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Important Drug Warning

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Dear Healthcare Professional:

Cangene Corporation and Baxter Healthcare Corporation are informing the medical community about important revisions to the labeling for WinRho® SDF (Rh_o(D) Immune Globulin Intravenous (Human)) to address **two (2)** safety concerns. In addition, to alert patients to the early signs and symptoms of Intravascular Hemolysis, a new Patient Information Sheet will be made available for distribution to ITP patients treated with WinRho® SDF.

Important Safety Information Regarding Intravascular Hemolysis in ITP Patients

The *Warnings, Precautions* and *Adverse Reactions* sections of the labeling for WinRho® SDF are being revised to alert ITP patients to immediately report symptoms of intravascular hemolysis (back pain, shaking chills, fever, discolored urine, decreased urine output, sudden weight gain, fluid retention/edema, and/or shortness of breath) to their physicians.

Through continuing postmarketing safety surveillance, rare, but severe and sometimes fatal, intravascular hemolysis and its potentially serious complications, including disseminated intravascular coagulation (DIC) have been observed in patients with ITP. The impact of age, gender, pretreatment renal function, pretreatment hemoglobin, other concomitantly administered blood/blood products or significant co-morbid conditions may have had in the onset of DIC in any of these reports are not known. Analysis of these events indicates that the etiology is complex and the potential association with anti-D is not clearly understood.

Important Safety Information on Potential Interference with Blood Glucose Measurement Following Administration of WinRho® SDF Liquid

This letter is also intended to alert healthcare professionals of the potential for falsely elevated glucose readings when using certain blood glucose testing systems that are not glucose-specific (for example systems based on glucose dehydrogenase pyrroloquinolinequinone (GDH-PQQ) or glucose-dye-oxidoreductase methods) in patients who have received maltose-containing parenteral products including WinRho® SDF Liquid.

The following provides a summary of the important safety information to be included in the prescribing information for WinRho® SDF to address the **two (2)** safety concerns noted above.

WARNINGS

Physicians should discuss the risks and benefits of WinRho® SDF and alert the patients who are being treated for ITP, about the signs and symptoms associated with the following rare serious adverse events reported through postmarketing surveillance:

Among patients treated for ITP, there have been rare postmarketing reports of signs and symptoms consistent with intravascular hemolysis[27] that included back pain, shaking chills, fever and discolored urine occurring, in most cases, within four hours of administration. Potentially serious complications of intravascular hemolysis that have also been reported include clinically compromising anemia, acute renal insufficiency or disseminated intravascular coagulation (DIC) that have, in some cases, been fatal[28]. The extent of risk of intravascular hemolysis and its complications is not known but is reported to be rare, especially for DIC, which is very rare [29]. In the rare cases reported following anti-D administration, there was no discernible contribution of age, gender, pretreatment renal function, pretreatment hemoglobin, concomitantly administered blood/blood products, co-morbid conditions or previous treatment with WinRho® SDF to the development of intravascular hemolysis and its complications. (See ADVERSE REACTIONS: Postmarketing.).

The liquid formulation of WinRho® SDF contains maltose. Maltose in IVIG 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 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 Liquid.

The product information of the blood glucose testing system, including that of the test strips, should be carefully reviewed 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.

PRECAUTIONS

Treatment of ITP

Following administration of WinRho® SDF, Rh_o(D) positive ITP patients should be monitored for signs and/or symptoms of intravascular hemolysis and its complications, which include:

- hemoglobinuria
- pallor
- hypotension
- tachycardia
- oliguria or anuria
- edema
- dyspnea
- increased bruising and prolongation of bleeding time and clotting time which may be difficult to detect in the ITP population.

The diagnosis of a serious complication of an intravascular hemolysis is dependent on laboratory testing (see PRECAUTIONS: Laboratory tests)

Information for Patients

ITP

Patients being treated for ITP should be **instructed to immediately report** symptoms of back pain, shaking chills, fever, discolored urine, decreased urine output, sudden weight gain, fluid retention/edema, and/or shortness of breath to their physicians.

Laboratory Tests

ITP

ITP patients presenting with signs and/or symptoms of intravascular hemolysis and its complications after anti-D administration should have confirmatory laboratory testing that may include, but is 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).

ADVERSE REACTIONS

The most serious adverse reactions have been observed in patients receiving WinRho® SDF for treatment of ITP. These include: intravascular hemolysis, clinically compromising anemia, acute renal insufficiency, DIC, and death. (See WARNINGS.)

Healthcare professionals should report serious adverse events possibly associated with the use of WinRho® SDF to Baxter Healthcare Corporation at 1-800-423-2090. Alternatively, this information may also be reported to FDA's MedWatch reporting system by phone (1-800-FDA-1088), online https://www.accessdata.fda.gov/scripts/medwatch/ or by fax (1-800-FDA-0178), or mailed using the MedWatch form FDA 3500 to FDA Medical Products Reporting Program, 5600 Fishers Lane, Rockville, MD 20852-9787.

Cangene Corporation and Baxter Healthcare Corporation are committed to providing updated information to healthcare professionals to ensure WinRho® SDF is used safely and effectively. Should you have any questions regarding the use of WinRho® SDF, please contact Baxter Medical Affairs at 1-866-424-6724.

Sincerely,

Cangene Corporation

M Genereux M.D.

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Medical Director

Baxter Healthcare Corporation

Richard Schiff MD, PhD

Richard Schiff, M.D., Ph.D.
Global Medical Director

Reference:

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