



08908853

08908853 (Rev. January 2005)

# Hepatitis B Immune Globulin (Human)

## HyperHEP B™ S/D

### Solvent/Detergent Treated

#### DESCRIPTION

Hepatitis B Immune Globulin (Human) — HyperHEP B™ S/D treated with solvent/detergent is a sterile solution of hepatitis B hyperimmune immune globulin for intramuscular administration; it contains no preservative. HyperHEP B S/D is prepared by cold ethanol fractionation from the plasma of donors with high titers of antibody to the hepatitis B surface antigen (anti-HBs). The immune globulin is isolated from solubilized Cohn Fraction II. The Fraction II solution is adjusted to a final concentration of 0.3% tri-*n*-butyl phosphate (TNBP) and 0.2% sodium cholate. After the addition of solvent (TNBP) and detergent (sodium cholate), the solution is heated to 30°C and maintained at that temperature for not less than 6 hours. After the viral inactivation step, the reactants are removed by precipitation, filtration and finally ultrafiltration and diafiltration. HyperHEP B S/D is formulated as a 15–18% protein solution at a pH of 6.4–7.2 in 0.21–0.32 M glycine. HyperHEP B S/D is then incubated in the final container for 21–28 days at 20–27°C. Each vial contains anti-HBs antibody equivalent to or exceeding the potency of anti-HBs in a U.S. reference hepatitis B immune globulin (Center for Biologics Evaluation and Research, FDA). The U.S. reference has been tested against the World Health Organization standard Hepatitis B Immune Globulin and found to be equal to 220 international units (IU) per mL.

The removal and inactivation of spiked model enveloped and non-enveloped viruses during the manufacturing process for HyperHEP B S/D has been validated in laboratory studies. Human Immunodeficiency Virus, Type 1 (HIV-1), was chosen as the relevant virus for blood products; Bovine Viral Diarrhea Virus (BVDV) was chosen to model Hepatitis C virus; Pseudorabies virus (PRV) was chosen to model Hepatitis B virus and the Herpes viruses; and Reo virus type 3 (Reo) was chosen to model non-enveloped viruses and for its resistance to physical and chemical inactivation. Significant removal of model enveloped and non-enveloped viruses is achieved at two steps in the Cohn fractionation process leading to the collection of Cohn Fraction II: the precipitation and removal of Fraction III in the processing of Fraction II + IIIW suspension to Effluent III and the filtration step in the processing of Effluent III to Filtrate III. Significant inactivation of enveloped viruses is achieved at the time of treatment of solubilized Cohn Fraction II with TNBP/sodium cholate.

#### CLINICAL PHARMACOLOGY

Hepatitis B Immune Globulin (Human) provides passive immunization for individuals exposed to the hepatitis B virus (HBV) as evidenced by a reduction in the attack rate of hepatitis B following its use.<sup>1-6</sup> The administration of the usual recommended dose of this immune globulin generally results in a detectable level of circulating anti-HBs which persists for approximately 2 months or longer. The highest antibody (IgG) serum levels were seen in the following distribution of subjects studied:<sup>7</sup>

DAY	% OF SUBJECTS
3	38.9%
7	41.7%
14	11.1%
21	8.3%

Mean values for half-life were between 17.5 and 25 days, with the shortest being 5.9 days and the longest 35 days.<sup>7</sup>

Cases of type B hepatitis are rarely seen following exposure to HBV in persons with preexisting anti-HBs. No confirmed instance of transmission of hepatitis B has been associated with this product.

In a clinical study in eight healthy human adults receiving another hyperimmune immune globulin product treated with solvent/detergent, Rabies Immune Globulin (Human), HyperRAB™ S/D, prepared by the same manufacturing process, detectable passive antibody titers were observed in the serum of all subjects by 24 hours post injection and persisted through the 21 day study period. These results suggest that passive immunization with immune globulin products is not affected by the solvent/detergent treatment.

