Hepatitis B Immune Globulin (Human)  
Nabi-HB®  
Solvent/Detergent Treated and Filtered

DESCRIPTION  
Hepatitis B Immune Globulin (Human), Nabi-HB, is a sterile solution of immunoglobulin (5 ± 1% protein) containing antibodies to hepatitis B surface antigen (anti-HBs). It is prepared from plasma pooled from a minimum of 22 donor units of individuals with high titers of anti-HBs. The plasma is processed using a modified Cohn 6 / Oncley 9 cold-alcohol fractionation process with two added viral reduction steps described below. Nabi-HB is formulated in 0.042-0.108 M sodium chloride, 0.10-0.20 M glycine, and 20-60 M sodium phosphate buffer pH 6.5. The product is supplied as a nonsting liquid in single dose vials and appears as clear to opalescent. It contains no preservative and is intended for single use by the intramuscular route only.

Each plasma donation used for the manufacture of Nabi-HB is tested for the presence of hepatitis B virus (HBV) surface antigen (HBsAg), human immunodeficiency viruses (HIV) 1/2, and hepatitis C virus (HCV) antibodies. In addition, pooled samples of Source Plasma used in the manufacture of this product are tested by FDA licensed Nucleic Acid Testing (NAT) for HIV, HCV and HCV and found to be negative. Investigational NAT for hepatitis A virus (HAV) and HBV is also performed on pooled samples of all Source Plasma used, and found to be negative. Human immunodeficiency virus (HIV) 1 and 2 viral RNA and DNA are not detected by NAT.

The manufacturing steps for Nabi-HB are designed to reduce the risk of transmission of viral disease. The solvent/detergent treatment step, using tri-n-butyl phosphate and Triton® X-100, is effective in inactivating known enveloped viruses such as hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV). Virus filtration, using a Planova® 35 nm Virus Filter, is effective in reducing some known enveloped and non-enveloped viruses. The inactivating and enveloping agents used in each of the enveloped and non-enveloped models were validated in laboratory studies as summarized in the following table:

<table>
<thead>
<tr>
<th>Table 1 Log Reduction of Test Viruses²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model Virus: U201VH</td>
</tr>
<tr>
<td>Envelope/Genome: yes/RNA</td>
</tr>
<tr>
<td>Manufacturing Step</td>
</tr>
<tr>
<td>Preactivation of Cohn</td>
</tr>
<tr>
<td>Fraction III</td>
</tr>
<tr>
<td>Cohn Filtration</td>
</tr>
<tr>
<td>Solvent/Detergent</td>
</tr>
<tr>
<td>Nanofiltration</td>
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<tr>
<td>Cumulative</td>
</tr>
</tbody>
</table>

Nabi-HB® (Hepatitis B Immune Globulin (Human)) is indicated for the prevention of HBV infection in the following settings:

- • Sexual Exposure to Blood Containing HBsAg
- • Perinatal Exposure of Infants Born to HBsAg-positive Mothers

In instances of exposure based upon the increased efficacy found with that regimen in one or more of the following populations:

- Infants born to HBsAg-positive mothers are at risk of being infected with HBV and becoming chronic carriers. HBV vaccine should be given immediately after birth and repeated at 2 and 6 months of age. Nabi-HB should be given at birth to infants born to HBsAg-positive mothers. Nabi-HB should be given to infants less than 12 months of age with Hepatitis B Immune Globulin (Human) and hepatitis B vaccine is indicated if the mother or primary caregiver is HBsAg-positive.

- Sexual partners of HBsAg-positive persons are at increased risk of acquiring HBV infection. A single dose of Hepatitis B Immune Globulin (Human) is 75% effective if administered within two weeks of the last sexual exposure to a person with acute hepatitis B®.

Pharmacokinetics

Pharmacokinetic trials of Nabi-HB, Hepatitis B Immune Globulin (Human), given intramuscularly to 50 healthy volunteers demonstrated pharmacokinetic parameters similar to those reported by Schürer and Kuvvet.¹ The half-life for Nabi-HB was 23 ± 5.5 days. The clearance rate was 0.5 ± 0.2 mL/kg/min and the terminal half-life was 12.4 ± 3.4 h.

Maximum concentration of Nabi-HB was reached in 6.5 ± 4.3 days. The maximum concentration of anti-HBs and the area under the time-concentration curve achieved by Nabi-HB were bioequivalent to the area under the curve of the hepatitis B immune globulin (Hepatitis B Immune Globulin (Human)) when compared in the same pharmacokinetic trial. Comparability of pharmacokinetics between Nabi-HB and a commercially available hepatitis B immunoglobulin indicate that similar efficacy of Nabi-HB should be anticipated.

