

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use WinRho® SDF safely and effectively. See full prescribing information for WinRho® SDF.

WinRho® SDF [Rh<sub>0</sub>(D) Immune Globulin Intravenous (Human)]  
Solution For Intravenous or Intramuscular Injection  
Initial U.S. Approval: 1995

### WARNING: INTRAVASCULAR HEMOLYSIS (IVH) IN IMMUNE THROMBOCYTOPENIC PURPURA (ITP)

See full prescribing information for complete boxed warning. This warning does not apply to Rh<sub>0</sub>(D)-negative patients treated for the suppression of Rh isoimmunization.

- Intravascular hemolysis (IVH) leading to death has been reported in patients treated for ITP with WinRho® SDF.
- IVH can lead to clinically compromising anemia and multi-system organ failure including acute respiratory distress syndrome (ARDS)
- Serious complications including severe anemia, acute renal insufficiency, renal failure and disseminated intravascular coagulation (DIC) have also been reported.
- Closely monitor patients treated with WinRho® SDF for ITP in a healthcare setting for at least eight hours after administration (5.2.1). Perform dipstick urinalysis to monitor for hematuria and hemoglobinuria at baseline and 2 hours, 4 hours and prior to the end of the monitoring period. Alert patients and monitor the signs and symptoms of IVH including back pain, shaking chills, fever, and discolored urine or hematuria. Absence of these signs and/or symptoms of IVH within eight hours do not indicate IVH cannot occur subsequently. Perform post-treatment laboratory tests if signs and/or symptoms of IVH are present or suspected after WinRho® SDF administration (5.2.1).

### INDICATIONS AND USAGE

WinRho® SDF is a Rh<sub>0</sub>(D) Immune Globulin Intravenous (Human) indicated for: Immune Thrombocytopenic Purpura (ITP) (1.1)

Raising platelet counts in Rh<sub>0</sub>(D) positive, non-splenectomized:

- children with chronic or acute ITP,
- adults with chronic ITP and
- children and adults with ITP secondary to HIV infection

### Suppression of Rhesus (Rh) Isoimmunization (1.2)

- Pregnancy and other obstetric conditions in non-sensitized, Rh<sub>0</sub>(D)-negative women with an Rh-incompatible pregnancy including:
  - Routine antepartum and postpartum Rh prophylaxis
  - Rh prophylaxis in obstetric complications or invasive procedures
- Incompatible transfusions in Rh<sub>0</sub>(D)-negative individuals transfused with blood components containing Rh<sub>0</sub>(D)-positive red blood cells (RBCs).

### DOSAGE AND ADMINISTRATION

#### ITP (2.2)

##### Intravenous administration only

- Recommended dose: 250 international unit/kg (50mcg/kg) body weight, given as a single injection over 3 to 5 minutes.

##### Suppression of Rh Isoimmunization (2.3)

##### Intravenous or intramuscular administration

- Pregnancy and other obstetric conditions
  - Rh-incompatible pregnancy: 1500 international unit (300 mcg) at 28 weeks gestation followed by 600 international unit (120 mcg) within 72 hours of delivery of a Rh<sub>0</sub>(D)-positive baby
  - Threatened abortion at any time: 1500 international unit (300 mcg) immediately
  - Amniocentesis and chorionic villus sampling before 34 weeks gestation: 1500 international unit (300 mcg) immediately following the procedure

- Abortion, amniocentesis, or any other manipulation after 34 weeks gestation: 600 international unit (120 mcg) within 72 hours
- Incompatible blood transfusions or massive fetal hemorrhage:
  - IV administration of 90 international unit (18 mcg) per 1 mL transfused RBC or per 2 mL transfused whole blood within 72 hours of exposure

### DOSAGE FORMS AND STRENGTHS

WinRho® SDF is a ready to use solution in single dose vials of 600 international unit (120 mcg), 1,500 international unit (300 mcg), 2,500 international unit (500 mcg), 5,000 international unit (1000 mcg) and 15,000 international unit (3,000 mcg).

### CONTRAINDICATIONS

- Patients with known anaphylactic or severe hypersensitivity responses to human immune globulin products.
- IgA-deficient patients with antibodies against IgA.
- Patients with a history of autoimmune hemolytic anemia, with pre-existing hemolysis or at high risk for hemolysis.
- Infants for the suppression of Rh<sub>0</sub>(D) isoimmunization.

### WARNINGS AND PRECAUTIONS

#### Both Indications (5.1)

- IgA deficient patients with known antibodies to IgA are at greater risk of developing severe hypersensitivity and anaphylactic reactions. (5.1.1)
- Risk of transmission of infectious agents: e.g., viruses and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent, from human plasma. (5.1.2)
- Interference with non-glucose-specific blood monitoring systems may result in elevated glucose readings that lead to untreated hypoglycemia or inappropriate insulin administration. (5.1.3)
- Monitor renal function, including blood urea nitrogen, serum creatinine, and urine output in patients at risk of developing acute renal failure. (5.1.4)
- Monitor patients with known risk factors for thrombotic events; consider baseline assessment of blood viscosity for those at risk of hyperviscosity. (5.1.5)
- Passive transfer of antibodies may confound serologic testing. (5.1.6)
- Monitor patients for pulmonary adverse reactions (transfusion-related acute lung injury [TRALI]). (5.1.7)

#### ITP (5.2)

- Risk of intravascular hemolysis (IVH) and its complications following administration of WinRho® SDF. (5.2.1)
- Hemolytic anemia can develop subsequent to WinRho® SDF therapy. Monitor patients for hemolysis and haemolytic anemia. (5.2.2)

#### Suppression of Rh Isoimmunization (5.3)

- Do not administer to the newborn infant.

### ADVERSE REACTIONS

The most common adverse reactions occurring in ≤ 2% of doses are headache, chills, fever, asthenia, pallor, diarrhea, nausea, vomiting, arthralgia, myalgia, dizziness, malaise, hyperkinesia, abdominal or back pain, hypotension, hypertension, increased LDH, somnolence, vasodilation, pruritus, rash and sweating. (6.1)

Serious adverse reactions, such as IVH, clinically compromising anemia, acute renal insufficiency and DIC have been observed in patients receiving WinRho® SDF for treatment of ITP. Some of these cases resulted in fatal outcome. (6.2)

To report SUSPECTED ADVERSE REACTIONS, contact Cangene Corporation at 1-800-768-2304 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

### DRUG INTERACTIONS

Immunoglobulin administration may transiently interfere with the immune response to live virus vaccines, such as measles, mumps and rubella. (7.1)

### USE IN SPECIFIC POPULATIONS

#### ITP

- Pregnancy: No human or animal data. Use only if clearly needed. (8.1)  
See 17 for PATIENT COUNSELING INFORMATION

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## FULL PRESCRIBING INFORMATION

### WARNING: INTRAVASCULAR HEMOLYSIS (IVH)

*This warning does not apply to Rh<sub>o</sub>(D)-negative patients treated for the suppression of Rh isoimmunization.*

