WinRho® SDF

RH(D) Immune Globulin Intravenous (Human) 
[articled in this document]

DESCRIPTION

WinRho® SDF, Rh(D) Immune Globulin Intravenous (Human) (Rh o(D) IGIV), is a single, freeze-dried preparation of Rehů’s reagent isolated by affinity chromatography from plasma donated by ABO-similar, Rh-negative volunteers who were not exposed to Rh o(D) antigens. WinRho® SDF is prepared from human plasma by an aseptic, virus-inactivation (Creutzfeldt-Jakob disease) procedure. The manufacturing process includes heat inactivation of virus at 60°C for 30 minutes, as well as ultraviolet (UV) light treatment and 2.3×10^12 ergs/cm2 that is effective in inactivating lipid enveloped viruses such as hepatitis B, hepatitis C, and HIV. WinRho® SDF is also inactivated by a 1% formalin solution for 72 hours, which has been validated to be effective in the inactivation of RNA viruses, non-enveloped viruses, and isonitritated RBCs included in the final formulation. WinRho® SDF is not completely inactivated by UV light treatment due to the presence of UV-sensitive transmissible viruses. WinRho® SDF contains anti-Rh o(D) immunoglobulin G (IgG) with a high affinity and capacity for neutralization of RBCs (WinRho® results in Rh o(D) positive RBCs). WinRho® SDF contains approximately 5.0 µg IgA. The product is stabilized with 0.1% p-iodobenzyl alcohol, 0.04 M sodium chloride, and 0.07%/polyethyleneglycol 8000 contains no preservatives.

Treatment of ITP

For use in the suppression of Rh isoimmunization, WinRho® SDF may be administered intramuscularly or intravenously.

PHARMACOKINETICS

In a clinical study involving Rh(D) negative volunteers, two subjects received 120 µg (600 IU) of Rh o(D) IGIV intramuscularly and two subjects received 120 µg (600 IU) of Rh o(D) IGIV intravenously. Peak levels (20-40 ng/ml) were reached within two hours of IV administration and peak levels (16-40 ng/ml) were reached within 24 hours of IM administration. The calculated area under the curve (AUC) for the IM route was 700% higher than for the IV route. The calculated half-life for the IM route was 24 days and the calculated half-life for the IV route was 12 days. The calculated clearance was 19.0 ml/kg/day for the IM route and 4.2 ml/kg/day for the IV route.

INDICATIONS AND CLINICAL USE

Treatment of ITP

WinRho® SDF, Rh(D) immune globulin Intravenous (Human), is recommended for the treatment of non-ITP serum sickness-like eruptions in children with chronic or acute ITP.

Suppression of Rh isoimmunization

For use in the suppression of Rh isoimmunization, WinRho® SDF may be administered either intramuscularly or intravenously.

Pregnancy and Other Obstetric Conditions

WinRho® SDF is recommended for the suppression of Rh isoimmunization in non-anti-Rh(D) negative individuals following exposure to Rh(D) positive RBCs (by intravenous hemolysis in Rhesus (Rh) negative neonates within two days and peak within 2 to 4 days after the transfusion. The duration of response is variable, however, the duration in subjects with minimal Rh sensitization is approximately 38 months. The resolution of Rh(D) sensitization is not complete upon treatment of Rh(D) sensitization and minimal Rh immunization. A second course of WinRho® SDF has been successfully used in patients who had failed to respond to initial treatment with WinRho® SDF. WinRho® SDF is not effective in suppressing Rh sensitization in the presence of Rho(D) incompatibility between mother and fetus. The safety and efficacy of WinRho® SDF have not been established in clinical trials for patients with non-ITP serum sickness-like eruptions, or in patients with splenectomy.

SuPPRIOn OF Rh isoimmunization

WinRho® SDF is effective in suppressing the responses to non-ethrination Rh(D) negative individuals following exposure to Rh(D) positive RBCs (by intravenous hemolysis during delivery of a Rh(D) positive infant). WinRho® SDF has been shown to suppress the immunizing potential of approximately 17-47 mL of RhO(D) positive RBCs. WinRho® SDF administration at a dose of 25 µg/kg (125 IU/kg) on days 1 and 2, 32 patients (84%) responded (platelet count ≥ 100,000/mm3) with a doubling of the baseline. Nineteen of 24 patients responded for an overall response rate of 79%, an average increase in platelet count of 32,000/mm3 (range 5,000 to 85,000) per dose of WinRho® SDF. The t1/2 for anti-Rho(D) was about 24 days following IV administration and about 33 days following IM administration.