INDICATIONS AND USAGE

Nabi-HB, Hepatitis B Immune Globulin (Human), is indicated for treatment of acute exposure to Hepatitis B virus (HBV) infection, perinatal exposure of infants born to HBsAg-positive mothers, sexual exposure to Hepatitis B virus (HBV) infection, and household exposure to persons with acute HBV infection in the following settings:

- • Acute Exposure to Blood Containing HBsAg
- • Perinatal Exposure of Infants Born to HBsAg-positive Mothers

Hepatitis B Immune Globulin (Human) should be given to a pregnant woman only if clearly indicated.

Nursing Mothers

If Nabi-HB is necessary to treat another drug this is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Nabi-HB is administered to a nursing mother.

Pregnancy Category C

Animal reproduction studies have not been conducted with Nabi-HB. It is also not known whether Nabi-HB can cause fetal harm when administered to a pregnant woman or can affect a woman's ability to conceive. Nabi-HB should be given to a pregnant woman only if clearly indicated.

Safety and effectiveness in the pediatric population have not been established for Nabi-HB. However, the safety and effectiveness of similar hepatitis B immune globulins have been demonstrated in infants and children.²

Geriatric Use

Clinical studies of Nabi-HB did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently than younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

ADVERSE REACTIONS

Fifty male and female volunteers received Nabi-HB, Hepatitis B Immune Globulin (Human), intramuscularly at doses of 20, 60, 120, 300, and 600 U/kg. The number of patients with reactions related to the administration of Nabi-HB included local reactions such as enanthema 6 (12%) and ache 2 (4%) at the injection site, as well as systemic reactions such as headache 7 (14%), myalgia 5 (10%), nausea 3 (6%), vomiting 2 (4%), and somnolence 2 (4%). The majority (92%) of reactions were reported as mild. The following adverse events were reported in the pharmacokinetic trials and were considered probably related to Nabi-HB:

- Elevated AST 1 (2%), decreased WBC 1 (2%), elevated creatinine 1 (2%).
- All adverse events were mild in intensity. There were no serious adverse events.

No anaphylactic reactions with Nabi-HB have been reported. However, these reactions, although rare, have been reported following the injection of human immunoglobulins.³
OVERDOSAGE
Although no data are available, clinical experience reported with other human immunoglobulin suggests that the only manifestations of overdose with Nabi-HB, Hepatitis B Immune Globulin (Human), would be pain and tenderness at the injection site.

DOSE AND ADMINISTRATION
This product is for intramuscular use only. The use of this product by the intravenous route is not indicated. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration.

It is important to use a separate vial, sterile syringe, and needle for each individual patient, in order to prevent transmission of infectious agents from one person to another. Any vial of Nabi-HB, Hepatitis B Immune Globulin (Human) that has been entered should not be used promptly. Do not reuse or save for future use. This product contains no preservative; therefore, partially used vials should be discarded immediately.

Hepatitis B Immune Globulin (Human) may be administered at the same time (but at a different site), or up to one month preceding hepatitis B vaccination without impairing the active immune response to hepatitis B vaccine.

- **Acute Exposure to Blood Containing HbsAg**
- **Prophylaxis Following Percutaneous or Perimucosal Exposure**

Table 2 summarizes prophylaxis for percutaneous (needlestick, bite, sharp), ocular, or mucocutaneous exposure to blood according to the source of exposure and vaccination status of the exposed person. For greatest effectiveness, passive prophylaxis with Hepatitis B Immune Globulin (Human) should be given as soon as possible after exposure, as its value after seven days following exposure is uncertain.

An injection of 0.06 mL/kg of body weight should be administered intramuscularly as soon as possible after exposure and within 24 hours if possible. Consult the hepatitis B vaccine package insert for dosage information regarding the vaccine.

For persons who refuse hepatitis B vaccine or are known non-responders to vaccine, a second dose of Hepatitis B Immune Globulin (Human) should be given one month after the first dose.