- **Intravascular hemolysis (IVH) leading to death has been reported in patients treated with WinRho<sup>®</sup> SDF for immune thrombocytopenic purpura (ITP).**
- **IVH can lead to clinically compromising anemia and multi-system organ failure including acute respiratory distress syndrome (ARDS).**
- **Serious complications including severe anemia, acute renal insufficiency, renal failure and disseminated intravascular coagulation (DIC) have also been reported.**
- **Closely monitor patients treated with WinRho<sup>®</sup> SDF for ITP in a healthcare setting for at least eight hours after administration. A dipstick urinalysis to monitor for hematuria and hemoglobinuria is to be performed at baseline and then after administration at 2 hours, 4 hours and prior to the end of the monitoring period. Alert patients and monitor the signs and symptoms of IVH including back pain, shaking chills, fever, and discolored urine or hemoglobinuria. Absence of these signs and/or symptoms of IVH within eight hours do not indicate IVH cannot occur subsequently. If signs and/or symptoms of IVH are present or suspected after WinRho<sup>®</sup> SDF administration, post-treatment laboratory tests should be performed including plasma hemoglobin, haptoglobin, LDH, and plasma bilirubin (direct and indirect).**

## 1 INDICATIONS AND USAGE

WinRho<sup>®</sup> SDF is an Rh<sub>o</sub>(D) Immune Globulin Intravenous (Human) (anti-D) product that is indicated for the treatment of ITP in Rh<sub>o</sub>(D)-positive patients and for the suppression of Rh isoimmunization in non-sensitized Rh<sub>o</sub>(D)-negative patients.

### 1.1 Treatment of ITP

WinRho<sup>®</sup> SDF is indicated for use in clinical situations requiring an increase in platelet count to prevent excessive hemorrhage in the treatment of non-splenectomized, Rh<sub>o</sub>(D)-positive

- children with chronic or acute ITP,
- adults with chronic ITP, or
- children and adults with ITP secondary to HIV infection

The safety and efficacy of WinRho<sup>®</sup> SDF have not been evaluated in clinical trials for patients with non-ITP causes of thrombocytopenia or in previously splenectomized patients or in patients who are Rh<sub>o</sub>(D)-negative.

### 1.2 Suppression of Rh Isoimmunization

#### Pregnancy and Other Obstetric Conditions

WinRho<sup>®</sup> SDF is indicated for the suppression of Rh isoimmunization in non-sensitized, Rh<sub>o</sub>(D)-negative (D-negative) women with an Rh-incompatible pregnancy, including:

- Routine antepartum and postpartum Rh prophylaxis
- Rh prophylaxis in cases of:
  - Obstetric complication (e.g., miscarriage, abortion, threatened abortion, ectopic pregnancy or hydatidiform mole, transplacental hemorrhage resulting from antepartum hemorrhage)
  - Invasive procedures during pregnancy (e.g., amniocentesis, chorionic biopsy) or obstetric manipulative procedures (e.g., external version, abdominal trauma)

An Rh-incompatible pregnancy is assumed if the fetus/baby is either Rh<sub>o</sub>(D)-positive or Rh<sub>o</sub>(D)-unknown or if the father is either Rh<sub>o</sub>(D)-positive or Rh<sub>o</sub>(D)-unknown.

### Incompatible Transfusions

WinRho<sup>®</sup> SDF is indicated for the suppression of Rh isoimmunization in Rh<sub>o</sub>(D)-negative individuals transfused with Rh<sub>o</sub>(D)-positive red blood cells (RBCs) or blood components containing Rh<sub>o</sub>(D)-positive RBCs.

WinRho<sup>®</sup> SDF is not indicated for use as immunoglobulin replacement therapy for immune globulin deficiency syndromes.

## 2 DOSAGE AND ADMINISTRATION

### 2.1 Preparation and Handling

- Bring WinRho<sup>®</sup> SDF to room temperature prior to use.
- Inspect WinRho<sup>®</sup> SDF for particulate matter and discoloration prior to administration. Do not use if the solution is cloudy or contains particulates.
- WinRho<sup>®</sup> SDF is for single use only. Discard any unused portion.
- The solution is ready to use, no reconstitution required. See Table 1 for the target fill volumes for each of the dosage sizes for WinRho<sup>®</sup> SDF.

**Table 1 Liquid WinRho<sup>®</sup> SDF Dosage size and target fill volumes**

Vial Size	Target Fill Volume
600 international unit (120 mcg)	0.5 mL
1,500 international unit (300 mcg)	1.3 mL
2,500 international unit (500 mcg)	2.2 mL
5,000 international unit (1,000 mcg)	4.4 mL
15,000 international unit (3,000 mcg)	13.0 mL

**Note:** Remove the entire contents of the vial to obtain the labelled dosage of WinRho<sup>®</sup> SDF. If partial vials are required for dosage calculation, withdraw the entire contents of the vial to

ensure accurate calculation of the dosage requirement. For ease in withdrawing the contents of the vial, draw back the plunger of a sterile syringe (with the needle and needle cover in place) to admit air into the syringe. Depress the plunger of the syringe to inject air into the vial. Invert vial and aspirate contents of vial into syringe.

## 2.2 Treatment of ITP

**ADMINISTER WinRho<sup>®</sup> SDF BY THE INTRAVENOUS ROUTE ONLY** (*see [Preparation and Handling \[2.1\]](#)*). **Do not administer intramuscularly.**

- Administer the entire dose of WinRho<sup>®</sup> SDF into a suitable vein over three to five minutes.
- Administer WinRho<sup>®</sup> SDF separately from other drugs.
- If dilution of WinRho SDF is preferred prior to intravenous administration, use normal saline as diluent. Do not use Dextrose (5%) in water (D5W). No other diluents have been tested.

*Initial Dosing:* An initial dose of 250 international unit/kg (50 mcg/kg) body weight, given as a single injection is recommended for the treatment of ITP. The initial dose may be administered in two divided doses given on separate days, if desired. If the patient has a hemoglobin level less than 10 g/dL, a reduced dose of 125 to 200 international unit/kg (25 to 40 mcg/kg) should be given to minimize the risk of increasing the severity of anemia in the patient. All patients should be monitored to determine clinical response by assessing platelet counts, RBCs, hemoglobin (Hgb), and reticulocyte levels [see [Warnings and Precautions \(5.2\)](#)].

*Subsequent Dosing:* If subsequent therapy is required to elevate platelet counts, an intravenous dose of 125 to 300 international unit/kg (25 to 60 mcg/kg) body weight of WinRho<sup>®</sup> SDF is recommended. The frequency of dosing and the dose used in maintenance therapy should be determined by the patient's clinical response by assessing platelet counts, RBCs, Hgb, and reticulocyte levels.

If a patient responded to initial dose with a satisfactory increase in platelets, maintenance dose at 125 to 300 international unit/kg (25 to 60 mcg/kg), individualized based on platelet and Hgb levels. An international consensus report on the investigation and management of primary immune thrombocytopenia states that treatment is rarely indicated in patients with platelet counts above  $50 \times 10^9/L$  and this has been generally accepted as the threshold for satisfactory response.<sup>1</sup> Evaluate whether patient responded with a satisfactory increase in platelets based on the clinical situation and bleeding risks for the individual patient.

If patient did not respond to initial dose, administer a subsequent dose based on Hgb:

If Hgb between 8-10 g/dL, redose between 125 to 200 international unit/kg (25 to 40 mcg/kg).

If Hgb >10 g/dL, redose between 250 to 300 international unit/kg (50 to 60 mcg/kg).

If Hgb < 8 g/dL, alternative treatments should be used.

