. Set the mode to **ICD/Grouper** and enter and select these ICD-10 codes for acute hepatic impairment and cirrhosis (K70.30, K70.31, K72.00. K72.01, K74.3, K74.4, K74.5, K74.60, K74.69)[4] that should be excluded. The **AND** operator can be changed by clicking the button and selecting **Exclude** from the dropdown menu.
    Note: If using a grouper, enter the cirrhosis grouper instead of the individual ICD-10 codes
21. If the filters are linked by encounter, unlink them (click the **chain icon** next to the filter criterion so it appears broken) to allow the search to be completed across encounters

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.

Patient Identification and Reporting (cont'd)

Instructions for SlicerDicer (cont'd)

22. Click the icon with the **detail table** in the **Visual Option** section to see the query results

23. The results can be exported to Reporting Workbench by right clicking the bar with the patient results and selecting Show Slice in Reporting Workbench

24. In Reporting Workbench, select the **Display tab** to set all display columns for the report. Search for any display information in the **Available Columns** pane. Select all desired display columns and click the right arrow to drag them to the Selected Columns pane

25. In the **Display tab,** navigate to the **Detailed Views** section and set additional information displays. Consider adding the current and past medications views

26. In the **General tab,** enter the desired report name (eg, **"Adult patients with chronic HBV without cirrhosis on NA therapy with HBsAg ≤3,000 IU/mL and platelets ≥100 × 10^9/L"**) and a description. Results can be shared with selected users or pools

27. Click **Save** and then **Run** to create the patient list. The list will display all patients matching the criteria

Instructions for Sidekick

Sidekick is Epic's generative AI assistant, introduced with SlicerDicer, that translates plain-language questions into report queries and analyses to streamline data exploration. For example, the following prompt could be considered:

- Show patients with chronic HBV (B18.1) currently on an NA therapy medication for at least 6 months who have an HBsAg lab test ≤3,000 IU/mL and a platelet count of ≥100 × 10^9/L, excluding patients with acute hepatic impairment or cirrhosis. Include medical record number (MRN), HBsAg value and date, liver function tests (LFTs) and complete blood count (CBC) with differential, HBV DNA, uACR, eGFR, current nucleos(t)ide analog therapy medication name, dose, route, and frequency

Note: Sidekick access and functionality may vary based on your organization's Epic configuration and enabled features. Users must complete the required Sidekick tutorial before using the tool for the first time

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

Adding Orders to a Preference List for an End User

Instructions for searching for the quantitative hepatitis B surface antigen test in Epic

1. In a patient's chart, access the **Order Entry** mode
2. In the **Order Search** screen, select the **Facility List** tab in the top right of the order search window. The **Facility List** tab includes all orders and procedures (including medications) that are orderable at a specific hospital or location. It typically will include all Pharmacy and Therapeutics (P&T) approved orders
3. In the search field enter "Hepatitis B surface antigen." All matches will display (note that naming conventions may vary by institution and synonyms may be used to find the desired order)



For illustrative purposes only. *Example of Order Search. The* ***Facility List*** *tab is selected on the top right. All matches will display in the list.*

Note: Not all criteria/information may be documented in structured fields in the EHR. Review current documentation practices and available data. It is recommended to manually review the patient's chart to confirm eligibility.

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.

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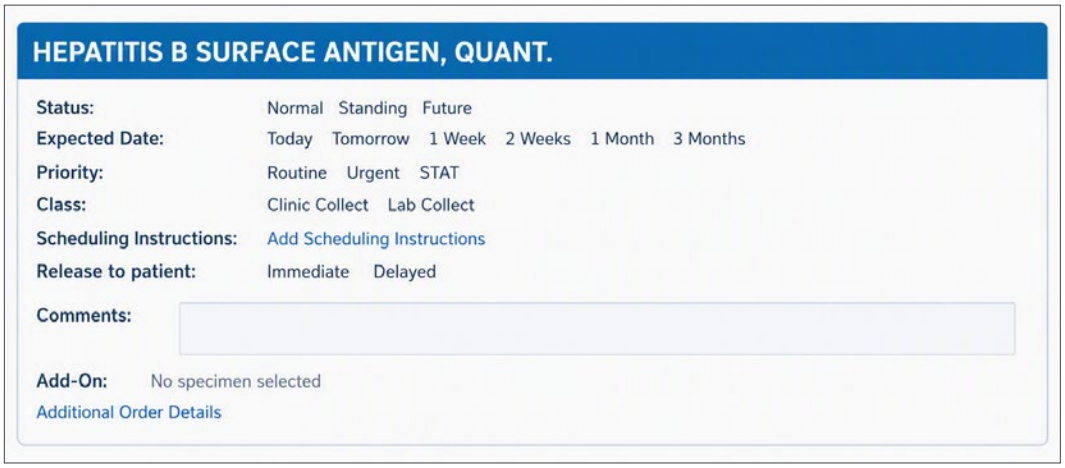
Adding Orders to a Preference List for an End User (cont'd)

