NEW ZEALAND DATA SHEET

1 PRODUCT NAME

Hepatitis B Immunoglobulin-VF 100 IU, solution for intramuscular injection

Hepatitis B Immunoglobulin-VF 400 IU, solution for intramuscular injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Human Hepatitis B Immunoglobulin

Hepatitis B Immunoglobulin-VF is a sterile solution containing 160 mg/mL human plasma protein of which at least 98% is immunoglobulin (mainly IgG), with a hepatitis B antibody titre of not less than 100 IU/mL.

Hepatitis B Immunoglobulin-VF contains less than 0.5 mg/mL immunoglobulin A (IgA).

Hepatitis B Immunoglobulin-VF is manufactured from human plasma donated by New Zealand's voluntary and non-remunerated donors.

Hepatitis B Immunoglobulin-VF contains 22.5 mg/mL glycine.

Hepatitis B Immunoglobulin-VF contains no preservatives.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for intramuscular injection.

The pH value of the ready-to-use solution is 6.6.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Hepatitis B Immunoglobulin-VF is indicated for post-exposure prophylaxis in persons who did not receive prior vaccination, or whose prior vaccination regimen is incomplete, or when the hepatitis B antibody level is inadequate (<10 IU/L).

Post-exposure prophylaxis should be considered following percutaneous or permucosal exposure to the hepatitis B virus surface antigen (HBsAg)-positive or suspected HBsAg-positive material, for example, by needle stick, oral ingestion or sexual exposure.

Hepatitis B Immunoglobulin-VF is also indicated for prophylaxis in infants born to HBsAg-positive mothers.

4.2 Dose and method of administration

Dose

Prophylaxis with Hepatitis B Immunoglobulin-VF in adults following percutaneous or permucosal exposure to HBsAg-positive or suspected HBsAg-positive material: Refer to **Table 1.**

Table 1: Prophylaxis with Hepatitis B Immunoglobulin-VF in adults following percutaneous or permucosal exposure to HBsAg-positive or suspected HBsAg-positive material

Source material	Vaccination history	
	No prior vaccination or incomplete vaccination regimen	**Completed vaccination regimen**
Confirmed positive for HBsAg	Give a single dose of 400 IU Hepatitis B Immunoglobulin-VF immediately[a] and initiate hepatitis B vaccination regimen at the same time.	Test exposed person for HBs antibody. If level is inadequate (<10 IU/L), give a single dose of 400 IU Hepatitis B Immunoglobulin-VF immediately plus a hepatitis B vaccine booster.
High risk for HBsAg, but not confirmed	Initiate hepatitis B vaccination regimen. Test source material for HBsAg and, if positive, give a single dose of 400 IU Hepatitis B Immunoglobulin-VF.	Test exposed person for HBs antibody. If level is inadequate (<10 IU/L), test source material for HBsAg and, if positive, give a single dose of 400 IU Hepatitis B Immunoglobulin-VF plus a hepatitis B vaccine booster.
Uncertain or low risk	Initiate hepatitis B vaccination regimen.	Nothing required.

[a] Hepatitis B Immunoglobulin-VF must be administered within 72 hours of exposure to the virus.

Prophylaxis in infants born to HBsAg-positive mothers:

Give infant 100 IU Hepatitis B Immunoglobulin-VF at birth and initiate hepatitis B vaccination regimen at the same time by giving first vaccine dose in a different limb.

Method of administration

Hepatitis B Immunoglobulin-VF should be brought to room temperature before use, and given slowly by deep intramuscular injection, using an appropriate sized needle. If a large dose is required, it is advisable to administer it in divided doses at different sites. This applies in the case of doses above 2 mL for children up to 20 kg body weight and doses above 5 mL for persons above 20 kg body weight.

Hyaluronidase and/or a suitable local anaesthetic may be added to the injection if desired.

Active immunisation with hepatitis B vaccine should always be commenced in conjunction with administration of Hepatitis B Immunoglobulin-VF in patients exposed to hepatitis B virus (see Table 1). In such case the immunoglobulin and the vaccine should be administered at different sites of the body.

For further instructions, see section 6.6.

4.3 Contraindications

Hepatitis B Immunoglobulin-VF is contraindicated in patients:

- who have had a true anaphylactic reaction to the active substance or to any of the components of the product
- with immunoglobulin A (IgA) deficiency, unless they have been tested and shown not to have circulating anti-IgA antibodies, since these patients may experience severe reactions to the IgA which is present in trace amounts
- who have severe thrombocytopenia or any coagulation disorder that would contraindicate intramuscular injections.
- who are HBsAg-positive.

  Hepatitis B Immunoglobulin-VF is unnecessary in those who already have adequate circulating hepatitis B antibody (≥10 IU/L).

4.4 Special warnings and precautions for use

Route of administration

Hepatitis B Immunoglobulin-VF MUST NOT be administered intravenously because of the potential for anaphylactic reactions. Injections must 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.