#### INDICATIONS AND USAGE

Recommendations on post-exposure prophylaxis are based on available efficacy data and on the likelihood of future HBV exposure for the person requiring treatment. In all exposures, a regimen combining Hepatitis B Immune Globulin (Human) with hepatitis B vaccine will provide both short- and long-term protection, will be less costly than the two-dose Hepatitis B Immune Globulin (Human) treatment alone, and is the treatment of choice.<sup>8</sup>

HyperHEP B S/D is indicated for post-exposure prophylaxis in the following situations:

##### Acute Exposure to Blood Containing HBsAg

After either parenteral exposure, e.g., by accidental "needlestick" or direct mucous membrane contact (accidental splash), or oral ingestion (pipetting accident) involving HBsAg-positive materials such as blood, plasma or serum. For inadvertent percutaneous exposure, a regimen of two doses of Hepatitis B Immune Globulin (Human), one given after exposure and one a month later, is about 75% effective in preventing hepatitis B in this setting.

##### Perinatal Exposure of Infants Born to HBsAg-positive Mothers

Infants born to HBsAg-positive mothers are at risk of being infected with hepatitis B virus and becoming chronic carriers.<sup>5,8-10</sup> This risk is especially great if the mother is HBeAg-positive.<sup>11-13</sup> For an infant with perinatal exposure to an HBsAg-positive and HBeAg-positive mother, a regimen combining one dose of Hepatitis B Immune Globulin (Human) at birth with the hepatitis B vaccine series started soon after birth is 85%–95% effective in preventing development of the HBV carrier state.<sup>8,14</sup> Regimens involving either multiple doses of Hepatitis B Immune Globulin (Human) alone or the vaccine series alone have 70%–90% efficacy, while a single dose of Hepatitis B Immune Globulin (Human) alone has only 50% efficacy.<sup>8,15</sup>

##### Sexual Exposure to an HBsAg-positive Person

Sex partners of HBsAg-positive persons are at increased risk of acquiring HBV infection. For sexual exposure to a person with acute hepatitis B, a single dose of Hepatitis B Immune Globulin (Human) is 75% effective if administered within 2 weeks of last sexual exposure.<sup>8</sup>



Since infants have close contact with primary care-givers and they have a higher risk of becoming HBV carriers after acute HBV infection, prophylaxis of an infant less than 12 months of age with Hepatitis B Immune Globulin (Human) and hepatitis B vaccine is indicated if the mother or primary care-giver has acute HBV infection.<sup>8</sup>

Administration of Hepatitis B Immune Globulin (Human) either preceding or concomitant with the commencement of active immunization with Hepatitis B Vaccine provides for more rapid achievement of protective levels of hepatitis B antibody, than when the vaccine alone is administered.<sup>16</sup> Rapid achievement of protective levels of antibody to hepatitis B virus may be desirable in certain clinical situations, as in cases of accidental inoculations with contaminated medical instruments.<sup>16</sup> Administration of Hepatitis B Immune Globulin (Human) either 1 month preceding or at the time of commencement of a program of active vaccination with Hepatitis B Vaccine has been shown not to interfere with the active immune response to the vaccine.<sup>16</sup>

## CONTRAINDICATIONS

None known.

## WARNINGS

**HyperHEP B S/D** is made from human plasma. Products made from human plasma may contain infectious agents, such as viruses, that can cause disease. The risk that such products will transmit an infectious agent has been reduced by screening plasma donors for prior exposure to certain viruses, by testing for the presence of certain current virus infections, and by inactivating and/or removing certain viruses. Despite these measures, such products can still potentially transmit disease. There is also the possibility that unknown infectious agents may be present in such products. Individuals who receive infusions of blood or plasma products may develop signs and/or symptoms of some viral infections, particularly hepatitis C. ALL infections thought by a physician possibly to have been transmitted by this product should be reported by the physician or other healthcare provider to Talecris Biotherapeutics, Inc. [1-800-520-2807].

The physician should discuss the risks and benefits of this product with the patient, before prescribing or administering it to the patient.