The following equations are provided to determine the dosage and number of vials needed for the treatment of ITP:

- $\text{weight in lbs}/2.21 = \text{weight in kg}$

- weight in kg X selected international unit (mcg) dosing level = dosage
- dosage / vial size = number of vials needed

Safety and efficacy of WinRho<sup>®</sup> SDF in the treatment of ITP at doses exceeding 300 international unit/kg (60 mcg/kg) has not been established.

## 2.3 Suppression of Rh Isoimmunization

### Intravenous or intramuscular use.

- For intravenous administration, administer WinRho<sup>®</sup> SDF separately from other drugs. WinRho<sup>®</sup> SDF should be administered at a rate of 2 mL per 5 to 15 seconds.
- For intramuscular administration, administer into the deltoid muscle of the upper arm or the anterolateral aspects of the upper thigh. Due to the risk of sciatic nerve injury, avoid the gluteal region. If the gluteal region is used, use only the upper, outer quadrant.

### Pregnancy and other Obstetric Indications

Table 2 provides dosing guidelines based on the condition being treated.

**Table 2      Obstetric Indications and Recommended Dose**

Indication	Timing of Administration	Dose (Administer IM or IV)
<b><i>Rh-incompatible Pregnancy:</i></b>		
Routine antepartum prophylaxis	28 weeks gestation*	1,500 international unit (300 mcg)
Postpartum (if newborn is Rh <sub>0</sub> (D)-positive)	Within 72 hours of birth**	600 international unit (120 mcg)
<b><i>Obstetric Conditions:</i></b>		
Threatened abortion at any time	Immediately	1,500 international unit (300 mcg)
Amniocentesis and chorionic villus sampling before 34 weeks gestation	Immediately after procedure†	1,500 international unit (300 mcg)
Abortion, amniocentesis, or any other manipulation after 34 weeks gestation	Within 72 hours	600 international unit (120 mcg)
<p>* If WinRho<sup>®</sup> SDF is administered early in the pregnancy, it is recommended that WinRho<sup>®</sup> SDF be administered at 12-week intervals in order to maintain adequate levels of passively acquired anti-Rh.</p> <p>** In the event that the Rh status of the baby is not known at 72 hours, WinRho<sup>®</sup> SDF should be administered to the mother at 72 hours after delivery. If more than 72 hours have elapsed, WinRho<sup>®</sup> SDF should not be withheld but administered as soon as possible up to 28 days after delivery.</p> <p>† Repeat every 12 weeks during pregnancy</p>		

### Incompatible Transfusion

Administer WinRho<sup>®</sup> SDF within 72 hours after exposure for treatment of incompatible blood transfusions or massive fetal hemorrhage.

Table 3 provides dosing guidelines based on the condition being treated.

**Table 3 Transfusion Indication and Recommended Dose**

Route of Administration	Rate of Administration	WinRho <sup>®</sup> SDF Dose	
		If exposed to Rh <sub>o</sub> (D)-Positive Whole Blood:	If exposed to Rh <sub>o</sub> (D)-Positive Red Blood Cells:
Intravenous	3,000 international unit (600 mcg) <b>every 8 hours</b>	45 international unit (9 mcg)/mL blood	90 international unit (18 mcg)/mL cells
Intramuscular	6,000 international unit (1,200 mcg) <b>every 12 hours</b>	60 international unit (12 mcg)/mL blood	120 international unit (24 mcg)/mL cells

### 3 DOSAGE FORMS AND STRENGTHS

WinRho<sup>®</sup> SDF, Rh<sub>o</sub>(D) Immune Globulin Intravenous (Human), is available as a ready to use solution for injection available in single dose vials of 600 international unit (120 mcg), 1,500 international unit (300 mcg), 2,500 international unit (500 mcg), 5,000 international unit (1000 mcg) and 15,000 international unit (3,000 mcg).

### 4 CONTRAINDICATIONS

WinRho<sup>®</sup> SDF is contraindicated in:

- Patients who have had known anaphylactic or severe systemic reaction to the administration of human immune globulin products.
- IgA deficient patients with antibodies to IgA and a history of hypersensitivity.
- Patients with autoimmune hemolytic anemia, with pre-existing hemolysis or at high risk for hemolysis.
- Infants for the suppression of Rh<sub>o</sub>(D) isoimmunization.

### 5 WARNINGS AND PRECAUTIONS

#### 5.1 Both Indications

##### 5.1.1 Hypersensitivity

Severe hypersensitivity reactions may occur [[see Contraindications \(4\)](#)]. If symptoms of allergic or early signs of hypersensitivity reactions (including generalized urticaria, tightness of the chest, wheezing, hypotension, and anaphylaxis) occur, discontinue WinRho<sup>®</sup> SDF infusion immediately and institute appropriate treatment. Have medications such as epinephrine available for immediate treatment of acute hypersensitivity reactions.

WinRho<sup>®</sup> SDF contains approximately 5 micrograms/mL IgA [[see Description \(11\)](#)]. Patients with known antibodies to IgA have a greater risk of developing potentially severe hypersensitivity and anaphylactic reactions. WinRho<sup>®</sup> SDF is contraindicated in patients with antibodies against IgA and a history of hypersensitivity reaction [[see Contraindications \(4\)](#)].

### **5.1.2 Transmissible Infectious Agents**

Because WinRho<sup>®</sup> SDF is made from human plasma; it may carry a risk of transmitting infectious agents, e.g., viruses and theoretically, the Creutzfeldt-Jakob disease (CJD) agent. The risk of transmitting an infectious agent has been reduced by screening plasma donors for prior exposure to certain pathogens, testing for the presence of certain current viral infections, and including virus inactivation/removal steps in the manufacturing process [[see Description \(11\)](#)].

Report all infections thought to have been transmitted by WinRho<sup>®</sup> SDF to Cangene Corporation at 1-800-768-2304. The physician should discuss the risks and benefits of this product with the patient.

### **5.1.3 Interference with Blood Glucose Testing: False High Blood Glucose Levels**

The liquid formulation of WinRho<sup>®</sup> SDF contains maltose. Maltose in IGIV products has been shown to give falsely high blood glucose levels in certain types of blood glucose testing systems [for example, by systems based on glucose dehydrogenase pyrroloquinolinequinone (GDH-PQQ) or glucose-dye-oxidoreductase methods]. Due to the potential for falsely elevated glucose readings, only use testing systems that are glucose-specific to test or monitor blood glucose levels in patients receiving maltose-containing parenteral products, including WinRho<sup>®</sup> SDF Liquid.

Carefully review the product information of the blood glucose testing system, including that of the test strips, to determine if the system is appropriate for use with maltose-containing parenteral products. If any uncertainty exists, contact the manufacturer of the testing system to determine if the system is appropriate for use with maltose-containing parenteral products.

### **5.1.4 Renal Dysfunction/Failure**

Acute renal dysfunction/failure, osmotic nephropathy, and death may occur upon use of Immune Globulin Intravenous (IGIV) products, including WinRho<sup>®</sup> SDF.<sup>2</sup> Ensure that patients are not volume depleted before administering WinRho<sup>®</sup> SDF. For patients at risk of renal dysfunction or failure, including those with any degree of pre-existing renal insufficiency, diabetes mellitus, advanced age (above 65 years of age), volume depletion, sepsis, paraproteinemia, or receiving known nephrotoxic drugs, administer WinRho<sup>®</sup> SDF at the minimum infusion rate practicable.

Assess renal function, including measurement of blood urea nitrogen (BUN) and serum creatinine, before the initial infusion of WinRho<sup>®</sup> SDF.