Hypersensitivity

Hepatitis B Immunoglobulin-VF contains trace amounts of IgA which may provoke anaphylaxis in patients with anti-IgA antibodies, such as those with IgA deficiency.

Hepatitis B Immunoglobulin-VF should be given with caution to patients with a history of prior systemic allergic reactions following the administration of human immunoglobulin preparations. Rarely, human Hepatitis B immunoglobulin can induce a precipitous fall in blood pressure with anaphylactic reaction, even in patients who had tolerated previous treatment with human Hepatitis B immunoglobulin. In case of anaphylactic reaction, the injection should be stopped immediately.

In the case of shock, treatment should follow the guidelines of shock therapy.

Patients should be observed for at least 20 minutes after administration of Hepatitis B Immunoglobulin-VF. Particularly in cases of inadvertent intravenous injection, patients should be observed for longer term (at least 1 hour) after administration.

Pathogen safety

This product is made from human plasma. Products made from human plasma may contain infectious agents, such as viruses and theoretically Creutzfeldt-Jakob Disease (CJD) agents, 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 infectious agents and by testing for the presence of certain viral markers.

In addition, virus removal and inactivation procedures are included in the manufacturing process. The current procedures applied in the manufacture of this product are effective against enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B virus (HBV) and hepatitis C virus (HCV), and the non-enveloped viruses, such as hepatitis A virus (HAV) and human parvovirus B19.

There is no evidence to date that parvovirus B19 can be transmitted by Hepatitis B Immunoglobulin-VF and the nanofiltration step of the manufacturing process has been shown to remove such viruses (or viruses of similar size). The product is known to contain antibodies to the virus.

Immunoglobulins for intramuscular injection, prepared by this process from plasma screened by current methods, have not been implicated in the transmission of viral infectious diseases including HIV. Studies using plasma spiked with HIV have shown that the Cohn cold-ethanol fractionation process produces a very large reduction in virus titre with undetectable levels in the immunoglobulin fraction. Epidemiological studies have not recognised any cluster of AIDS patients or HIV seroconversion in immunoglobulin recipients.

Despite these measures, such products may still potentially transmit disease. There is also the possibility that other known or unknown infectious agents may be present in such products. Vaccination for patients in receipt of medicinal products from human plasma should be considered where appropriate.

It is strongly recommended that every time Hepatitis B Immunoglobulin-VF is administered to a patient, the name and batch number of the product are recorded in order to maintain a link between the patient and the batch of the product.

Genotoxicity and carcinogenicity

No genotoxicity or carcinogenicity studies have been conducted with Hepatitis B Immunoglobulin-VF. There have been no reports of such effects associated with the use of CSL Behring's plasma-derived products.

Effects on laboratory tests

After injection of immunoglobulin, the transitory rise of the various passively transferred antibodies in the patient's blood may result in misleading positive results in serological testing. Passive transmission of antibodies to erythrocyte antigens (e.g., anti-A, anti-B, anti-D) may interfere with some serological tests for red cell allo-antibodies (e.g. Coombs' test).

4.5 Interaction with other medicines and other forms of interaction

Hepatitis B Immunoglobulin-VF should not be mixed with other pharmaceutical products, except as indicated (see section 4.2).

Hepatitis B vaccine

If hepatitis B vaccine is administered at the same time as Hepatitis B Immunoglobulin-VF it should be given in a different limb/site.

Vaccinations with live attenuated virus vaccines

Passively acquired antibody can interfere with the response to live, attenuated virus vaccines. Therefore, administration of such vaccines, e.g. poliomyelitis or measles, should be deferred until approximately three months after passive immunisation. In the case of measles, the decrease in efficacy may persist for up to one year. Therefore, patients receiving measles vaccine should have their antibody status checked. If Hepatitis B Immunoglobulin-VF is administered within two weeks of vaccination with a live attenuated virus vaccine, the efficacy of the vaccine may be compromised. Consideration should be given to re-vaccination approximately three months after Hepatitis B Immunoglobulin-VF was given.

4.6 Fertility, pregnancy and lactation

Pregnancy

The safety of this medicinal product for use in human pregnancy has not been established in controlled clinical trials. Hepatitis B Immunoglobulin-VF should therefore only be given with caution to pregnant women.

Breast-feeding

The safety of this medicinal product for use during lactation has not been established in controlled clinical trials. Hepatitis B Immunoglobulin-VF should therefore only be given with caution to breast-feeding mothers. Immunoglobulins are excreted in breast milk, however, it is not known whether this applies to passively administered Hepatitis B Immunoglobulin-VF.

Fertility

No reproductive toxicity studies have been conducted with Hepatitis B Immunoglobulin-VF. There have been no reports of such effects associated with the use of CSL Behring's plasma-derived products.

4.7 Effects on ability to drive and use machines

No effects on ability to drive and use machines have been observed.

4.8 Undesirable effects

Summary of the safety profile

Local tenderness, erythema and stiffness may occur at the site of injection and may persist for several hours. This may occur after any intramuscular injection.