Instructions for selecting the quantitative hepatitis B surface antigen test in Epic

1. Select the desired order from the list. A new window will display
2. Complete all order details in the new window with the test details
3. Click **Accept** when the order is complete



For illustrative purposes only. *Example of the order details screen. The provider should complete all order details.*

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.

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.

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HIBSAGO (bepirovirsen)
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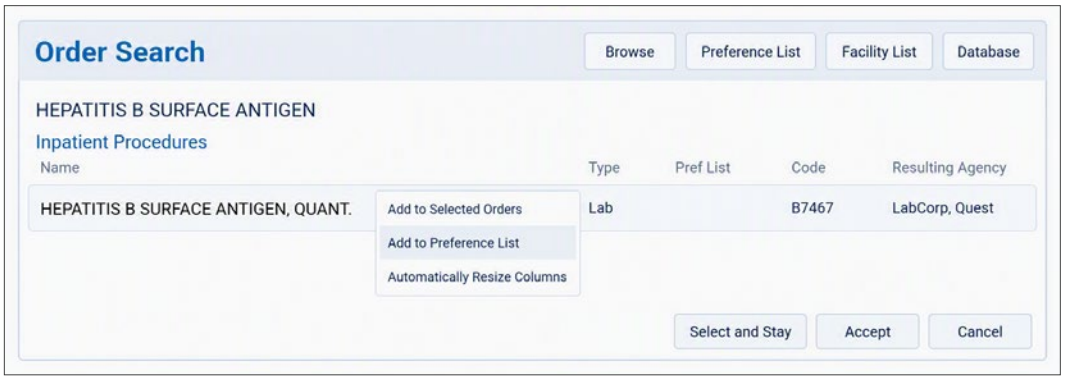
Adding Orders to a Preference List for an End User (cont'd)

Instructions for preferencing the quantitative hepatitis B surface antigen test in Epic

1. In the **Order Search** window, navigate to the list of orders
2. **Right-click** on the name of the order in the list
3. From a drop-down list, select **Add to Preference List** and select the desired order category



For illustrative purposes only. *Example of the order screen. After right-clicking the name of the order, the option to add the order to the Preference List (Favorites folder) will display.*

Instructions for making the HIBSAGO Therapy Plan a favorite in Epic

1. In the **Therapy Plan** search window, navigate to the list of therapy plans
2. **Click** on the star next to the name of the therapy plan in the list

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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Documentation and Macros

SmartPhrases are Epic's text-based macros ("dot phrases") that allow end users to quickly insert predefined text into notes, orders, messages, and other documentation fields. A SmartPhrase could be used to quickly insert instructions into an After-Visit Summary, for example. They are a widely used documentation shortcut that improves efficiency, consistency, and completeness within the EHR. Typing a SmartPhrase abbreviation (preceded by a period) in the chart expands the text into structured, reusable content that may include narrative text, prompts, and patient-specific data. SmartPhrases can be easily created and customized by end users in minutes, enabling rapid standardization of common documentation elements while still allowing clinician flexibility.

Instructions for SmartPhrase

1. Open the **SmartTool** Editor and select the **SmartPhrase** option (click the **Epic** logo in the top left and select **MySmartPhrases** or use the search feature)
2. Create a new **SmartPhrase** with a unique mnemonic according to the organization's naming conventions (eg, "HIBSAGOAVS")
3. Select the **General** button and copy and paste the suggested After-Visit Summary content from **Appendix** on pages 14-18
   Note: SmartLinks may be used to retrieve relevant patient chart information. SmartLinks can be adjusted as desired, as local naming conventions and available SmartLinks may vary
4. Click **Accept** once uploaded and formatted as desired. Some manipulation of the **SmartPhrase** content or the **SmartLinks** may be required
5. Open a patient chart and confirm the **SmartPhrase** renders the content as expected

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.