### **5.1.5 Thromboembolic Events**

Thromboembolic events may occur during or following treatment with WinRho<sup>®</sup> SDF and other IGIV products.<sup>3,4</sup> Patients at risk include those with a history of atherosclerosis, multiple cardiovascular risk factors, advanced age, impaired cardiac output, coagulation disorders, prolonged periods of immobilization, and/or known/suspected hyperviscosity.



Consider baseline assessment of blood viscosity in patients at risk for hyperviscosity including those with cryoglobulins, fasting chylomicronemia/markedly high triacylglycerols (triglycerides), or monoclonal gammopathies. For patients who are at risk of developing thromboembolic events, administer WinRho<sup>®</sup> SDF at the minimum rate of infusion practicable.

### **5.1.6 Interference with Serological Testing**

After administration of WinRho<sup>®</sup> SDF, a transitory increase of various passively transferred antibodies in the patient's blood may yield positive serological testing results, with the potential for misleading interpretation. Passive transmission of antibodies to erythrocyte antigens (e.g., A, B, C and E) and other blood group antibodies [for example, anti Duffy, anti Kidd (anti JKa) antibodies]<sup>5</sup> may cause a positive direct or indirect (Coombs') test.

A large fetomaternal hemorrhage late in pregnancy or following delivery may cause a weak mixed field positive D<sup>u</sup> test result. Assess such an individual for a large fetomaternal hemorrhage and adjust the dose of WinRho<sup>®</sup> SDF accordingly. The presence of passively administered anti Rh<sub>0</sub>(D) in maternal or fetal blood can lead to a positive direct Coombs' test. If there is an uncertainty about the father's Rh group or immune status, administer WinRho<sup>®</sup> SDF to the mother.

### **5.1.7 Transfusion-Related Acute Lung Injury (TRALI)**

Non-cardiogenic pulmonary edema may occur in patients following IGIV treatment, including WinRho<sup>®</sup> SDF.<sup>6</sup> TRALI is characterized by severe respiratory distress, pulmonary edema, hypoxemia, normal left ventricular function, and fever. Symptoms typically appear within 1 to 6 hours following administration of blood products.

Monitor patients for pulmonary adverse reaction. If TRALI is suspected, perform appropriate tests for the presence of anti-neutrophil antibodies and anti-HLA antibodies in both the product and patient serum. TRALI may be managed using oxygen therapy with adequate ventilatory support.

### **5.1.8 Monitoring: Laboratory Tests**

- For all ITP patients, blood type, blood count, reticulocyte count, DAT and dipstick urinalysis are recommended before deciding to treat patients with WinRho<sup>®</sup> SDF. In patients with evidence of hemolysis (reticulocytosis greater than 3%), or patients at risk of hemolysis (positive DAT not attributed to previous immune globulin administration) use other treatments.<sup>1</sup>
- Closely monitor patients administered WinRho<sup>®</sup> SDF for at least 8 hours post administration and perform a dipstick urinalysis to monitor for hematuria and hemoglobinuria at baseline and then after administration at 2 hours, 4 hours and prior to the end of the monitoring period.
- If signs and/or symptoms of IVH and its complications are present after anti-D administration, perform appropriate confirmatory laboratory testing including, but not

limited to, CBC (i.e. hemoglobin, platelet counts), haptoglobin, plasma hemoglobin, urine dipstick, assessment of renal function (i.e. BUN, serum creatinine), liver function (i.e. LDH, direct and indirect bilirubin) and DIC specific tests such as D-dimer or Fibrin Degradation Products (FDP) or Fibrin Split Products (FSP).

- Periodic monitoring of renal function and urine output in patients who are at increased risk of developing acute renal failure [[see Warnings and Precautions \(5.1.4\)](#)]. Assess renal function in these at-risk patients, including measurement of BUN and serum creatinine, before the initial infusion of WinRho<sup>®</sup> SDF and at appropriate intervals thereafter.
- If TRALI is suspected in ITP patients, perform appropriate tests for the presence of anti-neutrophil antibodies in both the product and patient serum [[see Warnings and Precautions \(5.1.7\)](#)].

## 5.2 Treatment of ITP

### 5.2.1 Intravascular Hemolysis (IVH)

IVH leading to death has been reported in patients treated for ITP with WinRho<sup>®</sup> SDF.

IVH can lead to clinically compromising anemia and multi-system organ failure including acute respiratory distress syndrome (ARDS).

Serious complications including severe anemia, acute renal insufficiency, renal failure and disseminated intravascular coagulation (DIC) have also been reported.<sup>7,8</sup>

Closely monitor patients treated with WinRho<sup>®</sup> SDF for ITP in a healthcare setting for at least eight hours after administration. Perform a dipstick urinalysis to monitor for hematuria and hemoglobinuria at baseline and then after administration at 2 hours, 4 hours and prior to the end of the monitoring period. Alert patients and monitor for signs and symptoms of IVH including back pain, shaking chills, fever, and discolored urine or hemoglobinuria. Absence of these signs and/or symptoms of IVH within eight hours do not indicate IVH cannot occur subsequently. If signs and/or symptoms of IVH are present or if IVH is suspected after WinRho<sup>®</sup> SDF administration, perform post-treatment laboratory tests including plasma hemoglobin, haptoglobin, LDH, and plasma bilirubin (direct and indirect).

### 5.2.2 Hemolysis

Although the mechanism of action of WinRho<sup>®</sup> SDF in the treatment of ITP is not completely understood it is postulated that anti-D binds to the Rh<sub>o</sub>(D) RBC resulting in formation of antibody-coated RBC complexes. Immune-mediated clearance of the antibody-coated RBC complexes would spare the antibody-coated platelets because of the preferential destruction of antibody-coated RBC complexes by the macrophages located in the reticuloendothelial system.<sup>9-11</sup> The side effect of this action is a decrease in hemoglobin levels (extravascular hemolysis).<sup>7</sup> The pooled data from ITP clinical studies demonstrated a mean decrease from baseline in hemoglobin levels of 1.2 g/dL within 7 days after administration of WinRho<sup>®</sup> SDF.

If the patient has lower than normal hemoglobin levels (less than 10 g/dL), a reduced dose of 125 to 200 international unit/kg (25 to 40 mcg/kg) should be given to minimize the risk of increasing the severity of anemia in the patient. Alternative treatments should be used in patients with hemoglobin levels that are less than 8 g/dL due to the risk of increasing the severity of the anemia [[see Dosage and Administration \(2.2\)](#)].

Significant anemia may present with pallor, hypotension, or tachycardia while acute renal insufficiency may present with oliguria or anuria, edema and dyspnea. Patients with IVH who develop DIC may exhibit signs and symptoms of increased bruising and prolongation of bleeding time and clotting time which may be difficult to detect in the ITP population. Consequently the diagnosis of this serious complication of IVH is dependent on laboratory testing [[see Warnings and Precautions \(5.1.7\)](#)]. Previous uneventful administration of WinRho<sup>®</sup> SDF does not preclude the possibility of an occurrence of IVH and its complications following any subsequent administration of WinRho<sup>®</sup> SDF. Have confirmatory laboratory testing on ITP patients presenting with signs and/or symptoms of IVH and its complications after anti-D administration [[see Warnings and Precautions \(5.1.7\)](#)].

If ITP patients are to be transfused, use Rh<sub>0</sub>(D)-negative red blood cells (PRBCs) so as not to exacerbate ongoing hemolysis.

