

# WinRho SDF™

## NAME OF THE DRUG

**Anti-D (Rh<sub>0</sub>) Immunoglobulin (Human) for injection**  
**600IU (120µg)**  
**Powder for Injection**  
**Passive Immunising Agent**

## DESCRIPTION

**WinRho SDF™**, Anti-D (Rh<sub>0</sub>) Immunoglobulin (Human), is a sterile freeze-dried gamma globulin (IgG) fraction containing antibodies to Rh<sub>0</sub> (D). **WinRho SDF™** is prepared from human plasma by an anion-exchange column chromatography method. Standard measures to minimize a possible transmission of infectious agent, resulting from the use of human plasma-derived products, have been applied during the manufacturing process of **WinRho SDF™**. These measures include selection of the plasma donors and screening of individual donations and pooled plasma for specific markers of viral infections. Additionally, the isolated Anti-D (Rh<sub>0</sub>) fraction eluted from the anion exchange procedure is subjected to solvent detergent treatment for viral inactivation of lipid enveloped viruses and Planova (20N) viral filtration for removal of lipid and some non-lipid enveloped viruses (for details see SPECIAL WARNING).

The product is stabilised with 0.1M glycine, 0.04M sodium chloride, and 0.01 % polysorbate 80. It contains no preservative. The product is reconstituted with the sterile diluent provided. The sterile diluent is a 0.8% Sodium Chloride solution containing sodium phosphate.

## SPECIAL WARNING

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 virus 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 (human immunodeficiency virus), hepatitis B and hepatitis C and West Nile viruses, and the non-enveloped viruses, hepatitis A and human parvovirus B19.

Despite these measures, such products may still potentially transmit disease. There is also the possibility that other 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.

## Pharmacology

### *Pharmacodynamics*

**WinRho SDF<sup>TM</sup>**, Anti-D (Rh<sub>0</sub>) Immunoglobulin (Human), is used to suppress the immune response of non-sensitised Rh<sub>0</sub> (D)-negative individuals who receive Rh<sub>0</sub> (D)-positive blood either by foetomaternal haemorrhage during delivery of an Rh<sub>0</sub> (D)-positive infant, abortion (either spontaneous or induced), following amniocentesis, abdominal trauma or transfusion. Administration of anti-Rh<sub>0</sub> (D) antibody to the Rh<sub>0</sub> (D)-negative mother prevents an immune response with subsequent anti-Rh<sub>0</sub> (D) antibody formation. The exact mechanism of action has yet to be determined.

**WinRho SDF<sup>TM</sup>**, when administered within 72 hours of a full-term delivery of an Rh<sub>0</sub> (D)-positive infant by an Rh<sub>0</sub> (D)-negative mother, will reduce the incidence of Rh alloimmunisation from 12 - 13% to 1 - 2%. The 1 - 2% is, for the most part, due to alloimmunisation during the last trimester of pregnancy. When treatment is given both antenatally at 28 weeks gestation and postpartum the Rh immunization rate drops to about 0.1%.

A clinical study was conducted with ten Rh<sub>0</sub> (D)-negative volunteers. All subjects were administered an IV infusion of Rh<sub>0</sub> (D)-positive foetal red cells. Two days after injection of the red cells, five subjects were given an IM injection of 600IU **Win Rho<sup>®</sup> <sup>TM</sup>** (an earlier formulation of **WinRho SDF<sup>TM</sup>**). Approximately 3mL of foetal red cells were cleared from the circulation of the subjects within eight hours of IV administration of the drug or within 24 hours of IM administration of the drug. None of the subjects had evidence of Rh alloimmunisation either by screening for anti-Rh<sub>0</sub> (D) (two stage papain, indirect Coombs saline and low ionic Autoanalyser techniques) or by challenge of the subjects with Rh<sub>0</sub> (D) foetal cells six months after first clearance of the red cells with **WinRho<sup>®</sup> <sup>TM</sup>**.

The half-life of anti-D is significantly shortened in pregnant women compared to non-pregnant subjects. When only 600IU of drug is administered to pregnant women, passive anti-Rh<sub>0</sub> (D) antibodies are not detectable in the circulation for more than six weeks and therefore a dose of 1,500IU should be used for antenatal administration.