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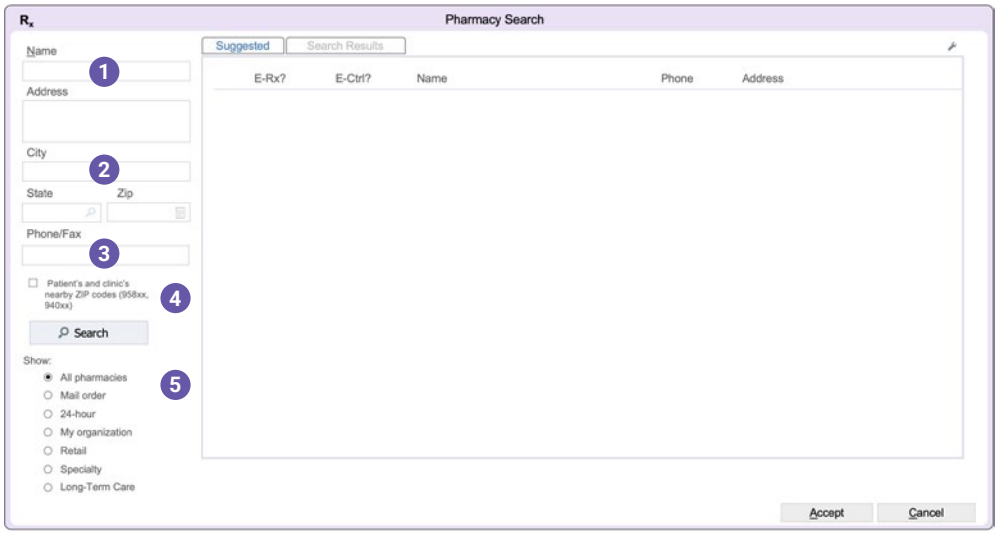
Subcutaneous Use 150 mg/mL

Instructions for Selecting the Specialty Pharmacy in the Epic system

HIBSAGO is primarily dispensed by PANTHERx Rare Pharmacy, and it's important to choose the appropriate pharmacy at the point of prescribing. The eligible specialty pharmacy is listed in the Surescripts pharmacy database and can be selected directly within the Epic EHR. This resource includes an image of the pharmacy selection solution in Epic and points out key considerations when searching for the specialty pharmacy for HIBSAGO. If applicable, providers should follow health system guidance regarding specialty pharmacy selection.

These instructions are not appropriate for other conditions or therapeutic areas or for other EHR systems. The processes outlined are variable and not all steps will apply to every user. Any steps or settings that are not part of a user's standard process should be excluded or modified accordingly. Any questions should be directed to the appropriate service provider.



Specialty pharmacy dispensing HIBSAGO

PANTHERx Rare Pharmacy

Phone: 855-726-8479

Fax: 855-246-3986

ERx NCPDP: 6008002

Address: 1120 Stevenson Mill Road
Coraopolis, PA 15108

Website: https://pantherxrare.com

For illustrative purposes only. *Example of the Pharmacy Search feature.*

1. Enter the full specialty pharmacy name in the **Name** field. Pharmacy chains will have multiple listings, but few will have the exact name referenced in the Certified Specialty Pharmacy resource
2. Add the **City** to narrow the results
3. Consider using the **Phone/Fax** field to refine your search
4. Uncheck this box, as it limits results to nearby pharmacies. The specialty pharmacy you need may not appear because of this geolocation feature
5. Check the **All pharmacies** radio button to ensure all pharmacy types are included in the search

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.

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

HIBSAGO (bepirovirsen)
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Appendix: After-Visit Summary[1]

What is the most important information I should know about HIBSAGO?

HIBSAGO may cause serious side effects, including:

- **flare-ups in liver enzyme levels during treatment.** HIBSAGO may cause increases in liver function blood tests. **Tell your healthcare provider right away if you get any of these symptoms**:
  - upper right stomach pain
  - dark or "tea-colored" urine
  - yellowing of your skin or the white part of your eyes
  - nausea and vomiting
  - loss of appetite
- **low platelet counts (thrombocytopenia).** HIBSAGO may cause your blood platelet levels to drop at any time during your treatment. When your platelet count is too low, your body cannot form blood clots properly. Low platelet counts can happen suddenly and without warning and can be life-threatening. **Stop using HIBSAGO and tell your healthcare provider right away if you get any of these symptoms:**
  - unusual bruising or a rash of tiny reddish-purple spots
  - bleeding from skin cuts that does not stop or oozes
  - bleeding from your gums or nose
  - blood in your urine or stools
  - abnormal or heavy periods (menstrual bleeding)
  - sudden severe headaches or neck stiffness
  - bleeding into the whites of your eyes

Your healthcare provider will do blood tests to check your liver and platelet count, before you start HIBSAGO, during treatment, and if you have abnormal blood tests for up to 24 weeks after you stop HIBSAGO.