### 5.3 Suppression of Rh Isoimmunization

Do not administer WinRho<sup>®</sup> SDF to Rh<sub>0</sub>(D)-negative individuals who are Rh immunized as evidenced by an indirect antiglobulin (Coombs') test revealing the presence of anti-Rh<sub>0</sub>(D) (anti-D) antibody. For postpartum use following an Rh-incompatible pregnancy administer WinRho<sup>®</sup> SDF to the mother only. Do not administer to the newborn infant.

## 6 ADVERSE REACTIONS

Serious adverse reactions, some of these cases resulted in fatal outcome, have been observed in patients receiving WinRho<sup>®</sup> SDF for the treatment of ITP. These include: intravascular hemolysis (IVH), clinically compromising anemia, acute renal insufficiency and DIC [[see Adverse Reactions, \(6.2\)](#)].

The most common adverse reactions observed for **all** indications are: headache, chills, fever, asthenia, pallor, diarrhea, nausea, vomiting, arthralgia, myalgia, dizziness, hyperkinesia, abdominal or back pain, hypotension, hypertension, increased LDH, somnolence, vasodilation, pruritus, rash and sweating. All adverse reactions listed occurred in ≤ 2% of WinRho<sup>®</sup> doses administered in clinical trials.

Adverse reactions observed in the use of WinRho<sup>®</sup> SDF for Suppression of Rh Isoimmunization are <0.1% in Rh<sub>0</sub>(D)-negative individuals.

### 6.1 Clinical Trials Experiences

*Because clinical studies are conducted under different protocols and widely varying conditions, adverse reaction rates observed in the clinical trials of a specific drug product*

cannot be directly compared to rates in clinical trials of another drug, and may not reflect rates observed in practice.

### Treatment of ITP

The safety of WinRho SDF was evaluated in clinical trials (n=161) in children and adults with acute and chronic ITP and adults and children with ITP secondary to HIV. Overall, 417 adverse events were reported by 91 patients (57%). The most common adverse events were headache (14% of the patients), fever (11% of the patients) and asthenia (11% of the patients). A total of 117 adverse drug reactions were reported by 46 patients (29%). Headache, chills, and fever were the most common related adverse events (Table 4). With respect to safety profile per administration, 60/848 (7%) of WinRho<sup>®</sup> infusions had at least one adverse reaction. The most common adverse reactions were headache (19 infusions; 2%), chills (14 infusions; < 2%), and fever (nine infusions; 1%).

**Table 4 Adverse Drug Reactions with an Incidence  $\geq$ 5% of Patients**

Body System	Adverse Event	All Studies	Children	Adults
		# of Patients (%)		
Body as a Whole	Headache	18 (11)	8 (11)	10 (12)
	Chills	13 (8)	4 (5)	9 (10)
	Fever	9 (6)	5 (7)	4 (5)
	Asthenia	6 (4)	2 (3)	4 (5)
	Infection	4 (3)	4 (5)	0 (0)
Nervous System	Dizziness	6 (4)	2 (3)	4 (5)

In four clinical trials of patients treated with the recommended initial intravenous dose of 250 international unit/kg (50 mcg/kg), the mean maximum decrease in hemoglobin was 1.70 g/dL (range: +0.40 to -6.1 g/dL). At a reduced dose, ranging from 125 to 200 international unit/kg (25 to 40 mcg/kg), the mean maximum decrease in hemoglobin was 0.81 g/dL (range: +0.65 to -1.9 g/dL). Only 5/137 (3.7%) of patients had a maximum decrease in hemoglobin of greater than 4 g/dL (range: -4.2 to -6.1 g/dL).

### Suppression of Rh Isoimmunization

In the clinical trial of 1,186 Rh<sub>0</sub>(D)-negative pregnant women, no adverse reactions were reported to Rh<sub>0</sub>(D) IGIV.

## 6.2 Post-marketing Experience

*Because post-marketing adverse reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to product exposure. The following adverse reactions have been identified during the post-approval use of WinRho<sup>®</sup> SDF.*

### Treatment of ITP

These adverse reactions are classified by system organ class.

**Intravascular hemolysis (IVH) leading to death has been reported in patients treated with WinRho<sup>®</sup> SDF for immune thrombocytopenic purpura (ITP).**

**Serious complications including severe anemia, acute renal insufficiency, renal failure and disseminated intravascular coagulation (DIC) have also been reported.**

**Infusion Reactions:** Anaphylactic reaction, Hypersensitivity

**Hematologic:** Intravascular hemolysis, Disseminated Intravascular Coagulation, Hemoglobinemia

**Cardiac:** Cardiac arrest, Cardiac failure, Myocardial infarction, Tachycardia

**Gastrointestinal:** Nausea

**General:** Chest pain, Fatigue, Edema

**Hepatologic:** Jaundice

**Musculoskeletal:** Myalgia, Muscle spasm, Pain in extremities

**Renal:** Renal failure, Renal impairment, Anuria, Chromaturia, Hemoglobinuria, Hematuria

**Respiratory:** Acute respiratory distress syndrome, Transfusion related acute lung injury

**Integumentary:** Hyperhidrosis

### **Suppression of Rh Isoimmunization**

**Infusion Reactions:** Hypersensitivity, anaphylactic reaction, induration, pruritus or swelling at injection site

**Integumentary:** Pruritus, Rash

Healthcare professionals should report serious adverse reactions following the administration of WinRho<sup>®</sup> SDF to Cangene Corporation at 1-800-768-2304 or FDA's MedWatch reporting system by phone (1-800-FDA-1088).

## **7 DRUG INTERACTIONS**

### **7.1 Live Virus Vaccines**

Administration of WinRho<sup>®</sup> SDF concomitantly with other drugs has not been evaluated. Passive transfer of antibodies may transiently impair the immune response to live attenuated virus vaccines such as measles, mumps, rubella, and varicella ([see Patient Counseling Information \[17.1\]](#)). Do not give immunization with live vaccines within 3 months after WinRho<sup>®</sup> SDF administration.

## **8 USE IN SPECIFIC POPULATIONS**

### **8.1 Pregnancy**

Pregnancy category C. Animal reproduction studies have not been conducted with WinRho<sup>®</sup> SDF. It is also not known whether WinRho<sup>®</sup> SDF can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. WinRho<sup>®</sup> SDF should be given to a pregnant woman only if clearly needed.

#### Treatment of ITP

WinRho<sup>®</sup> SDF has not been evaluated in pregnant women with ITP.

#### Suppression of Rh Isoimmunization

The available evidence suggests that WinRho<sup>®</sup> SDF does not harm the fetus or affect future pregnancies or reproduction capacity when given to pregnant Rh<sub>0</sub>(D)-negative women for suppression of Rh isoimmunization.<sup>12</sup>

### **8.3 Nursing Mothers**

#### Treatment of ITP

WinRho<sup>®</sup> SDF has not been evaluated in nursing mothers with ITP.

#### Suppression of Rh Isoimmunization

It is not known whether WinRho<sup>®</sup> SDF is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when WinRho SDF is administered to nursing women.

