NEW ZEALAND DATA SHEET

1 PRODUCT NAME (strength, pharmaceutical form)

HyperHEP B ≥ 220 IU / mL, solution for intramuscular injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Hepatitis B immunoglobulin, human

Each 1 mL contains:

Hepatitis B immunoglobulin, human	≥ 220 IU
Glycine, USP	15 mg
Water for injection, USP	up to 1 mL

Hepatitis B immunoglobulin, human is provided in a 0.5 mL syringe (≥ 110 IU); 1 mL syringe (≥ 220 IU); 1 mL vial (≥ 220 IU) and 5 mL vial (≥ 1100 IU).

Hepatitis B immunoglobulin, human is formulated as a 15% to 18% protein solution in 0.16 M to 0.26 M glycine. It contains no preservative and is latex-free.

Hepatitis B immunoglobulin, human is produced from the plasma of human donors with high titres of antibody to the hepatitis B surface antigen (anti-HBs).

Each vial or syringe 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, United States Food and Drug Administration). The U.S. reference has been tested against the World Health Organisation standard Hepatitis B Immunoglobulin and found to be equal to 220 international units (IU) per mL.

3 PHARMACEUTICAL FORM

Solution for intramuscular injection

Hepatitis B immunoglobulin, human is a clear or slightly opalescent, and colourless or pale yellow or light brown sterile solution.

The pH is 4.1 to 4.8.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Hepatitis B immunoglobulin, human is indicated for post-exposure prophylaxis in persons who did not receive prior vaccination, or whose prior vaccination regimen is incomplete or when the antibody level is inadequate i.e. < 10 IU/mL. A regimen combining Hepatitis B immunoglobulin, human with hepatitis B vaccine will provide both short and long-term protection. This post exposure prophylaxis should be considered following either parenteral exposure, direct mucous membrane contact, oral ingestion, sexual exposure to an HBsAg-positive person and for infants < 12 months, if the mother or

primary contact person has acute HBV infection. Infants born of HBsAg-positive mothers should receive Hepatitis B immunoglobulin, human in conjunction with the first dose of Hepatitis B Vaccine.

Administration of Hepatitis B immunoglobulin, human either preceding or concomitant with the commencement of active immunisation with Hepatitis B Vaccine provides for more rapid achievement of protective levels of hepatitis B antibody, than when the vaccine alone is administered. 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. Administration of Hepatitis B immunoglobulin, 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.

Hepatitis B immunoglobulin, human can also be considered for haemodialysis patients and receptors of certain blood products unable to develop adequate immune protection.

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 immunoglobulin, 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. This risk is especially great if the mother is HBeAg-positive. For an infant with perinatal exposure to an HBsAg-positive and HBeAg-positive mother, a regimen combining one dose of Hepatitis B immunoglobulin, human at birth with the hepatitis B vaccine series started soon after birth is 85% to 95% effective in preventing development of the HBV carrier state. Regimens involving either multiple doses of Hepatitis B immunoglobulin, human alone or the vaccine series alone have 70% to 90% efficacy, while a single dose of Hepatitis B immunoglobulin, human alone has only 50% efficacy.

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 immunoglobulin, human is 75% effective if administered within 2 weeks of last sexual exposure.

Household exposure to persons with acute HBV infection

Since infants have close contact with primary care-givers, 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 immunoglobulin, human and hepatitis B vaccine is indicated if the mother or primary care-giver has acute HBV infection.

4.2 Dose and method of administration

Dose

Acute exposure to blood containing HBsAg

Table 1 summarises 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 immunoglobulin, human should be given as soon as possible after exposure (its value beyond 7 days of exposure is unclear). If Hepatitis B immunoglobulin, human is indicated (see Table 1), an injection of 0.06 mL/kg of body weight should be administered intramuscularly (see 4.4 Special warnings and precautions for use) as soon as possible after exposure and within 24 hours, if possible. Consult Hepatitis B Vaccine Data Sheet (New Zealand) for dosage information regarding that product.