A retrospective survey of **WinRho SDF<sup>TM</sup>** use in Rh-negative pregnant women was conducted. Two hundred and twenty-six at-risk women were included in the survey, 225 of whom delivered an Rh-positive baby; the remaining patient had a spontaneous abortion with the Rh status of the foetus unknown. The women received an antenatal dose of 1,500IU, either at 28-weeks gestation or after a potentially sensitising event, and at 12 week intervals thereafter throughout the

pregnancy, and a post-partum dose of 600IU. There was no seroconversion at delivery versus an expected rate of 4/225 or 1.8% in the absence of effective prophylaxis.

### ***Pharmacokinetics***

There have been no pharmacokinetic studies conducted with **WinRho SDF™**.

In a clinical study with four non-pregnant Rh<sub>0</sub> (D)-negative volunteers, two subjects received 600IU **WinRho®™**, Anti-D (Rh<sub>0</sub>) Immunoglobulin (Human) via an intravenous (IV) route while two subjects were administered this dose via an intramuscular (IM) route. Peak levels of about 40ng/mL were reached within two hours of IV administration while peak levels of about 20ng/mL were reached at 5 - 10 days after IM administration. The calculated Areas Under the Plasma concentration-time Curve (AUC) were the same in this study regardless of the route of administration of drug. The t<sub>1/2</sub> for anti-Rh<sub>0</sub> (D) was about 24 days in this study.

## **INDICATIONS**

WinRho SDF™ is indicated for the prevention of Rh sensitisation in Rh<sub>0</sub> (D)-negative females at or below child bearing age.

## **CONTRAINDICATIONS**

### **Prevention of Rh Immunisation**

When **WinRho SDF™** is used to prevent Rh alloimmunisation, it should not be administered to:

1. Rh<sub>0</sub> (D)-positive individuals including babies
2. Rh<sub>0</sub> (D)-negative women who are Rh immunised as evidenced by standard manual Rh antibody screening tests (after due allowance for previously administered anti-D immunoglobulin)
3. Individuals with a history of anaphylactic or other severe systemic reaction to immunoglobulins.
4. Do not use **WinRho SDF™** in patients who are IgA deficient.

# PRECAUTIONS

## General

As is the case with all drugs of this nature, there is a remote chance of an idiosyncratic or anaphylactoid reaction with **WinRho SDF**<sup>TM</sup> in individuals with hypersensitivity to blood products. In the event of an immediate reaction (anaphylaxis) characterised by collapse, rapid pulse, shallow respiration, pallor, cyanosis, oedema or generalized urticaria, subcutaneous injection of adrenaline hydrochloride 0.3mL 1:1000 aqueous solution should be instituted followed by intravenous administration of hydrocortisone 50 to 100mg if necessary. Individuals known to have had an anaphylactic or severe systemic reaction to human globulin should not receive **WinRho SDF**<sup>TM</sup> or any other Immunoglobulin (Human).

**WinRho SDF**<sup>TM</sup> contains trace quantities of IgA. Individuals deficient in IgA have a potential for development of IgA antibodies and anaphylactic reactions after administration of blood components containing IgA. Therefore, **WinRho SDF**<sup>TM</sup> is contraindicated in these patients.

**WinRho SDF**<sup>TM</sup> is not approved in New Zealand for use in treating patients for Immune Thrombocytopenic Purpura (ITP). Serious adverse events of intravascular haemolysis (IVH) and its complications have been reported following treatment of ITP patients with **WinRho SDF**<sup>TM</sup>. A disproportionate number of IVH cases have been reported in patients with ITP secondary to haematological malignancies such as leukaemia or lymphoma, or active viral infections with HCV, EBV, and HIV. Some of these cases resulted in fatal outcomes. Clinically compromising haemolytic anaemia has the potential of precipitating acute respiratory distress syndrome (ARDS), renal failure or disseminated intravascular coagulation (DIC) in susceptible patients. In patients with predisposing conditions, renal and cardiovascular complications of IVH may occur more frequently in patients of advanced age (age of 65 or greater).

## Interactions with Other Drugs

Administration of **WinRho SDF**<sup>TM</sup> with other drugs has not been evaluated. It is recommended that **WinRho SDF**<sup>TM</sup> be administered separately from other drugs.

*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. By the same token, immunoglobulins should not be administered for at least two weeks after such a vaccine has been given.

## Use in Pregnancy

Animal reproduction studies have not been conducted with **WinRho SDF**<sup>TM</sup>. It is not known whether **WinRho SDF**<sup>TM</sup> can cause foetal harm when administered to a pregnant woman. **WinRho SDF**<sup>TM</sup> should be given to a pregnant woman only if clearly needed.