### **8.4 Pediatric Use**

The safety and effectiveness of WinRho<sup>®</sup> has been evaluated for the treatment of chronic or acute ITP in children and in children (<16 years of age) with ITP secondary to HIV infection [[see Adverse Reactions \(6.2\)](#)]. The dosing recommendation in the treatment of children with ITP is the same as in adults [[see Dosage and Administration \(2.2\)](#)],

### **8.5 Geriatric Use**

Clinical studies of WinRho<sup>®</sup> did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Post marketing clinical experience suggests that patients of advanced age (age over 65) with co-morbid conditions including but not limited to cardio-respiratory decompensation, renal failure or insufficiency or prothrombotic conditions are at increased risk of developing serious complications from acute hemolytic reactions such as IVH. Patients receiving doses in excess of 300 international unit/kg of WinRho<sup>®</sup> SDF may also be at an increased risk of developing increased hemolysis. Fatal outcomes associated with IVH and its complications have occurred most frequently in patients of advanced age (age over 65) with co-morbid conditions.

Use caution in dose selection for geriatric patients with consideration given to starting at the low end of the dosing range reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

## **10 OVERDOSAGE**

## Treatment of ITP and Suppression of Rh Isoimmunization

In post-marketing spontaneous reporting, there has been a limited number of medication error reports related to dosage calculations in which higher doses than that recommended for WinRho<sup>®</sup> SDF were administered (doses > 60 mcg/kg). Signs and laboratory findings of overdosage in Rh positive (ITP) patients have included hemoglobin decreases in excess of 1.2 g/dL. For the suppression of Rh isoimmunization, hemolytic reactions have been reported in cases of mis-matched blood transfusions where very large doses of WinRho SDF were administered.

In one ITP case report that involved an overdose due to confusion between mcg and international unit, a patient with significant co-morbidities developed IVH and had a fatal outcome. In the event of overdose, monitor patients closely for signs and symptoms of hemolysis and initiate symptomatic and supportive treatment.

## 11 DESCRIPTION

WinRho<sup>®</sup> SDF is a sterile, liquid gamma globulin (IgG) fraction containing antibodies to the Rh<sub>0</sub>(D) antigen (D antigen). WinRho<sup>®</sup> SDF is to be administered intravenously for the treatment of ITP and either intravenously or intramuscularly for the suppression of Rh isoimmunization.

WinRho<sup>®</sup> SDF is prepared from human plasma by an anion-exchange column chromatography method. The manufacturing process includes two steps implemented specifically for viral clearance. The solvent detergent treatment step (using tri-n-butyl phosphate and Triton<sup>®</sup> X-100) is effective in inactivating lipid enveloped viruses such as hepatitis B, hepatitis C, and HIV. Virus filtration, using a Planova<sup>™</sup> 20N virus filter is effective in the removal of some non-lipid enveloped viruses. These two processes are designed to increase product safety by reducing the risk of transmission of enveloped and non-enveloped viruses, respectively. In addition to the two specific steps, the anion-exchange chromatography step contributes to the removal of small non-lipid enveloped viruses.

The inactivation and reduction of known enveloped and non-enveloped model viruses were validated in laboratory studies as summarized in Table 5.

**Table 5 – Virus Reduction Values Obtained Through Validation Studies**

Enveloped	Enveloped			Non-Enveloped			
	RNA		DNA	RNA		DNA	
Virus	HIV-1	BVDV	PRV	HAV	EMC	MMV	PPV
Family	retro	flavi	herpes	picorna		parvo	
Size (nm)	80-100	50-70	120-200	25-30	30	20-25	18-24
Anion Exchange Chromatography (partitioning)	Not evaluated			2.3	n.e.	3.4	n.e.
20N Filtration	≥ 4.7	≥ 3.5	≥ 5.6*	n.e.	4.8	n.e.	4.1

(size exclusion)							
Solvent/Detergent (inactivation)	≥ 4.7	≥ 7.3	≥ 5.5	Not evaluated			
<b>Total Reduction (log<sub>10</sub>)</b>	<b>≥ 9.4</b>	<b>≥ 10.8</b>	<b>≥ 11.1</b>	<b>7.1</b>		<b>7.5</b>	

\* The PRV was retained by the 0.1 µm pre-filter during the virus validation. Since manufacturing employs a 0.1 µm pre-filter before the 20N filter, the claim of ≥5.6 reduction is considered applicable.

Abbreviations:

HIV-1: human immunodeficiency virus-1; relevant virus for human immunodeficiency virus-1 and model for HIV-2.

BVDV: bovine viral diarrhea virus; model virus for hepatitis C virus (HCV) and West Nile virus (WNV)

PRV: pseudorabies virus; model for large enveloped DNA viruses, including herpes

HAV: human hepatitis A virus; relevant virus for HAV and model for small non-enveloped viruses in general

EMC: encephalomyocarditis virus; model for HAV and for small non-enveloped viruses in general

MMV: murine minute virus; model for human parvovirus B19 and for small non-enveloped viruses in general

PPV: porcine parvovirus; model for human parvovirus B19 and for small non-enveloped viruses in general

n.e.: not evaluated

The product potency is expressed in international units by comparison to the World Health Organization (WHO) standard. In the past, a full dose of Rh<sub>0</sub>(D) Immune Globulin (Human) has traditionally been referred to as a “300 microgram” dose. Potency and dosing recommendations are now expressed in international units by comparison to the WHO anti-Rh<sub>0</sub>(D) standard. The conversion of “microgram” to “international units” is: 1 microgram = 5 international units. A 1,500 international unit (300 microgram [mcg]) vial contains sufficient anti-Rh<sub>0</sub>(D) to effectively suppress the immunizing potential of approximately 17 mL of Rh<sub>0</sub>(D) (D-positive) RBCs.

The liquid formulation is stabilized with 10% maltose and 0.03% polysorbate 80. There are no preservatives in the formulation. WinRho<sup>®</sup> SDF does not contain mercury. This product contains approximately 5 micrograms/mL IgA.

## 12 CLINICAL PHARMACOLOGY

### 12.1 Mechanism of Action

#### Treatment of ITP

WinRho<sup>®</sup> SDF has been shown to increase platelet counts in non-splenectomized, Rh<sub>0</sub>(D)-positive patients with ITP. Platelet counts usually rise within one to two days and peak within seven to 14 days after initiation of therapy. The mechanism of action is not completely understood, but is thought to be due to the formation of anti-Rh<sub>0</sub>(D)-coated RBC complexes, which are preferentially removed by the reticuloendothelial system, particularly the spleen. This results in Fc receptor blockade, thus sparing antibody-coated platelets.<sup>9,10</sup>

#### Suppression of Rh Isoimmunization

The mechanism by which Rh<sub>0</sub>(D) immune globulin suppresses immunization to Rh<sub>0</sub>(D)-positive RBCs is not completely understood.



WinRho<sup>®</sup> SDF when administered within 72 hours of a full-term delivery of a Rh<sub>o</sub>(D)-positive infant by a Rh<sub>o</sub>(D) negative mother will reduce the incidence of Rh isoimmunization from 12-13% to 1-2%. The 1-2% is, for the most part, due to isoimmunization 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%.<sup>13,14</sup>

When 600 international unit (120 mcg) of WinRho<sup>®</sup> SDF is administered to pregnant women, passive anti-Rh<sub>o</sub>(D) antibodies are not detectable in the circulation for more than six weeks and therefore a dose of 1,500 international unit (300 mcg) should be used for antenatal administration.

## **12.2 Pharmacodynamics**

In a clinical study with Rh<sub>o</sub>(D)-negative volunteers (nine males and one female), Rh<sub>o</sub>(D)-positive RBCs were completely cleared from the circulation within eight hours of intravenous administration of WinRho. There was no indication of Rh isoimmunization of these subjects at six months after the clearance of the Rh<sub>o</sub>(D)-positive RBCs.