**HyperHEP B S/D** should be given with caution to patients with a history of prior systemic allergic reactions following the administration of human immune globulin preparations. Epinephrine should be available.

In patients who have severe thrombocytopenia or any coagulation disorder that would contraindicate intramuscular injections, Hepatitis B Immune Globulin (Human) should be given only if the expected benefits outweigh the risks.

## PRECAUTIONS

### General

**HyperHEP B S/D** should not be administered intravenously because of the potential for serious reactions. Injections should be made intramuscularly, and care should be taken to draw back on the plunger of the syringe before injection in order to be certain that the needle is not in a blood vessel.

Intramuscular injections are preferably administered in the anterolateral aspects of the upper thigh and the deltoid muscle of the upper arm. The gluteal region should not be used routinely as an injection site because of the risk of injury to the sciatic nerve. An individual decision as to which muscle is injected must be made for each patient based on the volume of material to be administered. If the gluteal region is used when very large volumes are to be injected or multiple doses are necessary, the central region MUST be avoided; only the upper, outer quadrant should be used.<sup>17</sup>

### Laboratory Tests

None required.

### Drug Interactions

Although administration of Hepatitis B Immune Globulin (Human) did not interfere with measles vaccination,<sup>18</sup> it is not known whether Hepatitis B Immune Globulin (Human) may interfere with other live virus vaccines. Therefore, use of such vaccines should be deferred until approximately 3 months after Hepatitis B Immune Globulin (Human) administration. Hepatitis B Vaccine may be administered at the same time, but at a different injection site, without interfering with the immune response.<sup>16</sup> No interactions with other products are known.

### Pregnancy Category C

Animal reproduction studies have not been conducted with **HyperHEP B S/D**. It is also not known whether **HyperHEP B S/D** can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. **HyperHEP B S/D** should be given to a pregnant woman only if clearly needed.

### Pediatric Use

Safety and effectiveness in the pediatric population have not been established.

## ADVERSE REACTIONS

Local pain and tenderness at the injection site, urticaria and angioedema may occur; anaphylactic reactions, although rare, have been reported following the injection of human immune globulin preparations.<sup>19</sup>

## OVERDOSAGE

Although no data are available, clinical experience with other immunoglobulin preparations suggests that the only manifestations would be pain and tenderness at the injection site.

## DOSAGE AND ADMINISTRATION

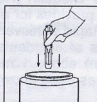
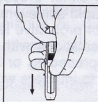
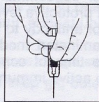
### Acute Exposure to Blood Containing HBsAg<sup>15</sup>

Table 1 summarizes prophylaxis for percutaneous (needlestick or bite), ocular, or mucous-membrane 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 (its value beyond 7 days of exposure is unclear). If Hepatitis B Immune Globulin (Human) is indicated (see Table 1), an injection of 0.06 mL/kg of body weight should be administered intramuscularly (see PRECAUTIONS) as soon as possible after exposure and within 24 hours, if possible. Consult Hepatitis B Vaccine package insert for dosage information regarding that product.



### Directions for Syringe Usage

1. Remove the prefilled syringe from the package. Lift syringe by barrel, **not** by plunger.
2. Twist the plunger rod clockwise until the threads are seated.
3. With the rubber needle shield secured on the syringe tip, push the plunger rod forward a few millimeters to break any friction seal between the rubber stopper and the glass syringe barrel.
4. Remove the needle shield and expel air bubbles. [Do not remove the rubber needle shield to prepare the product for administration until immediately prior to the anticipated injection time.]
5. Proceed with hypodermic needle puncture.
6. Aspirate prior to injection to confirm that the needle is not in a vein or artery.
7. Inject the medication.
8. Keeping your hands behind the needle, grasp the guard with free hand and slide forward toward needle until it is completely covered and guard clicks into place. If audible click is not heard, guard may not be completely activated. (See Diagrams A and B)
9. Place entire prefilled glass syringe with guard activated into an approved sharps container for proper disposal. (See Diagram C)



A number of factors beyond our control could reduce the efficacy of this product or even result in an ill effect following its use. These include improper storage and handling of the product after it leaves our hands, diagnosis, dosage, method of administration and biological differences in individual patients. Because of these factors, it is important that this product be stored properly and that the directions be followed carefully during use.

