WINRHO® SDF

Rh$_0$(D) Immunoglobulin
Intravenous (Human)

Treatment Overview With A Focus on Hypersensitivity Management

SAOL THERAPEUTICS

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Serious Warnings and Precautions

WinRho SDF(Rho(D) Immunoglobulin (Human) for Injection), prepared from pools of human plasma, may contain infectious agents such as viruses. Serious adverse events of intravascular hemolysis (IVH) and its complications have been reported following treatment with WinRho SDF.

A disproportionate number of IVH cases have been reported in patients with ITP secondary to hematological malignancies such as leukemia or lymphoma, or active viral infections with HCV and EBV. Some of these cases resulted in fatal outcome. Clinically compromising hemolytic anemia has the potential of precipitating acute respiratory distress syndrome (ARDS), and hemoglobinuria or hemoglobinemia may precipitate renal failure or DIC in susceptible patients. Patients of advanced age (> 65 years) with underlying cardiac, renal or hepatic co-morbidities are at increased risk of developing serious renal, hepatic or cardiovascular complications if they develop IVH. Physicians are advised that if a patient has evidence of hemolysis (reticulocytosis greater than 3%) or is at high risk for hemolysis (positive DAT not attributed to previous immune globulin administration), alternate therapies must be used. Physicians should discuss the risks and benefits of WinRho SDF and alert patients who are being treated for ITP, about the signs and/or symptoms.

Hypersensitivity reactions can occur in very rare cases of IgA deficiency or hypersensitivity to human globulin.

WinRho 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.

PRODUCT OVERVIEW

WinRho® SDF is a Rho(D) Immunoglobulin (Human) prepared from pools of human plasma and is available as a sterile liquid gamma globulin (IgG) fraction of human plasma containing antibodies to the Rho (D) antigen (D antigen). (1)

WinRho® SDF sterile solution is for injection and available in the following dosage forms:

Route of Administration	Dosage Form/ Strength	Clinically Relevant Nonmedicinal Ingredients[a]
Intravenous or Intramuscular	Solution for Injection: 600 IU (120 µg) 1500 IU (300 µg), 2500 IU (500 µg), 5000 IU (1000 µg), 15000 IU (3000 µg)	Maltose Polysorbate 80 Water for injection

[a]WinRho SDF may contain trace amounts of tri-n-butyl phosphate and octoxynol.

WINRHO® SDF
Rh_0(D) Immunoglobulin
Intravenous (Human)

Indications

PREGNANCY AND OTHER OBSTETRIC CONDITIONS

WinRho SDF, Rho (D) Immunoglobulin (Human) is indicated for the prevention of Rh immunization in Rho (D) negative mothers not previously sensitized to the Rho (D) factor. WinRho SDF is recommended for prevention of Rh immunization of Rho (D) negative women at risk of developing Rh antibodies. Rho (D) Immunoglobulin (Human) prevents the development of Rh antibodies in the Rho (D) negative and previously not sensitized mother carrying a Rho (D) positive fetus, thus preventing the occurrence of hemolytic disease in the fetus or the newborn.

The administration of WinRho SDF to women satisfying the above conditions should be done at about 28-weeks gestation when the child's father is either Rho (D) positive or unknown.

WinRho SDF should be administered within 72 hours after delivery if the baby is Rho (D) positive or unknown.

WinRho SDF administration is also recommended in these same women within 72 hours after spontaneous or induced abortion, amniocentesis, chorion villus sampling, ruptured tubal pregnancy, abdominal trauma or transplacental hemorrhage, unless the blood type of the fetus or father are confirmed to be Rho (D) negative. It should be administered as soon as possible in the case of maternal bleeding due to threatened abortion.

TRANSFUSION

WinRho SDF is recommended to prevent alloimmunization in Rho (D) negative female children and female adults in their child-bearing years transfused with Rho (D) positive RBCs or blood components with Rho (D) positive RBCs. Treatment should only then be carried out (without preceding exchange transfusion), if the transfused Rho (D) positive blood represents less than 20% of the total circulating red cells.