## **12.3 Pharmacokinetics**

### **IM versus IV Administration (Lyophilized Powder)**

In a clinical study involving Rh<sub>o</sub>(D)-negative volunteers, two subjects received 600 international unit (120 mcg) WinRho by intravenous (IV) administration and two subjects received this dose by intramuscular (IM) administration. Peak levels (36 to 48 ng/mL) were reached within two hours of IV administration and peak levels (18 to 19 ng/mL) were reached at five to 10 days after IM administration. Although no statistical comparisons were made, the calculated areas under the curve were comparable for both routes of administration. The  $t_{1/2}$  for anti-Rh<sub>o</sub>(D) was about 24 days following IV administration and about 30 days following IM administration.

### **Lyophilized Powder versus Liquid Formulation**

In two comparative pharmacokinetics studies, 101 volunteers were administered the liquid or lyophilized formulation of WinRho<sup>®</sup> SDF intravenously (n=41) or intramuscularly (n=60). The formulations were bioequivalent following IV administration based on area under the curve to 84 days and had comparable pharmacokinetics following IM administration. The average peak concentrations ( $C_{max}$ ) of anti-Rh<sub>o</sub>(D) for both formulations were comparable following IV or IM administration and occurred within 30 minutes or 2-4 days of administration, respectively. Both formulations also had similar elimination half-lives ( $t_{1/2}$ ) following IV or IM administration.

## **14 CLINICAL STUDIES**

### **14.1 Treatment of ITP**

Efficacy was documented in four subgroups of patients with ITP:

#### Childhood Chronic ITP

In an open-label, single arm, multicenter study, 24 non-splenectomized, Rh<sub>o</sub>(D)-positive children with ITP of greater than six months duration were treated initially with 250 international unit/kg (50 mcg/kg) WinRho [125 international unit/kg (25 mcg/kg) on days 1 and 2, with subsequent doses ranging from 125 to 275 international unit/kg (25 to 55 mcg/kg)]. Response was defined as a platelet increase to at least 50,000/mm<sup>3</sup> and a doubling of the baseline. Nineteen of 24 patients responded for an overall response rate of 79%, an overall mean peak platelet count of 229,400/mm<sup>3</sup> (range 43,300 to 456,000), and a mean duration of response of 36.5 days (range 6 to 84).<sup>15</sup>

#### Childhood Acute ITP

A multicenter, randomized, controlled trial comparing WinRho to high dose and low dose Immune Globulin Intravenous (Human) (IGIV) and prednisone was conducted in 146 non-splenectomized, Rh<sub>o</sub>(D)-positive children with acute ITP and platelet counts less than 20,000/mm<sup>3</sup>. Of 38 patients receiving WinRho [125 international unit/kg (25 mcg/kg) on days 1 and 2], 32 patients (84%) responded (platelet count  $\geq$  50,000/mm<sup>3</sup>) with a mean peak platelet count of 319,500/mm<sup>3</sup> (range 61,000 to 892,000), with no statistically significant differences compared to other treatment arms. The mean times to achieving  $\geq$  20,000/mm<sup>3</sup> or  $\geq$  50,000/mm<sup>3</sup> platelets for patients receiving WinRho were 1.9 and 2.8 days respectively. When comparing the different therapies for time to platelet count  $\geq$  20,000/mm<sup>3</sup> or  $\geq$  50,000/mm<sup>3</sup>, no statistically significant differences among treatment groups were detected, with a range of 1.3 to 1.9 days and 2.0 to 3.2 days, for IGIV and prednisone respectively.<sup>16,17</sup>

#### Adult Chronic ITP

Twenty-four non-splenectomized Rh<sub>o</sub>(D)-positive adults with ITP of greater than six months duration and platelet counts  $<$  30,000/mm<sup>3</sup> or requiring therapy were enrolled in a single-arm, open-label trial were treated with 100 to 375 international unit/kg (20 to 75 mcg/kg) WinRho [mean dose 231 international unit/kg (46.2 mcg/kg)]. Twenty-one of 24 patients responded (increase  $\geq$  20,000/mm<sup>3</sup>) during the first two courses of therapy for an overall response rate of 88% with a mean peak platelet count of 92,300/mm<sup>3</sup> (range 8,000 to 229,000).<sup>18,19</sup>

#### ITP Secondary to HIV Infection

Eleven children and 52 adults, who were non-splenectomized and Rh<sub>o</sub>(D)-positive, with all Walter Reed classes of HIV infection and ITP, with initial platelet counts of  $\leq$  30,000/mm<sup>3</sup> or requiring therapy, were treated with 100 to 375 international unit/kg (20 to 75 mcg/kg) WinRho in an open label trial. WinRho was administered for an average of 7.3 courses (range 1 to 57) over a mean period of 407 days (range 6 to 1,952). Fifty-seven of 63 patients responded (increase  $\geq$  20,000/mm<sup>3</sup>) during the first six courses of therapy for an overall response rate of 90%. The overall mean change in platelet count for six courses was 60,900/mm<sup>3</sup> (range -2,000 to 565,000), and the mean peak platelet count was 81,700/mm<sup>3</sup> (range 16,000 to 593,000).<sup>18-20</sup>

## **14.2 Suppression of Rh Isoimmunization**

A study was conducted in 1,186 non-sensitized, Rh<sub>o</sub>(D)-negative pregnant women in cases in which the blood types of the fathers were Rh<sub>o</sub>(D)-positive or unknown. WinRho was administered according to one of three regimens: 1) 93 women received 600 international unit (120 mcg) at 28 weeks; 2) 131 women received 1200 international unit (240 mcg) each

at 28 and 34 weeks; 3) 962 women received 1200 international unit (240 mcg) at 28 weeks. All women received a postnatal administration of 600 international unit (120 mcg) if the newborn was found to be Rh<sub>o</sub>(D)-positive. Of 1,186 women who received antenatal WinRho, 806 were given WinRho postnatal following the delivery of a Rh<sub>o</sub>(D)-positive infant, of which 325 women underwent testing at six months after delivery for evidence of Rh isoimmunization. Of these 325 women, 23 would have been expected to display signs of Rh isoimmunization, however, none was observed ( $p < 0.001$  in a Chi-square test of significance of difference between observed and expected isoimmunization in the absence of WinRho).

