AUSTRALIAN PRODUCT INFORMATION

Hepatitis B Immunoglobulin-VF
(Human hepatitis B immunoglobulin)

1 NAME OF THE MEDICINE

Human Hepatitis B Immunoglobulin

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Hepatitis B Immunoglobulin-VF is a sterile, preservative-free solution containing 160 mg/mL human plasma proteins and 22.5 mg/mL glycine. At least 98% of the protein is immunoglobulins (mainly IgG), with a hepatitis B antibody titre of not less than 100 IU/mL.

Hepatitis B Immunoglobulin-VF is manufactured from human plasma collected by Australian Red Cross Lifeblood.

3 PHARMACEUTICAL FORM

Solution for intramuscular injection.

The solution has a pH of 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 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

Dosage

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* 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.

* 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.

Administration

If the product appears to be turbid by transmitted light or contains any sediment it must not be used. **The product does not contain an antimicrobial preservative. It must, therefore, be used immediately after opening the vial. Any unused solution must be discarded appropriately.**

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 (more than 5 mL) is required, it is advisable to administer it in divided doses at different sites. 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.

4.3 CONTRAINDICATIONS

Hepatitis B Immunoglobulin-VF is contraindicated in individuals:

1. With isolated Immunoglobulin A (IgA) deficiency, unless they have been tested and shown not to have circulating anti-IgA antibodies.
2. Who have severe thrombocytopenia or any coagulation disorder that would contraindicate intramuscular injections.
3. 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

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.

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

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, the manufacturing process for Hepatitis B Immunoglobulin contains specific steps to reduce the possibility of viral transmission including pasteurisation for viral inactivation and nanofiltration for virus removal. 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. Additionally, the product contains specific antibodies directed against human parvovirus B19.

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

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 human immunodeficiency virus (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.

Use in the elderly

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's intramuscular immunoglobulin products.

Paediatric use

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's intramuscular immunoglobulin 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.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

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

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.

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. 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

Effects on 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's plasma-derived therapeutic medicines.

Use in 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.

Use in lactation

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.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

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

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

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. 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).

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.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

The consequences of overdosage are not known.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

Hepatitis B Immunoglobulin-VF contains specific neutralising antibodies (mainly IgG) against hepatitis B surface antigen (HBsAg). Donations are selected on the basis that they contain high levels of antibody to HBsAg. Pharmacological data is presented under Clinical trials.

Clinical trials

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

Refer to Section 5.1 Pharmacodynamic Properties.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

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

Carcinogenicity

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

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Refer to Section 2 Qualitative and quantitative composition.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store at 2°C to 8°C (Refrigerate. Do not freeze). Protect from light. Do not use after the expiry date shown on the label.

6.5 NATURE AND CONTENTS OF CONTAINER

Hepatitis B Immunoglobulin-VF solution for intramuscular injection is available in single vials containing 100 IU or 400 IU hepatitis B antibody. The actual volume in the vial is stated on the label.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure

Not applicable

CAS Number

None assigned

7 MEDICINE SCHEDULE (POISONS STANDARD)

S4

8 SPONSOR

CSL Behring (Australia) Pty Ltd
ABN 48 160 734 761
189–209 Camp Road
Broadmeadows VIC 3047
Australia

Distributed by

Australian Red Cross Lifeblood

For Medical/Technical Enquiries

TOLL FREE: 1800 642 865

For Customer Service Enquiries

TOLL FREE: 1800 063 892

customerservice@cslbehring.com.au

www.cslbehring.com.au

9 DATE OF FIRST APPROVAL

08 November 2006

10 DATE OF REVISION

7 May 2020

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
All	PI updated to the new format.
4.7	Information added about effects on ability to drive and use machines
8	Name changed to Australian Red Cross Lifeblood