It is important that you make sure you get these blood tests done.

What is HIBSAGO?

HIBSAGO is a prescription medicine used with other medicines called nucleos(t)ide analog reverse transcriptase inhibitors (NrtIs), to treat adults with chronic (long-term) hepatitis B virus (HBV) infection without advanced liver disease (cirrhosis):

- who have been on NrtI treatment for at least 6 months and have undetectable HBV deoxyribonucleic acid (DNA),
  and
- who have low levels of HBV surface antigen (HBsAg less than or equal to 3,000 IU/mL)

Your healthcare provider will perform tests to make sure HIBSAGO is right for you.

It is not known if HIBSAGO is safe and effective in children less than 18 years of age.

It is not known if HIBSAGO is safe and effective in people who also have hepatitis C virus (HCV) or hepatitis D virus (HDV) infection. HIBSAGO is not recommended in people with HDV infection as it may increase the chance of flare-ups in liver enzymes.

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.

HIBSAGO (bepirovirsen)
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Appendix: After-Visit Summary[1] (cont'd)

Who should not use HIBSAGO?

Do not use HIBSAGO if you have:

- a condition where your liver is currently not working as well as it should
- have **advanced liver disease (cirrhosis)**
- low platelet blood counts.

Talk to your healthcare provider if you are not sure if you have any of these conditions.

Before using HIBSAGO, tell your healthcare provider about all of your medical conditions, including if you:

- have bleeding problems or a history of bleeding problems
- have kidney problems
- have received an organ transplant
- have problems with your immune system (autoimmune disease), or have a history of blood vessel inflammation (vasculitis)
- have hepatitis D
- are pregnant or plan to become pregnant. It is not known if HIBSAGO will harm your unborn baby.
- are breastfeeding or plan to breastfeed. HIBSAGO may pass into your breast milk. Talk to your healthcare provider about the best way to feed your baby during treatment with HIBSAGO.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Using HIBSAGO with certain other medicines may increase the risk of side effects. Especially tell your healthcare provider if you take:

- medicines that prevent your blood from clotting or that lower your blood platelet count.
- medicines that may lower your kidney function.
- peginterferon alfa-2a.

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

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)
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Appendix: After-Visit Summary[1] (cont'd)

How should I use HIBSAGO?

Read the detailed Instructions for Use that comes with your HIBSAGO for information on how to inject a dose of HIBSAGO.

- Use HIBSAGO exactly as your healthcare provider tells you to.
- Treatment with HIBSAGO usually lasts 24 weeks. Do not take HIBSAGO for longer than 24 weeks.
- **HIBSAGO must be used in combination with NrtI treatment. You must remain on NrtI treatment for at least 24 weeks after stopping treatment with HIBSAGO.** Your healthcare provider will decide if you can stop your NrtI treatment.
- You will receive your first dose of HIBSAGO under the guidance and supervision of your healthcare provider. HIBSAGO is given as an injection under the skin (subcutaneous).
- Your healthcare provider will decide if you or your caregiver may inject HIBSAGO.
  - Your healthcare provider will show you or your caregiver how to inject HIBSAGO.
  - Your healthcare provider will tell you how much HIBSAGO to inject and when to inject it. **Do not** inject more than your prescribed dose.
- Your prescribed dose will generally require two injections. Your healthcare provider will do blood tests during your treatment with HIBSAGO and may decrease your dose to one injection, temporarily stop, or permanently stop your HIBSAGO treatment depending on the results.
  - If your dose is 300 mg, you will need to inject two HIBSAGO prefilled syringes.
  - If your dose is 150 mg, you will need to inject one HIBSAGO prefilled syringe. For a 150 mg dose, keep the second syringe in the carton and away from light.
- The recommended dosing schedule is shown in the table below. Your healthcare provider may tell you to reduce or temporarily stop doses based on your blood tests or how you are feeling. Follow your healthcare provider's instructions on how to use HIBSAGO.