### Table 2: Recommendations for Hepatitis B Prophylaxis Following Pericutaneous or Perimucosal Exposure

<table>
<thead>
<tr>
<th>Source</th>
<th>Unvaccinated</th>
<th>Vaccinated</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbsAg-positive</td>
<td>1. Initiate HB vaccine series</td>
<td>1. Test source for HbsAg only, if exposed is vaccine nonresponder; if source is HbsAg-positive, give Hepatitis B Immune Globulin (Human) immediately plus either HB vaccine booster dose or second dose of Hepatitis B Immune Globulin (Human) one month later&lt;sup&gt;‡&lt;/sup&gt;</td>
</tr>
<tr>
<td>Known Source - High Risk for HbsAg-positive</td>
<td>1. Initiate HB vaccine series</td>
<td>1. Test source for HbsAg only, if exposed is vaccine nonresponder; if source is HbsAg-positive, give Hepatitis B Immune Globulin (Human) immediately plus either HB vaccine booster dose or second dose of Hepatitis B Immune Globulin (Human) one month later&lt;sup&gt;‡&lt;/sup&gt;</td>
</tr>
<tr>
<td>Known Source - Low Risk for HbsAg-positive</td>
<td>Initiate HB vaccine series</td>
<td>Nothing required</td>
</tr>
<tr>
<td>Unknown Source</td>
<td>Initiate HB vaccine series</td>
<td>Nothing required</td>
</tr>
</tbody>
</table>

<sup>‡</sup> Hepatitis B Immune Globulin (Human) dose of 0.06 mL/kg IM.

<sup>§</sup> See manufacturers' recommendations for appropriate dose.

<sup>¶</sup> Less than 10 mIU/mL anti-HBs by radioimmunoassay, negative by enzyme immunoassay.

<sup>†</sup> Two doses of Hepatitis B Immune Globulin (Human) is preferred if no response after at least four doses of vaccine.

### Table 3: Recommended Schedule of Hepatitis B Immunoprophylaxis to Prevent Perinatal Transmission of Hepatitis B Virus Infection

<table>
<thead>
<tr>
<th>Age of Infant</th>
<th>First Vaccination&lt;sup&gt;‡&lt;/sup&gt;</th>
<th>Second Vaccination&lt;sup&gt;‡&lt;/sup&gt;</th>
<th>Third Vaccination&lt;sup&gt;‡&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant born to mother known to be HbsAg-positive</td>
<td>Birth (within 12 hours)</td>
<td>Birth (within 12 hours)</td>
<td>1 month</td>
</tr>
<tr>
<td>Infant born to mother not known to be HbsAg-positive</td>
<td>Birth (within 12 hours)</td>
<td>If mother is found to be HbsAg-positive, administer dose to infant as soon as possible, not later than 1 week after birth</td>
<td>6 months&lt;sup&gt;‡&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>‡</sup> See manufacturers' recommendations for appropriate dose.

<sup>§</sup> 0.5 mL administered IM at a site different than that used for the vaccine.

<sup>¶</sup> Using the manufacturer's recommendations.

<sup>†</sup> Sexual Exposure to HbsAg-positive Persons

Sexual exposure to HbsAg-positive persons is an acceptable route of infection. All susceptible persons whose sexual partners have acute hepatitis B infection should receive a single dose of Hepatitis B Immune Globulin (Human) (0.06 mL/kg) and should begin the hepatitis B vaccine series. If the sexual contact is not contraindicated, within 14 days of the last sexual contact or if sexual contact with the infected person will continue. Administering the vaccine with Hepatitis B Immune Globulin (Human) may improve the efficacy of post exposure treatment. The vaccine has the added advantage of conferring long-lasting protection.

- **Household Exposure to Persons with Acute HBV Infection**

Prophylaxis of an infant less than 12 months of age with 0.5 mL Hepatitis B Immune Globulin (Human) and hepatitis B vaccine is indicated if the mother or primary caregiver has acute HBV infection. Prophylaxis of other household contacts of persons with acute HBV infection is not indicated unless they had an identifiable blood exposure to the index patient, such as by sharing toothbrushes or razors. Such exposures should be treated like sexual exposures. If the index patient becomes an HBV carrier, all household contacts should receive hepatitis B vaccine.

### HOW SUPPLIED
- Nabi-HB, Hepatitis B Immune Globulin (Human), is supplied as:
- 59730-4202-1 a carton containing a 1 mL dose in a single-use vial (>312 IU) and package insert
- 59730-4203-1 a carton containing a 5 mL dose in a single-use vial (>1560 IU) and package insert

### STORAGE
Store between 2 to 8 °C (36 to 46 °F). Do not freeze. Do not use after expiration date. Use within 6 hours after the vial has been entered.

### REFERENCES
5. Unpublished data on file, Viral Validation Study Reports, Biotest Pharmaceuticals.

Manufactured by: Biotest Pharmaceuticals Corporation

Boca Raton, FL 33437

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