IMMUNE THROMBOCYTOPENIC PURPURA (ITP)

WinRho SDF is recommended in the treatment of destructive thrombocytopenia of an immune etiology in situations where platelet counts must be increased to control bleeding. Clinical studies have shown that the peak platelet counts occur about seven days after IV anti-Rho (D) treatment. The effect is not curative but is transient; platelet counts are usually elevated from several days to several weeks. For individuals with chronic ITP, a maintenance dosage is recommended with the dosage schedule determined on an individual basis.

WinRho SDF is recommended in clinical situations requiring an increase in platelet count to prevent excessive hemorrhage for the treatment of:

1) non-splenectomized Rho (D) positive children with chronic or acute ITP,

2) adults with chronic ITP, or

3) children and adults with ITP secondary to HIV infection.

The safety and efficacy of WinRho has not been evaluated in clinical trials for patients with non-ITP causes of thrombocytopenia or in previously splenectomized patients.

Geriatrics (> 65 years of age):

Differences in response to treatment in those aged 65 or over as compared to younger subjects cannot be determined due to a limited number of study subjects aged 65 or over enrolled in clinical studies with WinRho. Caution should be used when determining the dose for an elderly patient for the treatment of ITP and should take into account the increased frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy associated with advanced age. Doses starting at the low end of the dosing range should be considered when administering WinRho SDF to those aged 65 or older.

Pediatrics (< 16 years of age):

WinRho SDF has been evaluated in children for the treatment of chronic or acute ITP and in children with ITP secondary to HIV infection. The dosing recommendation in the treatment of children with ITP is the same as in adults (1).

WINRHO® SDF
Rh_0(D) Immunoglobulin
Intravenous (Human)

Contraindications

IMPORTANT – PATIENT GROUPS WHERE WINRHO SDF (RHO (D) IMMUNOGLOBULIN [HUMAN]) SHOULD NOT BE ADMINISTERED

WinRho SDF is contraindicated in the following patient groups and should not be administered to patients:

All Indications	• with a history of hypersensitivity, anaphylactic, or other severe systemic reaction to WinRho SDF or other human immune globulin drug products • with IgA deficiencies when the patient has antibodies to IgA or a history of IgA hypersensitivity • with a history of hypersensitivity, anaphylactic, or other severe systemic reaction to any ingredient in this formulation or component of the container
ITP	who are Rho(D) negative • who are splenectomized • with pre-existing hemolysis or at high risk for hemolysis
Prevention of Rh Isoimmunization	• who are Rho(D) positive • who are Rho(D) negative women who are Rh immunized as evidenced by standard Rh antibody screening tests (e.g. indirect antiglobulin test)

Hypersensitivity

Hypersensitivity is a state of altered reactivity in which the body reacts to a foreign agent with an increased immune response and is a pharmaceutical class effect that has been reported with the use of immunoglobulin products, including WinRho SDF (Rho (D) Immunoglobulin [Human]). Hypersensitivity describes the process of interaction between a particular antigen and the body's antibodies or lymphocytes (2).

Based on safety data for WinRho SDF, hypersensitivity has been classified as an important identified risk following use of the anti-D product for all indications. Hypersensitivity is therefore associated with all approved indications for the product and is not dose specific, whereas other complications are dose dependent and are only seen with higher doses, such as those used to treat ITP.

HYPERSENSITIVITY REACTION TYPES

Hypersensitivity reactions fall into one of four reaction types (Types I, II, III and IV), depending on the immune globulin proteins involved. WinRho SDF may lead to the onset of immediate or delayed hypersensitivity reactions (Types I or III, respectively).