Table 1. Recommendations for Hepatitis B Prophylaxis Following Percutaneous or Permucosal Exposure

Exposed Person		
Source	Unvaccinated	Vaccinated
HBsAg-Positive	1. Hepatitis B immunoglobulin, human x1 immediately* 2. Initiate Hepatitis B Vaccine Series †	1. Test exposed person for anti-HB's. 2. If inadequate antibody,‡ Hepatitis B immunoglobulin, human (x1) immediately plus Hepatitis B Vaccine booster dose, or 2 doses of Hepatitis B immunoglobulin, human*, one as soon as possible after exposure and the second 1 month later.
Known Source (High Risk)	1. Initiate Hepatitis B Vaccine Series 2. Test source for HBsAg. If positive, Hepatitis B immunoglobulin, human x1	1. Test source for HBsAg only if exposed is vaccine nonresponder; if source is HBsAg-positive, give Hepatitis B immunoglobulin, human) x1 immediately plus Hepatitis B Vaccine booster dose, or 2 doses of Hepatitis B immunoglobulin, human*, one as soon as possible after exposure and the second 1 month later.
Low Risk HBsAg-positive	Initiate Hepatitis B Vaccine series	Nothing required
Unknown source	Initiate Hepatitis B Vaccine series within 7 days of exposure.	Nothing required

* Hepatitis B immunoglobulin, human, dose 0.06 mL/kg IM.

† Hepatitis B Vaccine dose 20 µg IM for adults; 10 µg IM for infants or children under 10 years of age. First dose within 1 week; second and third doses, 1 and 6 months later.

‡ Less than 10 sample ratio units (SRU) by radioimmunoassay (RIA), negative by enzyme immunoassay (EIA).

For persons who refuse Hepatitis B Vaccine, a second dose of Hepatitis B immunoglobulin, human should be given 1 month after the first dose.

Perinatal exposure of infants born to HBsAg-positive mothers

Efficacy of prophylactic Hepatitis B immunoglobulin, human in infants at risk depends on administering Hepatitis B immunoglobulin, human on the day of birth. It is therefore vital that HBsAg-positive mothers be identified before delivery.

Hepatitis B immunoglobulin, human (0.5 mL) should be administered intramuscularly (IM) to the new-born infant after physiologic stabilisation of the infant and preferably within 12 hours of birth. Hepatitis B immunoglobulin, human efficacy decreases markedly if treatment is delayed beyond 48 hours. Hepatitis B Vaccine should be administered IM in three doses of 0.5 mL of vaccine (10 µg) each. The first dose should be given within 7 days of birth and may be given concurrently with Hepatitis B immunoglobulin, human) but at a separate site. The second and third doses of vaccine should be given 1 month and 6 months, respectively, after the first. If administration of the first dose of Hepatitis B Vaccine is delayed for as long as 3 months, then a 0.5 mL dose of Hepatitis B immunoglobulin, human should be repeated at 3 months. If Hepatitis B Vaccine is refused, the 0.5 mL dose of Hepatitis B immunoglobulin, human should be repeated at 3 and 6 months. Hepatitis B immunoglobulin, human administered at birth should not interfere with oral polio and diphtheria-tetanus-pertussis vaccines administered at 2 months of age.

Sexual exposure to an HBsAg-positive person

All susceptible persons, whose sex partners have acute hepatitis B infection, should receive a single dose of Hepatitis B immunoglobulin, human (0.06 mL/kg) and initiate Hepatitis B Vaccine series. If prophylaxis cannot be started within 14 days of the last sexual contact or if sexual contact with the infected person will continue, see Table 2 below. Administering the vaccine with Hepatitis B immunoglobulin, human may improve the efficacy of post-exposure treatment. The vaccine has the added advantage of conferring long-lasting protection.

Table 2. Recommendations for Post-exposure Prophylaxis for Sexual Exposure to Hepatitis B

Hepatitis B immunoglobulin, human		Vaccine	
Dose	Recommended timing	Dose	Recommended timing
0.06 mL/kg IM†	Single dose within 14 days of last sexual contact.	1.0 mL IM†	First dose at a time of Hepatitis B immunoglobulin, human treatment‡

† IM = Intramuscularly

‡ The first dose can be administered the same time as the Hepatitis B immunoglobulin, human dose but at a different site; subsequent doses should be administered as recommended for specific vaccine.

Household exposure to persons with acute HBV infection

Prophylactic treatment with a 0.5 mL dose of Hepatitis B immunoglobulin, human and hepatitis B vaccine is indicated for infants < 12 months of age, who have been exposed to a primary care-giver who has acute hepatitis B. Prophylaxis for other household contacts of persons with acute HBV infection is not indicated unless they have had 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.

Paediatric Population

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

Method of administration

Administer intramuscularly. Do not inject intravenously. Use only clear, particle free solution.

(For directions for syringe usage, see section 6.6).

Hepatitis B immunoglobulin, human may be administered at the same time (but at a different site), or up to 1 month preceding Hepatitis B Vaccination without impairing the active immune response from Hepatitis B Vaccination.