## Use in Lactation

Immunoglobulins are excreted into breast milk and may contribute to the transfer of protective antibodies to the neonate within the first few days of birth. However, it is not known whether passively administered anti-D (Rh<sub>0</sub>) immunoglobulin is excreted into the milk.

## Carcinogenicity, Mutagenicity and Impairment of Fertility

No mutagenicity, carcinogenicity or reproductive toxicity studies have been conducted with **WinRho SDF**<sup>TM</sup>.

## Effects on Laboratory Tests

In addition to anti-D, **WinRho SDF**<sup>TM</sup> contains trace amounts of anti-A, B, C, and E. These antibodies may be detected by laboratory screening tests.

In the prevention of Rh immunisation, the presence of passively administered Rh antibody in maternal or foetal blood can lead to a positive direct antiglobulin (Coombs) test. In case of doubt as to the individual's Rh group or immune status, **WinRho SDF**<sup>TM</sup> should be administered.

# ADVERSE REACTIONS

The Table below lists adverse reactions from post-marketing experience with **WinRho**<sup>®</sup>/**WinRho SD**<sup>®</sup> in Rh<sub>0</sub> (D)-negative women.

BODY SYSTEM	FREQUENCY	ADVERSE REACTION
<b>Body as a whole</b> <b>Digestive system</b> <b>Musculoskeletal system</b>	Common (≥ 1% and < 10%)	Headache, Chills, Fever, Discomfort and slight swelling at the site of injection Nausea, Vomiting Myalgia
<b>Body as a whole</b> <b>Cardiovascular system</b> <b>Musculoskeletal system</b> <b>Nervous system</b> <b>Skin and appendages</b>	Uncommon (≥ 0.1% and < 1%)	Asthenia, Abdominal or Back Pain, Sweating, Increased LDH Vasodilation Arthralgia Hypotension, Dizziness Pallor
<b>Body as a whole</b> <b>Nervous system</b> <b>Skin and appendages</b>	Rare (≥ 0.01% and < 0.1%)	Anaphylaxis Somnolence Allergic Reactions (erythema, pruritus, rash)

In a clinical study with five healthy Rh<sub>0</sub> (D)-negative male volunteers, Rh<sub>0</sub> (D)-positive foetal red cells were administered by IV infusion and then 1 - 2 days later the foetal red cells were cleared by IV administration of 600IU **WinRho SD**<sup>®</sup>. At 6 - 8 hours after administration of **WinRho SD**<sup>®</sup> to these subjects, there was an elevation in mean levels of granulocytes from 4.25 to 7.88 x 10<sup>9</sup>/L (p < 0.01) and monocytes from 0.38 to 0.64 x 10<sup>9</sup>/L (p < 0.02). Levels of phagocytic leucocytes returned to pretreatment levels by 24 hours after **WinRho SD**<sup>®</sup> treatment. This effect of **WinRho SD**<sup>®</sup> is believed to result from the anti-Rh<sub>0</sub> (D) mediated clearance of Rh<sub>0</sub> (D)-positive foetal red cells as it was not observed at much higher dosages of **WinRho SD**<sup>®</sup> when no Rh<sub>0</sub> (D)-positive red cells were present in the circulation.

Non-anaphylactic reactions are the most common type of reaction to intravenous immunoglobulin, being reported in up to 10% of patients receiving products in this class. The reactions are characterized by back or abdominal pain, nausea or vomiting within the first 30 minutes of the infusion. Usually there is no dyspnoea or other changes in vital signs. Chills, fever, headache, myalgia and fatigue may begin at the end of the infusion and continue for several hours.

## OVERDOSAGE

There are no reports of known overdoses in patients being treated for Rh isoimmunisation.

## DOSAGE AND ADMINISTRATION

Anti-D immunoglobulin may be administered intramuscularly or intravenously. Prophylaxis is effective if anti-D immunoglobulin is given within 72 hours of a sensitising event. The recommended doses for various situations are given in the Table below.