Type I reactions (i.e., immediate hypersensitivity reactions) involve IgE-mediated release of histamine and other mediators from mast cells and basophils. Examples of Type I reactions include asthma/wheezing, urticaria (hives), eczema, rhinitis (runny nose) or anaphylaxis.

Type III reactions (i.e., immune-complex reactions) involve circulating antigen-antibody immune complexes (aggregations of antigens, complement proteins, and IgG, IgA and IgM antibodies) that deposit in postcapillary venules, with subsequent complement fixation and the development of an acute inflammatory reaction resulting in tissue damage (3, 4). Type III reactions take a longer time to develop as compared to Type I reactions and it may take 3 to 6 hours to develop. Examples of Type III reaction include skin vasculitic lesions, nephritis and joint pain.

Individuals with hypersensitivity to blood products are at risk of developing an allergic or anaphylactoid reaction following administration of WinRho SDF.

WinRho SDF contains antibodies to the Rho (D) antigen (D antigen) and so can cause a drop-in blood pressure associated with an anaphylactic reaction, even in patients who have tolerated previous treatments with human immune globulin. The drop in blood pressure (called hypotension) is due to the release of several chemicals, such as histamine, tryptase and proteoglycans, from mast cells and/or basophils. (5)

WinRho SDF also contains trace amounts of IgA (less than or equal to 40 µg). Patients with known antibodies to IgA may have greater risk of developing severe hypersensitivity and anaphylactic reactions. (1)

Although WinRho SDF has been used successfully to treat selected IgA deficient individuals, the physician must weigh the potential benefit of treatment with WinRho SDF against the potential for hypersensitivity reactions. Individuals deficient in IgA have a potential for development of IgA antibodies and anaphylactic reactions after administration of blood components containing IgA; Burks et al. (1986) have reported that as little as 15 µg IgA/mL of blood product has elicited an anaphylactic reaction in IgA deficient individuals. Individuals known to have had an anaphylactic or severe systemic reaction to human globulin should not receive WinRho SDF or any other immune globulin (Human).

Anaphylaxis is characterized by life-threatening respiratory distress, hypotension, vascular collapse and shock and accompanied by rapid pulse, shallow respiration, pallor, cyanosis, pruritus and angioedema and/or urticaria.

Clinical Management of Hypersensitivity after Administration of WinRho SDF (Rho (D) Immunoglobulin [Human])

Hypersensitivity reactions can present with a wide variance of symptoms and severity, from very mild or moderate reactions, to life threatening severe reactions.

To minimize the risk of harm to a patient, early identification of reactions and rapid clinical assessment are essential. (6) It is recommended that all patients receiving WinRho SDF are administered the drug in a clinical area where they can be monitored and observed for signs and symptoms of hypersensitivity or an acute allergic reaction.

WinRho SDF should be administered in a setting where appropriate equipment, medication and personnel trained in the management of hypersensitivity, anaphylaxis and shock are available. (1).

SIGNS AND SYMPTOMS

The initial clinical assessment of patients seeks to quickly identify reactions which are serious or life threatening so that treatment and/or resuscitation can be initiated immediately.

Acute reactions can present with a range of signs and symptoms of varying severity.

These include:

- ✓ Fever and related inflammatory symptoms or signs, such as chills, rigours, myalgia, nausea or vomiting
- ✓ Cutaneous symptoms and signs including urticaria (hives), other skin rashes and pruritus
- ✓ Angioedema (localized oedema of the subcutaneous or submucosal tissues), which may be preceded by tingling
- ✓ Respiratory symptoms and signs including dyspnoea, stridor, wheeze and hypoxia
- ✓ Hypotension
- ✓ Pain
- ✓ Severe anxiety or ‘feeling of impending doom’
- ✓ Bleeding diathesis with acute onset

Rapidly developing features of airway, breathing or circulation problems, usually associated with skin and mucosal change would suggest anaphylaxis. (6)

OBSERVATION

The patient's pulse rate, blood pressure, temperature and respiratory rate should be monitored, and abnormal clinical features, such as fever, rashes or angioedema, frequently assessed.