4.3 Contraindications

Intolerance to homologous immunoglobulins**.**

Severe thrombocytopenia or any coagulation disorder that would contraindicate intramuscular injections.

4.4 Special warnings and precautions for use

HyperHEP B should **not** be administered intravenously because of the potential for serious reactions. Injections should be administered intramuscularly, and care should be taken to draw back the plunger of the syringe before injection in order to be certain that the needle is not in a blood vessel. Patients should be observed for at least 20 minutes after administration. 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 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.

True allergic response to Hepatitis-B IgG given intramuscularly is rare. In the case of shock, treatment should follow guidelines for shock therapy. Intolerance to immunoglobulins is likely to develop in the very rare cases of IgA deficiency when the patient has antibodies against IgA. Suspicion of allergic or anaphylactic type reaction requires immediate discontinuation of the injection.

HyperHEP B is made from human plasma. When medicinal biological products are administered, the possibility of infectious diseases due to transmission of pathogens cannot be totally excluded. However, in the case of products prepared from human plasma, the risk of transmission of pathogens

is reduced by: (1) epidemiological controls on the donor population and selection of individual donors by a medical interview and screening of individual donations and plasma pools for viral infection markers; (2) testing of plasma for hepatitis C virus (HCV), human immunodeficiency virus (HIV), hepatitis B virus (HBV), HAV, and human parvovirus (B19V) genomic material; and (3) manufacturing procedures with demonstrated capacity to inactivate/remove pathogens.

All infections, thought by a physician, to possibly have been transmitted by this product should be reported by the physician or other healthcare provider to Pharmacy Retailing (NZ) Ltd t/a Healthcare Logistics Phone (09) 918 5100.

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

It is strongly recommended that each time the healthcare staff administer a dose of HyperHEP B they record the name of the medication and lot number in order to keep a record of the batches used.

4.5 Interactions with other medicines and other forms of interaction

Live attenuated virus vaccine

Although administration of Hepatitis B immunoglobulin, human did not interfere with measles vaccination, it is not known whether Hepatitis B immunoglobulin, human may impair, for a period of 5 weeks and up to 3 months, the efficacy of live attenuated virus vaccine. Therefore, use of such vaccines should be deferred until approximately 3 months after Hepatitis B immunoglobulin, human administration. Hepatitis B Vaccine may be administered at the same time, but at a different injection site, without interfering with the immune response. No interactions with other products are known.

Interference with serological testing

After injection of immunoglobulins, the transitory rise of various passively transferred antibodies in the patient's blood may result in misreading positive results in serological testing.

4.6 Fertility, pregnancy and lactation

Animal reproduction studies have not been conducted with HyperHEP B. The safety of this medicinal product for use in human pregnancy has not been established in a controlled clinical trial, therefore, it should be administered with caution to pregnant or breast feeding women. Long lasting clinical experience with immunoglobulin (Ig), in particular the application of anti-D-Ig, does indicate that no harmful effects on the course of pregnancy, on the foetus and the neonate are to be expected. Immunoglobulins are excreted into the milk and may contribute to transfer of protective antibodies to the neonates.

4.7 Effects on ability to drive and use machines

There is no indication that Hepatitis B immunoglobulin, human may impair the ability to drive and use machines.

4.8 Undesirable effects

Local pain and tenderness at the injection site, urticaria and angioedema may occur. This can be prevented by dividing larger doses over several sites. Occasionally fever, cutaneous reactions and chills occur. In rare cases the following symptoms are reported: nausea, vomiting, hypotension, tachycardia, allergic or anaphylactic type reactions including shock.

When medicinal products prepared for human blood or plasma are administered, infectious diseases due to transmission of infective agents cannot be totally excluded. This also applies to pathogens of hitherto unknown nature.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://pophealth.my.site.com/carmreportnz/s/

4.9 Overdose

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.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: immune sera and immunoglobulins, hepatitis B immunoglobulin, ATC code: J06BB04

Hepatitis B immunoglobulin, human contains specific neutralising antibodies (mainly IgG) that provide passive immunisation for individuals exposed to the hepatitis B virus (HBV) as evidenced by a reduction in the attack rate of hepatitis B following its use.

5.2 Pharmacokinetic properties

The administration of the usual recommended dose of this immunoglobulin 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:

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

Mean value for half-life were between 17.5 and 25 days, with the shortest being 5.9 days and the longest 35 days.

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.