Mild pyrexia, malaise, drowsiness and urticaria have been reported occasionally after injections of immunoglobulins. True allergic responses are rare. Skin lesions, headache, dizziness, nausea, generalised hypersensitivity reactions and convulsions have been reported on rare occasions.

Clinical studies

In the clinical trial with Hepatitis B Immunoglobulin, the following general and local reactions were recorded in the 58 healthy subjects (total number of events, up to and including 7 days post injection; pasteurised/unpasteurised product): malaise (20/22 events), drowsiness (13/17 events), induration (10/4 events), sensation of fever (4/4 events), chills (3/3 events), sweating (3/1 events) and warmth/heat when touched (0/4 events). There was an overall higher reporting of local tolerance adverse events at the injection site for the unpasteurised product, such as pain (32/52 events), bruising (10/22 events), redness (2/8 events) and irritation (2/4 events).

Paediatric population

The use of this product in the paediatric population has not been established in appropriate studies. To date, this population is not over-represented in spontaneous reports of adverse events associated with the use of CSL Behring's intramuscular immunoglobulin products.

Elderly population

The use of this product in the elderly population has not been established in appropriate studies. To date, this population is not over-represented in spontaneous reports of adverse events associated with the use of CSL Behring's intramuscular immunoglobulin products.

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://nzphvc.otago.ac.nz/reporting/

4.9 Overdose

The consequences of overdosage are not known.

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, human hepatitis B immunoglobulin.

ATC code: J06BB04

Hepatitis B Immunoglobulin-VF is prepared from human plasma. Donations are selected on the basis that they contain high levels of antibody to HBsAg. The manufacturing process for Hepatitis B Immunoglobulin-VF contains specific steps to reduce the possibility of viral transmission including pasteurisation for viral inactivation and nanofiltration for virus removal.

Mechanism of action

Hepatitis B Immunoglobulin-VF contains specific neutralising antibodies (mainly IgG) against HBsAg.

Clinical efficacy and safety

A comparative clinical trial was conducted to investigate the effect of pasteurisation on the *in vivo* behaviour of intramuscular immunoglobulins using Hepatitis B Immunoglobulin (pasteurised and unpasteurised) as the representative of this group of products.

Fifty-eight (58) healthy subjects (28 males and 30 females) each received an intramuscular injection of pasteurised (viral inactivated) or unpasteurised Hepatitis B Immunoglobulin. No significant clinical differences were observed.

Twenty-eight (28) subjects received the viral inactivated product. Maximal serum concentration of IgG was reached after 8.0±5.5 days (mean±s.d.), and the estimated half-life of IgG was 27.2±6.6 days (mean±s.d.). The IgG levels remained at protective levels for at least 6 weeks. These values are consistent with ranges observed with other intramuscular immunoglobulin products.

A clinical trial with Hepatitis B Immunoglobulin-VF has not been conducted.

5.2 Pharmacokinetic properties

Absorption and Distribution

Hepatitis B Immunoglobulin-VF for intramuscular administration is bioavailable in the recipient's circulation after 2 to 3 days. Human hepatitis B immunoglobulin has a half-life of about 3 to 4 weeks. This half-life may vary from patient to patient.

Elimination

IgG and IgG-complexes are broken down in cells of the reticuloendothelial system.

5.3 Preclinical safety data

Animal reproduction studies have not been conducted with Hepatitis B Immunoglobulin-VF.

Hepatitis B Immunoglobulin-VF with hepatitis B IgG as the active ingredient is derived from human plasma and acts like an endogenous constituent of plasma. Preclinical studies with repeated dose applications (chronic toxicity, carcinogenicity and mutagenicity) cannot be reasonably performed in conventional animal models due to the development of antibodies following the application of heterologous human proteins.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycine
Water for injections

6.2 Incompatibilities

This medicine must not be mixed with other medicines, diluents, or solvents except those mentioned in section 4.2.

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6.3 Shelf life

3 years

Shelf life after first opening:

The product does not contain an antimicrobial preservative. It must, therefore, be used immediately after opening the vial.

6.4 Special precautions for storage

Store at 2°C to 8°C (Refrigerate. Do not freeze).

Protect from light.

For storage conditions of the medicine after first opening, see section 6.3.

6.5 Nature and contents of container

Solution in a single glass vial, with a rubber stopper, an aluminium seal and a plastic flip-top cap.

Pack sizes

1 vial with 100 IU hepatitis B antibody

1 vial with 400 IU hepatitis B antibody

The actual volume in the vial is stated on the label.

Hepatitis B Immunoglobulin-VF is packaged in latex free materials.

6.6 Special precautions for disposal and other handling

Hepatitis B Immunoglobulin-VF is a sterile, ready-to-use solution.

If the product appears to be turbid by transmitted light or contains any sediment it must not be used.

Any unused solution must be discarded appropriately.

7 MEDICINE SCHEDULE

Prescription Medicine

8 SPONSOR

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9 DATE OF FIRST APPROVAL

11 February 1999

10 DATE OF REVISION OF THE TEXT

8 June 2022

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
2	Addition of immunoglobulin A value.