### HOW SUPPLIED

HyperHEP B S/D is supplied in a 0.5 mL neonatal single dose syringe with attached needle, a 1 mL single dose syringe with attached needle and a 1 mL and a 5 mL single dose vial.

#### NDC Number

13533-636-03  
13533-636-02  
13533-636-01  
13533-636-05

#### Size

0.5 mL syringe  
1 mL syringe  
1 mL vial  
5 mL vial

### STORAGE

Store at 2–8°C (36–46°F). Do not freeze. Do not use after expiration date.

### CAUTION

R<sub>x</sub> only

U.S. federal law prohibits dispensing without prescription.

### REFERENCES

1. Grady GF, Lee VA: Hepatitis B immune globulin — prevention of hepatitis from accidental exposure among medical personnel. *N Engl J Med* 293(21):1067–70, 1975.
2. Seeff LB, Zimmerman HJ, Wright EC, et al: Efficacy of hepatitis B immune serum globulin after accidental exposure. *Lancet* 2(7942):939–41, 1975.
3. Krugman S, Giles JP: Viral hepatitis, type B (MS-2-strain). Further observations on natural history and prevention. *N Engl J Med* 288(15):755–60, 1973.
4. Current trends: Health status of Indochinese refugees: malaria and hepatitis B. *MMWR* 28(39):463–4; 469–70, 1979.
5. Jhaveri R, Rosenfeld W, Salazar JD, et al: High titer multiple dose therapy with HBIG in newborn infants of HBsAg positive mothers. *J Pediatr* 97(2):305–8, 1980.
6. Hoofnagle JH, Seeff LB, Bales ZB, et al: Passive-active immunity from hepatitis B immune globulin. *Ann Intern Med* 91(6):813–8, 1979.
7. Scheierrmann N, Kuwert EK: Uptake and elimination of hepatitis B immunoglobulins after intramuscular application in man. *Dev Biol Stand* 54:347–55, 1983.
8. Recommendations of the Immunization Practices Advisory Committee (ACIP): Hepatitis B Virus: A Comprehensive Strategy for Eliminating Transmission in the United States Through Universal Childhood Vaccination. Appendix A: Postexposure Prophylaxis for Hepatitis B. *MMWR* 40(RR-13):21–25, 1991.
9. Stevens CE, Beasley RP, Tsui J, et al: Vertical transmission of hepatitis B antigen in Taiwan. *N Engl J Med* 292(15):771–4, 1975.
10. Shiraki K, Yoshihara N, Kawana T, et al: Hepatitis B surface antigen and chronic hepatitis in infants born to asymptomatic carrier mothers. *Am J Dis Child* 131(6):644–7, 1977.
11. Recommendation of the Immunization Practices Advisory Committee (ACIP): Immune globulins for protection against viral hepatitis. *MMWR* 30(34):423–8; 433–5, 1981.
12. Okada K, Kamiyama I, Inomata M, et al: e antigen and anti-e in the serum of asymptomatic carrier mothers as indicators of positive and negative transmission of hepatitis B virus to their infants. *N Engl J Med* 294(14):746–9, 1976.
13. Beasley RP, Trepo C, Stevens CE, et al: The e antigen and vertical transmission of hepatitis B surface antigen. *Am J Epidemiol* 105(2):94–8, 1977.
14. Beasley RP, Hwang LY, Lee GCY, et al: Prevention of perinatally transmitted hepatitis B virus infections with hepatitis B immune globulin and hepatitis B vaccine. *Lancet* 2(8359): 1099–102, 1983.
15. Recommendation of the Immunization Practices Advisory Committee (ACIP): Recommendations for protection against viral hepatitis. *MMWR* 34(22):313–35, 1985.
16. Szmunes W, Stevens CE, Olesko WR, et al: Passive-active immunisation against hepatitis B: immunogenicity studies in adult Americans. *Lancet* 1:575–77, 1981.
17. Recommendations of the Immunization Practices Advisory Committee (ACIP): General recommendations on immunization. *MMWR* 38(13):205–14; 219–27, 1989.
18. Beasley RP, Hwang LY: Measles vaccination not interfered with by hepatitis B immune globulin. *Lancet* 1:161, 1982.
19. Ellis EF, Henney CS: Adverse reactions following administration of human gamma globulin. *J Allerg* 43(1):45–54, 1969.
20. Recommendations of the Immunization Practices Advisory Committee (ACIP): Update on Adult Immunization. Table 9. Recommendations for postexposure prophylaxis for percutaneous or mucosal exposure to hepatitis B, United States. *MMWR* 40(RR-12):70, 1991.
21. Recommendations of the Immunization Practices Advisory Committee (ACIP): Update on Adult Immunization. Table 10. Recommendations for post-exposure prophylaxis for perinatal and sexual exposure to hepatitis B, United States. *MMWR* 40(RR-12):71, 1991.