5.3 Preclinical safety data

Immunoglobulins are normal constituents of the human body. In animals, single dose toxicity testing is of no relevance since higher doses result in overloading. Repeated dose toxicity testing and embryofoetal toxicity studies are impractical due to induction of and interference with human antibodies. Effects of the product on the immune system of the newborn have not been studied. Since clinical experience provides no hint for tumourigenic and mutagenic effects of immunoglobulins, experimental studies, particularly in heterologous species are not considered necessary.

In the manufacturing process of HyperHEP B, there are several steps with the capacity for viral inactivation or removal. The main steps of the manufacturing process that contribute to the virus clearance capacity are as follows:

- Caprylate precipitation/depth filtration
- Caprylate incubation
- Depth filtration
- Column chromatography
- Nanofiltration
- Low pH final container incubation

To provide additional assurance of the pathogen safety of the final product, the capacity of the HyperHEP B manufacturing process to remove and/or inactivate viruses has been demonstrated by laboratory spiking studies on a scaled down process model using a wide range of viruses with diverse physicochemical properties.

The combination of all of the above mentioned measures provides the final product with a high margin of safety from the potential risk of transmission of infectious viruses.

The caprylate/chromatography manufacturing process was also investigated for its capacity to decrease the infectivity of an experimental agent of transmissible spongiform encephalopathy (TSE), considered as a model for the variant Creutzfeldt-Jakob disease (vCJD), and Creutzfeldt-Jakob disease (CJD) agents. These studies provide reasonable assurance that low levels of vCJD/CJD agent infectivity, if present in the starting material, would be removed by the caprylate/chromatography manufacturing process.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycine, USP.

Water for injection, USP.

6.2 Incompatibilities

Hepatitis B immunoglobulin, human should not be mixed with other medicinal products.

6.3 Shelf life

36 months when stored at 2°C to 8°C (refrigerate, do not freeze).

6.4 Special precautions for storage

Store at 2°C to 8°C. Do not freeze. Do not use after expiration date.

6.5 Nature and contents of container

Hepatitis B immunoglobulin, human - HyperHEP B is supplied in a 0.5 mL neonatal single dose syringe with attached needle, a 1 mL single dose syringe with attached needle, a 1 mL single dose vial, and a 5 mL single dose vial**.**

Package quantities

1 X 0.5 mL neonatal single dose syringe with attached needle

1 X 1 mL single dose syringe with attached needle

1 X 1 mL single dose vial

1 X 5 mL single dose vial

6.6 Special precautions for disposal and other handling

Do not use if the solution is cloudy or has particles.

Hepatitis B immunoglobulin, human — HyperHEP B is supplied in a syringe with an attached needle guard for your protection and convenience, as well as in vials. Please follow instructions below for proper use of syringe and needle guard.

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. Do not use if the syringe is prematurely engaged.

3. With the needle shield secured on the syringe tip, push the plunger rod forward a few millimeters to break any friction seal between the stopper and the glass syringe barrel.

4. Remove the needle shield and expel air bubbles. [Do not remove the needle shield to prepare the product for administration until immediately prior to the anticipated injection time.]

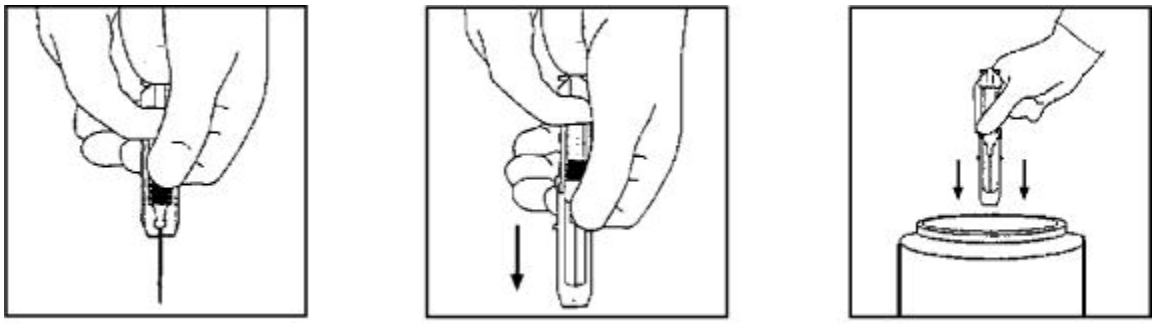
5. Proceed with hypodermic needle puncture.

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 B C

A number of factors 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.

7 MEDICINE SCHEDULE

Prescription Medicine

8 SPONSOR

Distributed by:

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10 DATE OF REVISION OF THE TEXT

27 September 2024

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
4.4	Change to contact
4.8	Updated URL address
6.3	Updated shelf life to 36 months
8	Sponsor change