A patient who has experienced a transfusion reaction should be observed directly until the clinical picture has improved. (6)

SEVERE ANAPHYLACTIC REACTIONS

In the event of a severe reaction seek medical attention immediately and discontinue WinRho SDF administration.

Prompt initial treatment is essential in anaphylaxis and delays in recognizing and treating symptoms could be life-threatening and even result in death.

If possible maintain IV access and reposition the patient if in discomfort.

International guidelines and emergency room studies concur that the best treatment option for the initial treatment of anaphylaxis is epinephrine injection. (7)

The following therapies are commonly used and widely accepted emergency procedures, although it is recognized that practice patterns may vary somewhat by country/region.

- Oxygen. Administer oxygen at high flow rates.
- Epinephrine

Absorption and subsequent achievement of maximum plasma concentration after subcutaneous administration is slower and may be significantly delayed with shock. Thus, intramuscular (IM) administration is favored.

- Administer epinephrine by IM injection early to all patients with signs of a systemic reaction, especially hypotension, airway swelling, or definite difficulty breathing.
- Use an IM dose of 0.3 to 0.5 mg (1:1000) repeated every 15 to 20 minutes if there is no clinical improvement.

Administer IV epinephrine if anaphylaxis appears to be severe with immediate life threatening manifestations.

- Use epinephrine (1:10 000) 0.1 mg IV slowly over 5 minutes. Epinephrine may be diluted to a 1:10 000 solution before infusion.
- An IV infusion at rates of 1 to 4 µg/min may prevent the need to repeat epinephrine injections frequently.

Close monitoring is critical because fatal overdose of epinephrine has been reported.

Patients who are taking ß-blockers have increased incidence and severity of anaphylaxis and can develop a paradoxical response to epinephrine. Consider glucagon as well as ipratropium for these patients.

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Additional Therapies

- Aggressive fluid resuscitation. Give isotonic crystalloid (eg. normal saline) if hypotension is present and does not respond rapidly to epinephrine. A rapid infusion of 1 to 2 L or even 4L may be needed initially.
- Antihistamines. Administer antihistamines slowly IV or IM (eg, 25 to 50 mg of diphenhydramine).
- H2 blockers. Administer H2 blockers such as cimetidine (300 mg orally, IM, or IV).
- Inhaled ß-adrenergic agents. Provide inhaled albuterol if bronchospasm is a major feature. Inhaled ipratropium may be especially useful for treatment of bronchospasm in patients receiving P-blockers. Note that some patients treated for near-fatal asthma actually had anaphylaxis, so they received repeated doses of conventional bronchodilators rather than epinephrine.
- Corticosteroids. Infuse high-dose IV corticosteroids (i.e. 200 mg of Hydrocortisone) early in the course of therapy. Beneficial effects are delayed at least 4 to 6 hours. (8)

PREGNANT WOMEN

Pregnant women with anaphylaxis require not only prompt epinephrine treatment but also high-flow supplemental oxygen and positioning on the left side so that the gravid uterus does not compress the Inferior Vena Cava, thus impeding venous return to the heart. The systolic blood pressure should be maintained at or above 90 mm Hg to ensure that placental blood perfusion is adequate. Continuous maternal and fetal monitoring is suggested. Emergency caesarean delivery is sometimes necessary.

Dosing and Administration

Proper care should be taken when calculating the dose of WinRho SDF (Rho (D) Immunoglobulin [Human])to be administered. **A confusion between International Units (IU) and micrograms (µg) of product, or between pounds (lbs) and kilograms (kg) for the patient's body weight could result in either an overdose that could lead to a severe hemolytic reaction or a dose too low to be effective.**

Please refer to the WinRho SDF label for complete information.

