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CSL Biotherapies

Australian Red Cross BLOOD SERVICE

17 November 2011

Re: Rh(D) Immunoglobulin-VF

As part of CSL Biotherapies' on-going commitment to enhance the utility of plasma-derived therapies fractionated under the Australian Fractionation Agreement, CSL Biotherapies advises that approval has been received from the Therapeutic Goods Administration (TGA) to formulate Rh(D) Immunoglobulin-VF (Human Anti-D Rh_o Immunoglobulin) with 22.5 mg/mL glycine buffer at pH 6.6.

Rh(D) Immunoglobulin-VF has previously been formulated with Normal Immunoglobulin-VF (Normal Human Immunoglobulin 16% formulated with 22.5 mg/mL glycine at pH 6.6). The change to formulate with 22.5 mg/mL glycine buffer will spare approximately 7.5 tonne of plasma equivalent annually from direction to the manufacture of Normal Immunoglobulin-VF as a diluent for Rh(D) Immunoglobulin-VF, for redirection to the manufacture of the intravenous immunoglobulin INTRAGAM® P (Human Normal Immunoglobulin).

The purification process for the product is not altered, the total anti-D Rh_o immunoglobulin content and composition remain unchanged, and the formulation complies with the British and European Pharmacopoeial (BP/EP) monograph for Human Anti-D Rh_o Immunoglobulin.

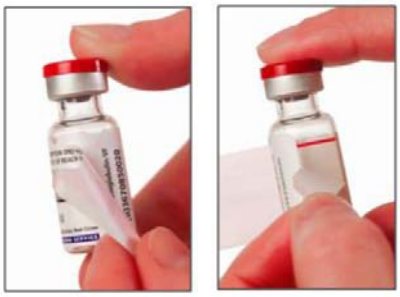
The change to formulate with 22.5 mg/mL glycine buffer results in Rh(D) Immunoglobulin-VF having a lower total immunoglobulin G content and in turn a lower protein concentration (≥10 mg/mL for a 250 IU vial and ≥30 mg/mL for a 625 IU vial)[1]. The efficacy of low protein concentration Rh(D) immunoglobulin preparations has been examined and documented in the literature[2], and the indications for Rh(D) Immunoglobulin-VF are unchanged.

The ARTG numbers for Rh(D) Immunoglobulin-VF are unchanged :

- 250 IU - AUST R 76643
- 625 IU - AUST R 61217.

Rh(D) Immunoglobulin-VF peel-off labels

To facilitate simple record keeping and enhance traceability, the label on each vial of Rh(D) Immunoglobulin-VF retains three peel-off stickers located beneath the outer wraparound label, as introduced recently. Each peel off sticker states the product name and batch number.



The National Blood Authority has now advised CSL Biotherapies to commence manufacture of Rh(D)Immunoglobulin-VF formulated with glycine, and based on current inventory and demand levels CSL Biotherapies anticipates distribution to the Australian Red Cross Blood Service will commence during December 2011 (625 IU presentation) and February 2012 (250 IU presentation).

Minor changes to the product carton and label to align with updated CSL Biotherapies' packaging design guidelines will follow later in 2012.

Yours sincerely,

Dr Elizabeth Campbell
Director, Commercial Operations
Plasma-Derived Therapies

Dr Joanne Pink
Chief Medical Officer
Australian Red Cross Blood Service

Reference:

1) Rh(D) Immunoglobulin-VF approved Product Information. Date of TGA approval: 9 November 2011
2) Bowman JM, Chown B, Pollock J. Low Protein Rh Immunoglobulin (Rh IgG)-Purity, Stability, Activity, and Prophylactic Value. Vox Sang. 1973. 24: 301-316.

Before prescribing, please review the Approved Product Information available on request from CSL Biotherapies

PBS Information: This product is not listed on the PBS. These products are funded under arrangements implemented by the National Blood Authority. Please refer to the National Blood Authority for details

The Medicines Australia Code of Conduct defines standards for the content of materials produced, and the conduct of promotional activities undertaken, by pharmaceutical companies within Australia. As a member of Medicines Australia, CSL Biotherapies willingly complies with the Medicines Australia Code of Conduct (www.medicinesaustralia.com.au).

Minimum Product Information. Rh(D) Immunoglobulin-VF (Human Anti-D Rh_o Immunoglobulin, solution for intramuscular injection) **Indications**: The prevention of Rh sensitisation in Rh(D) negative females at or below child bearing age. **Contraindications:** Individuals who are Rh(D) positive or D^u positive; Rh negative and D^u negative individuals previously sensitised to the Rh(D) antigen; individuals with IgA deficiency, unless they do not have circulating anti-IgA antibodies; individuals with coagulation disorders that would contraindicate intramuscular injections. **Precautions:** Rh(D) Immunoglobulin-VF must not be administered intravenously. It should be given with caution to patients with a history of prior systemic allergic reactions following the administration of human immunoglobulin preparations. Rh(D) Immunoglobulin-VF should not be given to the Rh(D) positive postpartum infant. Safety and/or efficacy has not been established in pregnancy, lactation, the elderly or paediatric patients. Rh(D) Immunoglobulin-VF 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, and by dedicated virus removal and inactivation procedures included in the manufacturing process. Despite these measures, such products may still potentially transmit disease. Vaccination for patients in receipt of medicinal products from human plasma should be considered where appropriate. **Interactions:** Rh(D) Immunoglobulin-VF should not be mixed with other pharmaceutical products, except as indicated. Rh(D) Immunoglobulin-VF may affect responses to live attenuated virus vaccines, and serological testing. Blood typing and antibody testing are affected by the anti-D immunoglobulin administration. Take blood for red cell antibody screening prior to administration. **Adverse Effects:** Local tenderness, erythema and stiffness at the injection site. Mild pyrexia, malaise, drowsiness and urticaria have been occasionally reported after injections of immunoglobulins. Rarely, true allergic reactions, skin lesions, headache, dizziness, nausea, generalised hypersensitivity reactions and convulsions. **Dosage & Administration:** 250 IU after sensitising events during the first trimester of pregnancy; this should be increased to 625 IU for twin and multiple pregnancies. 625 IU after sensitising events beyond the first trimester. If the gestational age is not known with certainty, 625 IU should be given. For mismatched transfusions or large foeto-maternal bleeds (>6mL), 100 IU Rh(D) Immunoglobulin-VF should be administered for each 1.0 mL of Rh(D) positive red cells. For foeto-maternal bleeds up to 6mL of Rh(D) positive red cells, a 625IU dose can be used. The dose should be given as early as possible and within 72 hours of exposure. Rh(D) Immunoglobulin-VF should be given by deep intramuscular injection. Administer large doses > 5 mL in divided doses at different sites. Review approved PI for further details. Contains no antimicrobial agent, use immediately after opening. Based on Rh(D) Immunoglobulin-VF Product Information date of TGA approval: 9 November 2011. (Version 11/11)

Ref. CSL 2295