**Talecris**  
BIOTHERAPEUTICS

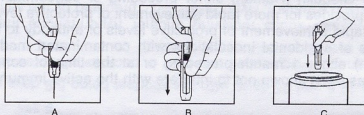
Talecris Biotherapeutics, Inc.  
Research Triangle Park, NC 27709 USA  
U.S. License No. 1716

08908853  
(Rev. January 2005)



### Directions for Syringe Usage

1. Remove the prefilled syringe from the package. Lift syringe by barrel, **not** by plunger.
2. Twist the plunger rod clockwise until the threads are seated.
3. With the rubber needle shield secured on the syringe tip, push the plunger rod forward a few millimeters to break any friction seal between the rubber stopper and the glass syringe barrel.
4. Remove the needle shield and expel air bubbles. [Do not remove the rubber needle shield to prepare the product for administration until immediately prior to the anticipated injection time.]
5. Proceed with hypodermic needle puncture.
6. Aspirate prior to injection to confirm that the needle is not in a vein or artery.
7. Inject the medication.
8. Keeping your hands behind the needle, grasp the guard with free hand and slide forward toward needle until it is completely covered and guard clicks into place. If audible click is not heard, guard may not be completely activated. (See Diagrams A and B)
9. Place entire prefilled glass syringe with guard activated into an approved sharps container for proper disposal. (See Diagram C)



A number of factors beyond our control could reduce the efficacy of this product or even result in an ill effect following its use. These include improper storage and handling of the product after it leaves our hands, diagnosis, dosage, method of administration and biological differences in individual patients. Because of these factors, it is important that this product be stored properly and that the directions be followed carefully during use.

### HOW SUPPLIED

HyperHEP B S/D is supplied in a 0.5 mL neonatal single dose syringe with attached needle, a 1 mL single dose syringe with attached needle and a 1 mL and a 5 mL single dose vial.

NDC Number  
13533-636-03  
13533-636-02  
13533-636-01  
13533-636-05

Size  
0.5 mL syringe  
1 mL syringe  
1 mL vial  
5 mL vial

### STORAGE

Store at 2–8°C (36–46°F). Do not freeze. Do not use after expiration date.

### CAUTION

R<sub>x</sub> only

U.S. federal law prohibits dispensing without prescription.