ADMINISTRATION

- WinRho SDF is for single use only.
- Bring WinRho SDF to room or body temperature prior to dosing.
- Inspect the product prior to use and do not use if the solution is cloudy or contains particulates.
- Administer WinRho SDF separately from other drugs.
- Aseptically administer the product intravenously in a suitable vein with a rate of injection of 1500 IU (300 µg)/5 to 15 seconds. 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.
- Intramuscular injections are made into the deltoid muscle of the upper arm or the anterolateral aspects of the upper thigh. Due to the risk of sciatic nerve injury, the gluteal region should not be used as a routine injection site. If the gluteal region is used, use only the upper, outer quadrant.
- Discard any unused portion.
- The following table describes the target fill volumes for each of the dosage sizes for WinRho SDF

Vial Size	Target Fill Volume*
600 IU (120 µg)	0.5 mL
1500 IU (300 µg)	1.3 mL
2500 IU (500 µg)	2.2 mL
5000 IU (1,000 µg)	4.4 mL
15 000 IU (3,000 µg)	13.0 mL

*Extractable volumes are confirmed using a 21-gauge needle as per USP General Chapters <1> Injections.

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• Note: The entire contents of the vial should be removed to obtain the labelled dosage of WinRho SDF, Rho (D) Immunoglobulin (Human). If partial vials are required for dosage calculation, then calculation should be based on the target fill volume. 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 content of vial into syringe.

RECOMMENDED DOSE AND DOSE ADJUSTMENT

Prophylaxis of Rh Immunization

Pregnancy and Other Obstetric Conditions

WinRho SDF should be administered by intravenous or intramuscular injection. The below table provides dosing guidelines based on the condition being treated.

Obstetric Indications and Recommended Dose

Indication	Timing of Administration	Dose (Administer IM or IV)
Pregnancy		
Routine antepartum prophylaxis	At Week 28-30 of gestation*	1500 IU (300 µg)
Postpartum prophylaxis (required only if the newborn is Rho(D)-positive or unknown)	Within 72 hours of birth of Rh (D) positive baby**	600 IU (120 µg)
Obstetric Conditions		
Obstetric complications (e.g., miscarriage, abortion, threatened abortion, ectopic pregnancy or hydatidiform mole, transplacental hemorrhage resulting from antepartum hemorrhage)	Within 72 hours of complication	1500 IU (300 µg)
Invasive procedures during pregnancy (e.g., amniocentesis, chorionic biopsy) † or obstetric manipulative procedures (e.g., external version, abdominal trauma)	Within 72 hours of procedure	1500 IU (300 µg)

IU, international units; µg, micrograms

*If WinRho SDF is administered early in the pregnancy, it is recommended that WinRho SDF be administered at 12 week intervals in order to maintain adequate levels of passively acquired anti-Rh.

** In the event that the Rh status of the baby is not known at 72 hours, WinRho SDF should be administered to the mother at 72 hours after delivery. If more than 72 hours have elapsed, WinRho SDF should not be withheld but administered as soon as possible up to 28 days after delivery.

†For amniocentesis and chorionic villus sampling repeat every 12 weeks during pregnancy

Transfusion

WinRho SDF, Rho (D) Immunoglobulin (Human) should be administered for treatment of incompatible blood transfusions or massive fetal hemorrhage as outlined in the table below:

Transfusion Indication and Recommended Dose

Route of Administration	WinRho SDF Dose	
	If exposed to Rho (D) Positive Whole Blood	If exposed to Rho (D) Positive Red Blood Cells
Intravenous	45 IU (9 µg)/mL blood	90 IU (18 µg)/mL of red blood cells
Intramuscular	60 IU (12 µg)/mL blood	120 IU (24 µg)/mL of red blood cells

Administer 3,000 IU (600 µg) every 8 hours **via the intravenous route** until the total dose, calculated from the above table, is administered.

Administer 6,000 IU (1,200 µg) every 12 hours **via the intramuscular route** until the total dose, calculated from the above table, is administered.

