Tetanus Immunoglobulin-VF (For Intramuscular Use)

Human Tetanus Immunoglobulin, solution for intramuscular injection

Product Information

Australia

NAME OF THE MEDICINE

Human Tetanus Immunoglobulin, solution for intramuscular injection

DESCRIPTION

Tetanus 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 tetanus antitoxin activity of not less than 100 IU/mL.

Tetanus Immunoglobulin-VF is prepared by Cohn cold-ethanol fractionation of human plasma obtained from voluntary blood donors. Donations are selected on the basis that they contain high levels of specific antibodies against the toxin of *Clostridium tetani*. 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 Tetanus Immunoglobulin-VF contains specific steps to reduce the possibility of viral transmission including pasteurisation for viral inactivation and nanofiltration for virus removal.

PHARMACOLOGY

Tetanus Immunoglobulin-VF contains high levels of antibodies (mainly IgG) against tetanus toxin.

CLINICAL TRIALS

A comparative clinical trial was conducted to investigate the effect of pasteurisation on the *in vivo* behaviour of intra-muscular 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 intra-muscular injection of pasteurised (viral inactivated) or unpasteurised Hepatitis B Immunoglobulin. No significant 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 Tetanus Immunoglobulin-VF has not been conducted.

INDICATIONS

Tetanus Immunoglobulin-VF is indicated for the passive protection of individuals who have sustained a tetanus-prone wound and who have either not been actively immunised against tetanus or whose immunisation history is doubtful. It should also be given to the fully immunised patient with a tetanus-prone wound if more than 10 years have elapsed since the last vaccine dose. In all the above instances, active immunisation with a tetanus vaccine should be commenced at the same time (refer to Table 1) according to current recommendations. Although Tetanus Immunoglobulin-VF and vaccine can be given at the same time, they should be administered in opposite limbs, using separate syringes.

CONTRAINDICATIONS

Tetanus 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

Tetanus Immunoglobulin-VF (for intramuscular use) 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. (Tetanus Immunoglobulin for intravenous use is available when an intravenous product is required).

Tetanus 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-Jacob 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 HIV, hepatitis B and hepatitis C viruses (HBV and HCV), and the non-enveloped viruses, such as hepatitis A (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.

Table 1. Guide to tetanus prophylaxis in wound management (refer to **INDICATIONS**)

History of active immunisation	Type of wound			
	Clean, minor wound		All other wounds	
	Tetanus Vaccine*	Tetanus Immuno-globulin-VF	Tetanus Vaccine*	Tetanus Immuno-globulin-VF
Not immunised or less than 3 doses	Yes	No	Yes	Yes
3 doses or more: < 5 years since last dose	No	No	No	No
5 to 10 years since last dose	No	No	Yes	No
> 10 years since last dose	Yes	No	Yes	Yes

* For children less than 8 years old, use of a combined diphtheria/tetanus/pertussis (DTPa) vaccine is recommended in preference to tetanus vaccine alone. For persons 8 years of age or older use a combined diphtheria/tetanus (dT) vaccine in preference to tetanus vaccine alone.

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 Tetanus 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. Tetanus 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 Tetanus 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
Tetanus 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.

Inactivated vaccines: Inactivated vaccines may be administered concurrently with passive antibody (although in separate syringes) to induce active immunity as is sometimes done for tetanus-prone wounds.

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 Tetanus 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
Good medical care is essential in the prevention of tetanus from fresh wounds. Thorough cleansing and removal of all foreign and necrotic material from the site of injury is important.

The minimum routine prophylactic dose of Tetanus Immunoglobulin-VF (for intramuscular use) for adults or children is 250 IU. The dose should be doubled if the wound is grossly contaminated or if more than 24 hours have elapsed between wounding and the seeking of medical attention.

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**.

Tetanus 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.

An intravenous preparation of tetanus immunoglobulin (Tetanus Immunoglobulin for intravenous use) is available for patients where large doses are indicated (i.e. treatment of tetanus), or when the patient has a significant haemostatic defect which may cause bleeding following intramuscular injection.

OVERDOSAGE
The consequences of overdosage are not known.

PRESENTATION
Tetanus Immunoglobulin-VF solution for intra-muscular injection is available in single vials containing 250 IU human tetanus antitoxin. The actual volume in the vial is stated on the label.

STORAGE CONDITIONS
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.

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Distributed by:
Australian Red Cross Blood Service

POISON SCHEDULE OF THE MEDICINE
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