### REFERENCES

1. Grady GF, Lee VA: Hepatitis B immune globulin — prevention of hepatitis from accidental exposure among medical personnel. *N Engl J Med* 293(21):1067–70, 1975.
2. Seeff LB, Zimmerman HJ, Wright EC, et al: Efficacy of hepatitis B immune serum globulin after accidental exposure. *Lancet* 2(7942):939–41, 1975.
3. Krugman S, Giles JP: Viral hepatitis, type B (MS-2-strain). Further observations on natural history and prevention. *N Engl J Med* 288(15):755–60, 1973.
4. Current trends: Health status of Indochinese refugees: malaria and hepatitis B. *MMWR* 28(39):463–4; 469–70, 1979.
5. Jhaveri R, Rosenfeld W, Salazar JD, et al: High titer multiple dose therapy with HBIG in newborn infants of HBsAg positive mothers. *J Pediatr* 97(2):305–8, 1980.
6. Hoofnagle JH, Seeff LB, Bales ZB, et al: Passive-active immunity from hepatitis B immune globulin. *Ann Intern Med* 91(6):813–8, 1979.
7. Scheiermann N, Kuwert EK: Uptake and elimination of hepatitis B immunoglobulins after intramuscular application in man. *Dev Biol Stand* 54:347–55, 1983.
8. Recommendations of the Immunization Practices Advisory Committee (ACIP): Hepatitis B Virus: A Comprehensive Strategy for Eliminating Transmission in the United States Through Universal Childhood Vaccination. Appendix A: Postexposure Prophylaxis for Hepatitis B. *MMWR* 40(RR-13):21–25, 1991.
9. Stevens CE, Beasley RP, Tsui J, et al: Vertical transmission of hepatitis B antigen in Taiwan. *N Engl J Med* 292(15):771–4, 1975.
10. Shiraki K, Yoshihara N, Kawana T, et al: Hepatitis B surface antigen and chronic hepatitis in infants born to asymptomatic carrier mothers. *Am J Dis Child* 131(6):644–7, 1977.
11. Recommendation of the Immunization Practices Advisory Committee (ACIP): Immune globulins for protection against viral hepatitis. *MMWR* 30(34):423–8; 433–5, 1981.
12. Okada K, Kamiyama I, Inomata M, et al: e antigen and anti-e in the serum of asymptomatic carrier mothers as indicators of positive and negative transmission of hepatitis B virus to their infants. *N Engl J Med* 294(14):746–9, 1976.
13. Beasley RP, Trepo C, Stevens CE, et al: The e antigen and vertical transmission of hepatitis B surface antigen. *Am J Epidemiol* 105(2):94–8, 1977.
14. Beasley RP, Hwang LY, Lee GCY, et al: Prevention of perinatally transmitted hepatitis B virus infections with hepatitis B immune globulin and hepatitis B vaccine. *Lancet* 2(8359): 1099–102, 1983.
15. Recommendation of the Immunization Practices Advisory Committee (ACIP): Recommendations for protection against viral hepatitis. *MMWR* 34(22):313–35, 1985.
16. Szmunes W, Stevens CE, Olesko WR, et al: Passive-active immunisation against hepatitis B: immunogenicity studies in adult Americans. *Lancet* 1:575–77, 1981.
17. Recommendations of the Immunization Practices Advisory Committee (ACIP): General recommendations on immunization. *MMWR* 38(13):205–14; 219–27, 1989.
18. Beasley RP, Hwang LY: Measles vaccination not interfered with by hepatitis B immune globulin. *Lancet* 1:161, 1982.
19. Ellis EF, Henney CS: Adverse reactions following administration of human gamma globulin. *J Allerg* 43(1):45–54, 1969.
20. Recommendations of the Immunization Practices Advisory Committee (ACIP): Update on Adult Immunization. Table 9. Recommendations for postexposure prophylaxis for percutaneous or percutaneous exposure to hepatitis B, United States. *MMWR* 40(RR-12):70, 1991.
21. Recommendations of the Immunization Practices Advisory Committee (ACIP): Update on Adult Immunization. Table 10. Recommendations for post-exposure prophylaxis for perinatal and sexual exposure to hepatitis B, United States. *MMWR* 40(RR-12):71, 1991.

**Talecris**  
BIOTHERAPEUTICS

Talecris Biotherapeutics, Inc.  
Research Triangle Park, NC 27709 USA  
U.S. License No. 1716

08908853  
(Rev. January 2005)