### *Anti-D (Rh<sub>0</sub>) Immunoglobulin (WinRho SDF™) Dose*

<b>Indication</b>	<b>Dose</b>
<i>At 28 weeks gestation</i> in Rh <sub>0</sub> (D)-negative women	1,500IU
<i>During Pregnancy</i> , in Rh <sub>0</sub> (D)-negative women who experience a sensitising event in which there is a risk of foetal blood crossing in to the maternal circulation, unless the blood type of the foetus is confirmed to be Rh <sub>0</sub> (D)-negative. Such events include spontaneous or induced abortion, amniocentesis, chorion villus sampling, ruptured tubal pregnancy, abdominal trauma or transplacental haemorrhage.	< 34 weeks gestation: 1,500IU repeated every 12 weeks ≥ 34 weeks gestation: 600IU For massive foeto-maternal haemorrhage, see During Transfusion.
<i>Post-partum</i> in Rh <sub>0</sub> (D)-negative women who deliver Rh <sub>0</sub> (D)-positive babies or Rh status of the baby is unknown	600IU
<i>Post-abortion</i> , in Rh <sub>0</sub> (D)-negative women, unless the blood type of the foetus is confirmed to be Rh <sub>0</sub> (D)-negative	600IU
<i>During transfusion</i> , in Rh <sub>0</sub> (D)-negative females at or below child-bearing age who are transfused with Rh <sub>0</sub> (D)-positive red blood cells or blood components containing red blood cells, provided the transfused blood represents less than 20% of total circulating red cells.	If exposed to Rh <sub>0</sub> (D)-positive whole blood: 45IU/mL blood IV or 60IU/mL blood IM If exposed to Rh <sub>0</sub> (D)-positive red blood cells: 90IU/mL cells IV or 120IU/mL cells IM Max 3,000IU q8h IV and 6,000IU q12h IM

## Reconstitution

**WinRho SDF™** should be reconstituted only with the accompanying vial of sterile diluent. Use aseptic technique throughout.

1. Before reconstitution allow the vial of **WinRho SDF™** and vial of sterile diluent, to reach a temperature between 20°C and 30°C.
2. Reconstitute shortly before use.
3. Remove caps from the Diluent and product vials.
4. Wipe exposed central portion of the rubber stopper with suitable disinfectant.
5. Withdraw Diluent using a suitable syringe and needle. Use 1.25 to 2.5mL of sterile diluent for intravenous injection or 1.25mL for intramuscular injection for 600IU (see table below). Discard unused portion.
6. Inject Diluent slowly at an angle so that the liquid is directed onto the inside wall of the vial containing the freeze dried pellet.
7. Wet pellet by gently tilting and inverting the vial. Avoid frothing. Gently swirl vial upright until dissolved (less than ten minutes).

### Reconstitution of WinRho SDF™

Vial Size	Volume of Diluent to be Added to Vial	Nominal Concentration per mL
<i>Intravenous Injection</i>		
600IU	1.25mL - 2.5mL	480IU/mL - 240IU/mL
<i>Intramuscular Injection</i>		
600IU	1.25mL	480IU/mL

## Injection

Inspect the product for particulate matter and discoloration prior to injection.

*Intravenous.* Inject into a suitable vein at a rate of 1,500IU over 5 to 15 seconds.

*Intramuscular.* Inject into the deltoid muscle of the upper arm or the anterolateral aspect of the upper thigh.

**WinRho SDF™** is **FOR SINGLE USE ONLY**. Discard any unused portion appropriately. If the product is not used immediately following reconstitution, it can be stored at room temperature for up to 12 hours.

## PRESENTATION

**WinRho SDF™** is available in a single dose vial containing 600IU of anti-Rh<sub>0</sub> (D). Each single pack contains one single dose vial of product and one single dose vial of diluent, sterile non-pyrogenic for reconstitution of **WinRho SDF™**.

## STORAGE

Store **WinRho SDF™**, Anti-D (Rh<sub>0</sub>) Immunoglobulin (Human) at 2 - 8°C. Do not freeze. Do not use after expiration date. Discard any unused portion. Protect from light.

## MEDICINE CLASSIFICATION

Prescription Medicine.

## NAME AND ADDRESS

### Manufacturer

Cangene Corporation  
Winnipeg, Canada R3T 5Y3

### Sponsor

#### *New Zealand*

Baxter Healthcare Ltd  
33 Vestey Drive  
Mt Wellington  
Auckland 1060

#### *Australia*

Baxter Healthcare Pty Ltd  
1 Baxter Drive  
Old Toongabbie  
NSW 2146

## **DATE OF PREPARATION**

10 June 2010.

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*Based on Australian PI approved 29 June 2000, most recent amendment 6 May 2010.*

*Product Monograph 15 February 2010*