Recommended dose		
When	**How much**	**How often**
Weeks 1 and 2	300 mg (inject **2** syringes)	**Two times** a week Allow 3 or 4 days between each dose
Weeks 3 to 24	300 mg (inject **2** syringes)	**One time** a week Inject on the same day each week

- Where possible, give each dose on the same day(s) each week.
- If you miss a dose, and your next dose is in 3 days or more:
  - inject the missed dose as soon as you remember. Then continue your treatment as before.
- If you miss a dose, and your next dose is in less than 3 days:
  - skip the missed dose and inject the dose at your usual time. Then continue your treatment as before.
- If you take too much HIBSAGO, call your healthcare provider or the Poison Help line at 1-800-222-1222 or go to the nearest hospital emergency room right away.

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

Appendix: After-Visit Summary[1] (cont'd)

After you finish your treatment with HIBSAGO, do not stop taking your NrtI treatment unless your healthcare provider tells you to. If you stop taking NrtI treatment, your HBV may return. It is important that you make sure you still get blood tests done. If you also have human immunodeficiency virus (HIV) and are taking an NrtI as part of your HIV treatment, do not stop the NrtI unless your HIV healthcare provider has told you to stop.

Taking HIBSAGO does not stop you from passing HBV to others. You should continue to practice safety habits to stop from passing HBV to other people.

What are the possible side effects of HIBSAGO?

HIBSAGO may cause serious side effects, including:

- **Increased liver laboratory tests:** See "What is the most important information I should know about HIBSAGO?"
- **Bleeding because of low platelet counts:** See "What is the most important information I should know about HIBSAGO?"
- **Worsening kidney function.** Your healthcare provider will do blood tests to check your kidneys before and during treatment, and for up to 12 weeks after you stop HIBSAGO if you have abnormal kidney function blood tests.
  It is important that you make sure you get these blood tests done.
- **Inflammatory or immune system problems.** Tell your healthcare provider if you get any of these symptoms:
  - flu-like symptoms
  - purple rashes or spots on the legs
  - scaly, raised or red patches
  - swelling and itchiness
  - joint pain that does not go away by itself
- **Serious side effects when HIBSAGO is not injected correctly.**
  - Make sure the injection sites are changed (rotated) from one week to the next and that the two injections given weekly are separated by at least 2 inches (5 cm).
  - Do not give injections into areas where the skin is tender, bruised, red, or hard.

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.

Appendix: After-Visit Summary[1] (cont'd)

The most common side effects of HIBSAGO include:

- injection site reactions
- tiredness
- fever
- headache

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of HIBSAGO.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store HIBSAGO?

- Store HIBSAGO at room temperature up to 86°F (30°C) for up to 12 weeks.
- Do not freeze HIBSAGO.
- Store HIBSAGO in the original carton to protect from light.
- Throw away (discard) HIBSAGO in an FDA-cleared sharps disposal container after if the expiration date has passed, or it has been 12 weeks since you received your carton, whichever comes first.
- HIBSAGO must be injected within 6 hours after you remove it from the carton. If the HIBSAGO syringes are not used within 6 hours, throw them away.

Keep HIBSAGO and all medicines out of the reach of children.

General information about the safe and effective use of HIBSAGO.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use HIBSAGO for a condition for which it was not prescribed. Do not give HIBSAGO to other people, even if they have the same symptoms that you have. It may harm them.

Throw away (discard) any unused syringes when your healthcare provider tells you that your HIBSAGO treatment is complete.

You can ask your pharmacist or healthcare provider for information about HIBSAGO that is written for health professionals.

What are the ingredients in HIBSAGO?

Active ingredient: bepirovirsen sodium

Inactive ingredients: water for injection, hydrochloric acid or sodium hydroxide to adjust to pH 8

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 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.

Disclaimers

- The user (eg, physician, medical group, integrated delivery network) shall be solely responsible for implementation, testing, and monitoring of the instructions to ensure proper orientation in each user's EHR system
- Capabilities, functionality and set-up (customization) for each individual EHR system vary. GSK shall not be responsible for revising the implementation instructions it provides to any user if user modifies or changes its software or the configuration of its EHR system after such time as the implementation instructions have been initially provided by GSK
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References: 1. HIBSAGO (bepirovirsen). Prescribing Information. GSK; 2026. **2.** Cornberg M, et al. *J Hepatol.* 2017;66(2):398-411. **3.** Vachon A, et al. *Viruses*. 2021;13(6):951. **4.** ICD-10. Centers for Medicare & Medicaid Services. Accessed October 12, 2026. https://www.cms.gov/medicare/coding-billing/icd-10-codes

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