Patients receiving an incompatible transfusion and those with ITP, who receive doses of anti-D immunoglobulin exceeding 300 IU/kg (60 µg/kg), are at an increased risk of developing chills, fever and headache as well as a larger hemoglobin decrease and IVH.

Treatment of ITP

For all ITP patients, blood type, blood count, reticulocyte count, DAT and dipstick urinalysis are recommended before deciding to treat patients with WinRho SDF. In patients with evidence of hemolysis or patients at risk of hemolysis, other treatments MUST be used.

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WinRho SDF, Rho (D) Immunoglobulin (Human), must be given by intravenous administration for the treatment of ITP. An intravenous dose of 125 to 300 IU/kg (25 to 60 µg/kg) body weight is recommended for individuals with ITP. **Since WinRho SDF is administered on a weight- based regimen per kilogram (kg), patient weight determination must be taken in kilograms (kg) as inappropriate use of pounds (lbs) will result in significant overdosing of WinRho SDF.**

Safety and efficacy of WinRho SDF in the treatment of ITP at doses exceeding 300 IU/kg (60 µg/kg) has not been evaluated and is not recommended.

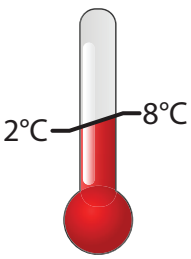
Initial Dosing

After confirming that the patient is Rho (D) positive, an initial dose of 250 IU/kg (50 µg/kg) body weight is recommended for the treatment of ITP. If the patient has a hemoglobin level between 8-10 g/dL, a reduced dose of 125 to 200 IU/kg (25 to 40 µg/kg) should be given to minimize the risk of increasing the severity of anemia in the patient. The initial dose may be administered in two divided doses given on separate days, if desired. In patients with a hemoglobin level less than 8 g/dL, alternative treatments should be used due to the risk of increasing the severity of the anemia.

Subsequent Dosing

If subsequent therapy is required to elevate platelet counts, an intravenous dose of 125 to 300 IU/kg (25 to 60 µg/kg) body weight of WinRho SDF, Rho (D) Immunoglobulin (Human), is recommended. The frequency and dose used should be administered based on the patient's clinical response by assessing platelet counts, red cell counts, hemoglobin, and reticulocyte levels.

Storage and Stability



WinRho SDF, Rho (D) Immunoglobulin (Human) is stable at 2-8°C until the expiry date indicated on the label.

Store WinRho SDF, Rho (D) Immunoglobulin (Human) at 2-8°C.

Do not freeze.

Do not use after expiration date.

Protect from light.

Special Handling Instructions

The product should be brought to room or body temperature immediately prior to use.

WinRho SDF contains no preservatives.

Discard any unused portion.

Do not use solutions that appear cloudy or contain deposits. (1)

Patient Consultation and Screening

Before administering WinRho SDF, Rho (D) Immunoglobulin (Human) to any patient it is important to understand if the patient is a suitable candidate to receive the drug. Healthcare professionals should be aware of the risks associated with WinRho SDF and **always** consult the product label prior to administration.

Patients should be well informed of the drug they are receiving and the potential adverse reactions, particularly hypersensitivity and its associated signs and symptoms, including hives, generalized urticaria, chest tightness, wheezing, hypotension, and anaphylaxis. (1)

Although severe allergic and anaphylactic reactions can present almost immediately, it is not uncommon for signs and symptoms to present at least several hours after administration. Patients should be informed to be aware of any signs and symptoms and instructed to contact their healthcare professional or local emergency department if experiencing any adverse effects.

Important Safety Information for WinRho SDF, Rho (D) Immunoglobulin (Human)

Serious Warnings and Precautions

WinRho SDF, prepared from pools of human plasma, may contain infectious agents such as viruses.

Serious adverse events of intravascular hemolysis (IVH) and its complications have been reported following treatment with WinRho SDF.

