Product Information

Hepatitis B Immunoglobulin-VF

Australia

NAME OF THE MEDICINE

Human Hepatitis B Immunoglobulin, solution for intramuscular injection.

DESCRIPTION

Hepatitis B Immunoglobulin-VF is a sterile, preservative-free solution containing 160 mg/mL human plasma proteins and 22.5 mg/mL glycine. The solution has a pH of 6.6. 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 plasma donated by Australia's voluntary and non-remunerated donors. Donations are selected on the basis that they contain high levels of antibody to hepatitis B surface antigen (HBsAg). 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. 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.

PHARMACOLOGY

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

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.

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).

PRECAUTIONS

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, virus removal and inactivation steps 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. Additionally, the product contains specific antibodies directed against human parvovirus B19.

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.

Genotoxicity, carcinogenicity and impairment of fertility

No genotoxicity, carcinogenicity or 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 products.

Use in pregnancy and lactation

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

Paediatric use and use in the elderly

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

Interactions with other medicines

Hepatitis B Immunoglobulin-VF should not be mixed with other pharmaceutical products, except as indicated (see **DOSAGE AND 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.

Passive transfer of antibodies and effect 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.

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).

ADVERSE 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.

DOSAGE AND 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.

OVERDOSAGE

The consequences of overdosage are not known.

PRESENTATION AND STORAGE CONDITIONS

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.

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.

NAME AND ADDRESS OF THE SPONSOR

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

DISTRIBUTED BY

Australian Red Cross Blood Service

POISON SCHEDULE OF THE MEDICINE

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DATE OF THERAPEUTIC GOODS ADMINISTRATION APPROVAL

08 November 2006

DATE OF MOST RECENT AMENDMENT

22 September 2014

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