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## 16 HOW SUPPLIED/STORAGE AND HANDLING

- Store at 2 to 8°C (36 to 46°F)
- Do not freeze
- Do not use after expiration date

WinRho<sup>®</sup> SDF is available in packages containing:

### Liquid

NDC Number	Product Description
53270-3120-1	A single dose vial of 600 international unit (120 mcg) anti-Rh <sub>o</sub> (D) IGIV
53270-3300-1	A single dose vial of 1,500 international unit (300 mcg) anti-Rh <sub>o</sub> (D) IGIV
53270-3500-1	A single dose vial of 2,500 international unit (500 mcg) anti-Rh <sub>o</sub> (D) IGIV
53270-3100-1	A single dose vial of 5,000 international unit (1,000 mcg) anti-Rh <sub>o</sub> (D) IGIV
53270-3000-1	A single dose vial of 15,000 international unit (3,000 mcg) anti-Rh <sub>o</sub> (D) IGIV

## 17 PATIENT COUNSELING INFORMATION

### Information for Patients

#### See FDA-Approved Patient Labeling

- **ITP and Suppression of Rh Isoimmunization**
  - Inform patients of the early signs of hypersensitivity reactions to WinRho<sup>®</sup> SDF including hives, generalized urticaria, chest tightness, wheezing, hypotension, and anaphylaxis.
  - Advise patients to notify their physicians if they experience any of the above symptoms.
- **Blood Glucose Monitoring**
  - Advise patients that the maltose contained in WinRho<sup>®</sup> SDF can interfere with some types of blood glucose monitoring systems.
  - Advise patients to use only testing systems that are glucose specific for monitoring blood glucose levels as the interference of maltose could result in falsely elevated glucose readings. This could lead to untreated hypoglycemia or to inappropriate insulin administration, resulting in life-threatening hypoglycemia.
- **Transmittable Infectious Agents**
  - Inform patients that WinRho<sup>®</sup> SDF is prepared from human plasma and may contain infectious agents (e.g., viruses and, theoretically, the CJD agent) 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 viruses, by testing for the presence of current virus infections, and by inactivating and/or removing certain viruses during manufacturing.
  - Advise patients to report any symptoms that concern them and that may be related to viral infections.
- **Live Virus Vaccines**
  - Advise patients that WinRho<sup>®</sup> SDF may impair the effectiveness of certain live virus vaccines (e.g., measles, rubella, mumps, and varicella).
  - Instruct patients to notify their treating physician of this potential interaction when they are receiving vaccinations.
- **Immune Thrombocytopenic Purpura (ITP)**
  - Instruct patients being treated with WinRho<sup>®</sup> SDF for ITP to **immediately report** symptoms of intravascular hemolysis including back pain, shaking chills, fever, discolored urine, decreased urine output, sudden weight gain, fluid retention/edema, and/or shortness of breath to their physicians.
  - Prior to discharge, instruct patients to continue to self-monitor for the signs and symptoms of IVH over 72 hours, especially for discoloration of urine, and to seek

medical attention immediately in the event that signs/symptoms of IVH occur following WinRho<sup>®</sup> SDF administration.

- **Laboratory Tests**

- Assess renal function in patients judged to be at an increased risk of developing acute renal failure, including measurement of BUN and serum creatinine, before the initial infusion of WinRho<sup>®</sup> SDF.

## **17.1 FDA Approved Patient Labeling – (Patient Prescribing Information)**

### **WinRho<sup>®</sup> SDF**

[pronounced win – row –S-D-F]

You should read this leaflet carefully each time before you are scheduled to receive a treatment for your Immune Thrombocytopenic Purpura (ITP) with WinRho<sup>®</sup> SDF. This letter is a summary of the important information you need to know about your medicine, and does not take the place of talking with your doctor and does not contain all of the information available about WinRho<sup>®</sup> SDF. If you have any questions after reading this leaflet, make sure you ask your doctor or nurse.

#### **1. What is the most important information I should know about WinRho<sup>®</sup> SDF?**

Some patients taking WinRho<sup>®</sup> SDF for immune thrombocytopenic purpura (ITP) have had severe, life threatening bleeding and clotting problems. For this reason, you need to remain under observation for at least 8 hours following each treatment with WinRho<sup>®</sup> SDF and your doctor will ask you to take blood and urine tests before and after infusion with WinRho<sup>®</sup> SDF.

Some patients taking WinRho<sup>®</sup> SDF have had problems with their kidneys and other organs.

Problems usually occur within 4 to 8 hours after getting an infusion. Tell your doctor or healthcare provider right away if you have any of the following signs or symptoms after getting a WinRho<sup>®</sup> SDF infusion:

- back pain
- shaking
- chills
- fever
- dark or oddly colored urine
- decreased urination
- swelling or sudden weight gain
- shortness of breath
- rash
- dizziness

Continue monitoring for these signs and symptoms for 72 hours after each treatment with WinRho<sup>®</sup> SDF.

WinRho<sup>®</sup> SDF contains maltose, which can give false readings on some glucose testing meters. If you are diabetic, ask your doctor what types of glucose testing meters can be used safely while you are getting WinRho<sup>®</sup> SDF.

## **2. What is WinRho<sup>®</sup> SDF?**

WinRho<sup>®</sup> SDF is a protein product, called an “immune globulin,” which is made from human plasma. It has antibodies to the “D” antigen that people with “Rh-positive” blood have in their blood.

WinRho<sup>®</sup> SDF is used to increase the number of platelets in the blood of Rh-positive people who have a problem called immune thrombocytopenic purpura (ITP). People with ITP bruise and bleed easily because they have a very low number of platelets in their blood.

WinRho<sup>®</sup> SDF is also used to treat Rh-negative girls and women who need a blood transfusion using Rh-positive blood and/or are carrying an Rh-positive baby.

## **3. Who should not use WinRho<sup>®</sup> SDF?**

You should not use WinRho<sup>®</sup> SDF for any treatment if you:

- have ever had a severe allergic reaction (such as trouble breathing, hives, passing out) after getting any blood product or blood product transfusion.
- have an immune globulin A (IgA) deficiency.

You should not use WinRho<sup>®</sup> SDF for treatment of ITP if you:

- have Rh-negative blood.
- have had your spleen removed.
- have a problem called “autoimmune hemolytic anemia.”
- have other pre-existing bleeding problems.

## **4. How will I get WinRho<sup>®</sup> SDF?**

Your doctor will give you WinRho<sup>®</sup> SDF as an injection into your vein. For the treatment of ITP, it will usually take 3 to 5 minutes for an injection. Your doctor will decide if you need one or more injections.

For protection against Rh-positive blood, your doctor may decide to give you WinRho<sup>®</sup> SDF as a shot in your arm or thigh.

## **5. What should I avoid while using WinRho<sup>®</sup> SDF?**

WinRho<sup>®</sup> SDF may interfere with your immune response to routine immunizations. Tell your doctor if you have recently been vaccinated or are planning to be vaccinated.

WinRho<sup>®</sup> SDF can interfere with certain blood tests. It is important to tell the person taking your blood and the doctor that you got WinRho<sup>®</sup> SDF.

## **6. What are the possible or reasonably likely side effects of WinRho<sup>®</sup> SDF?**

The most common side effects of WinRho<sup>®</sup> SDF are

- headache
- chills

- fever
- weakness
- diarrhea
- nausea and vomiting
- achy muscles
- feeling light-headed or dizziness
- fainting
- flushing
- rash
- sweating

Tell your doctor right away if you have:

- a fever over 100°F
- shaking or chills that continue or get worse
- a painful lump or swelling (because this may be a sign of a blood clot)
- bruising that is increasing in diameter (because this may be a sign of a clotting problem)
- oddly colored urine
- trouble urinating
- severe back pain
- severe abdominal pain
- swelling, especially around the ankles
- hives
- shortness of breath

Talk to your doctor about any side effects that concern you.

Additional prescribing information is available to healthcare professionals.

#### **7. What other information do I need to know about WinRho<sup>®</sup> SDF?**

WinRho<sup>®</sup> SDF is made from human plasma. Donors are carefully screened and the plasma is carefully cleaned, but it does have a very small risk of giving you viruses from the donor.

Talk to your doctor if you have any symptoms that concern you.

You may report side effects to Cangene Corporation at 1-800-768-2304 or FDA's MedWatch reporting system by phone (1-800-FDA-1088)

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