A disproportionate number of IVH cases have been reported in patients with ITP secondary to hematological malignancies such as leukemia or lymphoma, or active viral infections with HCV and EBV. Some of these cases resulted in fatal outcome. Clinically compromising hemolytic anemia has the potential of precipitating acute respiratory distress syndrome (ARDS), and hemoglobinuria or hemoglobinemia may precipitate renal failure or DIC in susceptible patients. Patients of advanced age (> 65 years) with underlying cardiac, renal or hepatic co- morbidities are at increased risk of developing serious renal, hepatic or cardiovascular complications if they develop IVH. Physicians are advised that if a patient has evidence of hemolysis (reticulocytosis greater than 3%) or is at high risk for hemolysis (positive DAT not attributed to previous immune globulin administration), alternate therapies must be used. Physicians should discuss the risks and benefits of WinRho SDF and alert patients who are being treated for ITP, about the signs and/or symptoms.

Hypersensitivity reactions can occur in very rare cases of IgA deficiency or hypersensitivity to human globulin.

WinRho 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.

INDICATIONS AND USAGE

- WinRho® SDF is a clear to opalescent sterile liquid containing purified immune globulin G (IgG) fraction of human plasma containing antibodies to Rho (D) antigen
- WinRho® SDF is indicated for the treatment of Immune Thrombocytopenia Purpura (ITP) in Rho(D)-positive patients and prevention of Rh isoimmunization in pregnancy, other obstetric conditions and incompatible transfusions

CONTRAINDICATIONS

WinRho SDF should not be administered to the following patients:

All Indications

- with a history of hypersensitivity, anaphylactic, or other severe systemic reaction to WinRho SDF or other human immune globulin drug products
- with IgA deficiencies when the patient has antibodies to IgA and/or a history of IgA hypersensitivity
- with a history of hypersensitivity, anaphylactic, or other severe systemic reaction to any ingredient in this formulation or component of the container.

ITP

- who are Rho(D) negative
- who are splenectomised
- with autoimmune haemolytic anemia, with pre-existing hemolysis or at high risk for hemolysis

Prevention of Rh Isoimmunization

- who are Rho(D) positive
- who are Rho(D) negative and Rh immunized as evidenced by standard Rh antibody screening tests (e.g. indirect antiglobulin test) in women

SPECIAL WARNINGS AND SPECIAL PRECAUTIONS

- Transfusion-Related Acute Lung Injury (TRALI) typically occurs within 1 to 6 hours after blood or blood product transfusions and may occur in patients receiving immune globulin treatment. TRALI is characterized by severe respiratory distress, non-cardiogenic pulmonary edema or fluid overload, hypoxemia, and fever.
- Monitor for pulmonary adverse reactions. If TRALI is suspected, perform tests for the presence of anti-HLA and anti-neutrophil antibodies in the product and patient serum.
- Thrombosis may occur in patients receiving immune globulin treatment. Consider baseline assessment of blood viscosity in patients at risk for hyperviscosity.

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- Acute renal dysfunction, acute renal failure, osmotic nephropathy, acute tubular necrosis, proximal tubular nephropathy, and death may occur in patients receiving immune globulin treatment, including WinRho SDF. Assess renal function, including measurement of blood urea nitrogen (BUN) and serum creatinine before the initial infusion of WinRho SDF, Rho (D) Immunoglobulin (Human).
- Hypersensitivity reactions may occur with WinRho administration.
- Because WinRho is made from human plasma, it may carry a risk of transmitting blood-borne infectious agents, e.g., viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent, and, theoretically, the Creutzfeld-Jakob disease (CJD) agent.
- WinRho SDF must be administered via the intravenous route for the treatment of ITP as its efficacy has not been established by the intramuscular or subcutaneous routes. Serious adverse events of intravascular hemolysis (IVH) and its complications have been reported following treatment with WinRho SDF. Closely monitor patients for at least 8 hours following treated with WinRho SDF for signs and symptoms of IVH.

