Product Information

Zoster Immunoglobulin-VF

Australia

NAME OF THE MEDICINE

Human Zoster Immunoglobulin, solution for intramuscular injection.

DESCRIPTION

Zoster 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). It contains not less than 200 IU/vial varicella-zoster antibody.

Zoster Immunoglobulin-VF is manufactured from plasma donated by Australia's voluntary and non-remunerated donors who have recently recovered from shingles or chickenpox. Donations are selected on the basis that they contain high levels of antibodies against *Herpesvirus varicellae*. 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 Zoster Immunoglobulin-VF contains specific steps to reduce the possibility of viral transmission including pasteurisation for viral inactivation and nanofiltration for virus removal.

PHARMACOLOGY

Zoster Immunoglobulin-VF contains high levels of antibodies (mainly IgG) against the varicella-zoster virus.

Zoster Immunoglobulin-VF has been shown to prevent varicella in susceptible contacts of an index case, and has been used successfully to prevent the spread of this infection in high-risk patients. Greatest effectiveness is to be expected when treatment commences within 96 hours of exposure; treatment after 96 hours is of uncertain value. High-risk patients are those with an immune deficiency or who are on immunosuppressive therapy.

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.). These values are consistent with ranges observed with other intramuscular immunoglobulin products.

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

INDICATIONS

Zoster Immunoglobulin-VF is indicated for prophylaxis against varicella in patients who meet all four of the criteria listed below:

1. One of the following underlying illnesses or conditions:
    a. Neoplastic disease (leukaemia or lymphoma).
    b. Congenital or acquired immunodeficiency.
    c. Immunosuppressive therapy with steroids or antimetabolites.

2. One of the following types of exposure to chickenpox or shingles patients:
    a. Household contact.
    b. Playmate contact (>1 hour play indoors).
    c. Hospital contact (in same 2 to 4 bedroom or adjacent beds in a large ward).
    d. Newborn contact (newborn of mother who had onset of chickenpox <5 days before delivery or within 48 hours after delivery).
    e. Premature infant (≥28 weeks gestation) whose mother lacks a prior history of chickenpox.
    f. Premature infant (<28 weeks gestation or ≤1000 g) regardless of maternal history.
3. Negative or unknown prior history of chickenpox.
4. If Zoster Immunoglobulin-VF can be administered within 96 hours after exposure.

Zoster Immunoglobulin-VF, Normal Immunoglobulin-VF (immunoglobulin for intramuscular use) or plasma are of no value in the treatment of established varicella or zoster infection. High levels of circulating antibody do not prevent dissemination of infection.

Zoster Immunoglobulin-VF is not indicated for prophylactic use in immunodeficient children or adults when there is a history of varicella, unless the patient's immunosuppressed status is that which is associated with bone marrow transplantation.

CONTRAINDICATIONS

Zoster 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.

PRECAUTIONS

Zoster 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.

Zoster 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 Zoster 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 medical product for use in human pregnancy or during lactation has not been established in controlled clinical trials. Zoster 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 Zoster 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

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

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 Zoster 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 Zoster 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 Zoster 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 injection site 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).

Angioedema, 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

The following dose schedule is recommended for Zoster Immunoglobulin-VF administration:

Dose of Zoster Immunoglobulin-VF based on body weight		
Weight of patient (kg)	**Dose (IU)**	**No. of vials**
0–10	125	1
10.1–20	250	2
20.1–30	375	2
30.1–40	500	3
over 40	600	3

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.**

Zoster 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.

OVERDOSAGE

The consequences of overdosage are not known.

PRESENTATION AND STORAGE CONDITIONS

Zoster Immunoglobulin-VF solution for intramuscular injection is available in single vials containing 200 IU varicella-zoster 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.

Note: Supplies of suitable plasma for Zoster Immunoglobulin-VF production are scarce. Healthy adults recovering from shingles or chickenpox should be urged to enrol as voluntary blood donors.

NAME AND ADDRESS OF THE SPONSOR

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DISTRIBUTED BY

Australian Red Cross Blood Service

POISON SCHEDULE OF THE MEDICINE

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DATE OF THERAPEUTIC GOODS ADMINISTRATION APPROVAL

07 April 2005

DATE OF MOST RECENT AMENDMENT

22 September 2014

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