CLINICAL PHARMACOLOGY

Transfusion

WinRho® SDF, Rh(D) immune globulin Intravenous (Human), has been shown to increase platelet counts in non-splenectomized Rh(D) negative patients with ITP. Platelet counts usually rise within 2 to 2 days and peak within 1 to 4 days after administration of WinRho® SDF. The criteria for an Rh-incompatible pregnancy requiring administration of WinRho® SDF may be administered either intramuscularly or intravenously.

For use in the suppression of Rh isoimmunization, WinRho® SDF may be administered either

CLINICAL PHARMACOLOGY

Intravenous (Human), administration. Interpretation of direct and indirect antiglobulin tests must be made with caution, as WinRho® SDF contains trace amounts of Rh immune globulin in the IgG fraction, and may result in false-positive reactions. Clinical trials of patients treated with the recommended dose of WinRho® SDF did not show any adverse events associated with therapy. WinRho® SDF was shown to be effective and safe in suppressing Rh sensitization in patients with minimal Rh sensitization, and minimal Rh immunization. No serious adverse events associated with therapy have been reported.

ADVERSE REACTIONS

Treatment of ITP

In a clinical trial involving Rh(D) negative volunteers, two subjects received 120 µg (600 IU) of Rh o(D) IGIV intramuscularly and two subjects received 120 µg (600 IU) of Rh o(D) IGIV intravenously. Peak levels (20-40 ng/ml) were reached within two hours of IV administration and peak levels (16-40 ng/ml) were reached within 24 hours of IM administration. The calculated area under the curve (AUC) for the IM route was 700% higher than for the IV route. The calculated half-life for the IM route was 24 days and the calculated half-life for the IV route was 12 days. The calculated clearance was 19.0 ml/kg/day for the IM route and 4.2 ml/kg/day for the IV route.

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Suppression of Rh Isoimmunization

Adverse reactions to Rh(D) immune globulin (Intraluminal) are infrequent in Rh(D) negative individuals. In the clinical trials, 1% of Rh(D) negative pregnant women, 0% of Rh(D) negative primiparous women, and 2% of Rh(D) negative multiparous women were reported to have experienced Rh(D) sensitization. Delayed and slight swelling at the site of injection and slight tenderness in the injection area have been reported infrequently as adverse reactions. Intraluminal administered by either the intramuscular or intravenous routes has not been associated with anaphylactoid or anaphylactic reactions with WinRho® SDF in individuals with hypersensitivity to blood products. Aseptic reconstitution of the product and dilution with aseptically reconstituted diluent slowly onto the inside wall of the vial and gently swirl until dissolved.

Symptoms and Treatment of Overdose

There are no reports of known overdoses in patients being treated for Rh isoimmunization or ITT in clinical trials. There were no Rh(D) positive women who received more than 300 µg (1500 IU) of Rh(D) IgG. There were no deaths or signs that suggested medical intervention. However, some subjects were associated with a rash, fever, or transient systemic reactions.

Dosage and Administration

Intramuscular injection

WinRho® SDF ( Rh(D) immune globulin Intraluminal) should be reconstituted only with the sterile diluent accompanying the vial of Sterile Diluent (0.8% sodium chloride, 10mM sodium phosphate). It should not be administered concurrently with other products.

Reconstitution

Aseptically reconstitute the product shortly before use with 2.5 mL of Sterile Diluent for 120 µg (600 IU) and 5 mL of Sterile Diluent for 300 µg (1,500 IU). Mix gently. The reconstituted product should be used immediately. Do not shake.

Injection

Parenteral products such as WinRho® SDF should be inspected for particulate matter and discoloration prior to administration. Use the product within 24 hours of reconstitution. Do not use any portion of the reconstituted product after expiration time as stated on the vial. Due to the risk of severe anaphylactic reaction, initial therapy should be administered intramuscularly. Due to the risk of severe anaphylactic reaction, initial therapy should be administered intramuscularly.

Intravenous injection

Aseptically reconstitute the product shortly before use with 2.5 mL of Sterile Diluent for 120 µg (600 IU) and 5 mL of Sterile Diluent for 300 µg (1,500 IU). Mix gently. The reconstituted product should be used immediately. Do not shake.

Reconstitution of WinRho® SDF

Reconstitute with 2.5 mL of Sterile Diluent for 120 µg (600 IU) or 5 mL of Sterile Diluent for 300 µg (1,500 IU).

IN VITRO STUDIES

In vitro studies with WinRho® SDF and WinRho® SDF Immune Globulin Intraluminal demonstrated that the immunosuppressive activity of WinRho® SDF is due to an inhibitory effect on B-lymphocytes, primarily characterised by decreased growth and reduced IL-2 production.

References