DRUG INTERACTIONS

- Immune globulin administration may transiently impair the efficacy of live attenuated vaccines such as measles, rubella, mumps and varicella. Do not give vaccinations with live virus vaccines until approximately three months after administration of WinRho SDF. Revaccinate patients who received WinRho SDF shortly after live virus vaccination three months after the administration of WinRho SDF.
- Interactions with other drugs have not been established. It is recommended that WinRho SDF be administered separately from other drugs.

LABORATORY INTERACTIONS

- The liquid formulation of WinRho SDF contains maltose. Maltose in immune globulin products has been shown to give falsely high blood glucose levels when certain types of blood glucose testing systems. Due to the potential for falsely elevated glucose readings, only testing systems that are glucose-specific should be used to test or monitor blood glucose levels in patients receiving maltose-containing parenteral products, including WinRho SDF.
- Antibodies present in WinRho SDF may also interfere with some serological tests. After administration of immune globulins like WinRho SDF, a transitory increase of passively transferred antibodies in the patient's blood may result in positive results in serological testing (e.g. Coombs' test).

ADVERSE REACTIONS

- The most serious adverse reactions have been observed in patients receiving WinRho SDF for the treatment of ITP. These include: intravascular hemolysis (IVH), clinically compromising anemia, acute renal insufficiency and disseminated intravascular coagulation (DIC), leading in some cases to death.
- The most common adverse reactions observed for all indications are: headache, chills, fever, asthenia, abdominal or back pain, hypotension, pallor, diarrhea, increased LDH, arthralgia, myalgia, dizziness, nausea, vomiting, hypertension, hyperkinesia, somnolence, vasodilation, pruritus, rash and sweating.
- As is the case with all drugs of this nature, there is a chance of an allergic or anaphylactoid reaction with WinRho SDF in individuals with hypersensitivity to blood products.

USE IN SPECIAL POPULATIONS

- WinRho SDF has not been evaluated in pregnant women with ITP. WinRho SDF is not indicated for the treatment of ITP in pregnancy. WinRho SDF should be given to a pregnant woman with ITP only if clearly needed based on a risk-benefit assessment.
- This medicine is intended for use during pregnancy. Epidemiological studies indicate that well-controlled WinRho SDF treatment produces no adverse effects on pregnancy or on the health of the fetus/newborn when given to pregnant Rho (D)-negative women for prevention of Rh isoimmunization.
- WinRho SDF has not been evaluated in nursing mothers with ITP. Because many drugs are excreted in human milk, exercise caution when WinRho SDF is administered to nursing women. It is not known whether WinRho SDF is excreted in human milk.
- The safety and effectiveness of WinRho has been evaluated in children (<16 years of age) for the treatment of chronic or acute ITP and in children with ITP secondary to HIV infection. The dosing recommendation and safety profile in the treatment of children with ITP is the same as in adults.
- The safety and effectiveness of WinRho have not been established in clinical trials for the prevention of Rh isoimmunization in infants.
- Differences in response to treatment in those aged 65 or over as compared to younger subjects cannot be determined due to a limited number of these study subjects enrolled in clinical studies with WinRho. Use caution in dose selection for geriatric patients and consider starting at the low end of the dosing range.

REPORTING OF ADVERSE REACTIONS

To report any adverse reactions to WinRho SDF, Rho (D) Immunoglobulin (Human) or any Saol Product please contact our adverse event toll free hotline at 1-833-644-4216.

References:

(1) WinRho® SDF Product Monograph 11th January 2018

(2) AMA encyclopaedia of Medicine, edited by Leiken JB, Lipsky M. 2003 Random House; page 694)

(3) Fauci AS, Braunwald E, Isselbaucher KJ, Wilson JD, Martin JB, Kasper, DL, et al. Harrison's Principles of Internal Medicine. 14th ed. New York: McGraw-Hill; 1998.

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