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Important Drug Warning

Month XX, 2010

Dear Healthcare Professional:

Cangene Corporation and Baxter Healthcare Corporation are informing the medical community about important risk information for WinRho® SDF (Rh_o(D) Immune Globulin Intravenous (Human)). Cases of Intravascular Hemoloysis (IVH) and its complications have been reported in patients treated for Immune Thrombocytopenic purpura (ITP) with WinRho® SDF. Some of these cases of IVH and its complications have been fatal. Accordingly, Cangene has added a Boxed Warning to the labeling for the product which strengthens the warnings related to the risk of developing IVH in the ITP population. This letter does not apply to patients receiving WinRho® SDF for the suppression of Rh isoimmunization.

Clinicians are advised to carefully review the **BOXED WARNING, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS** and **DOSAGE AND ADMINISTRATION** below.(a copy of the full prescribing information is also enclosed):

WARNING: INTRAVASCULAR HEMOLYSIS

Intravascular hemolysis (IVH) leading to death has been reported in patients treated for immune thrombocytopenic purpura (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 health care setting for at least eight hours after administration. Perform a dipstick urinalysis at baseline, 2 hours, 4 hours after administration 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. If signs and/or symptoms of IVH are present or suspected after WinRho®administration, post-treatment laboratory tests should be performed, including plasma hemoglobin, microscopic and dipstick urinalysis, haptoglobin, LDH, and plasma bilirubin (direct and indirect).

- **CONTRAINDICATIONS**
  - …Do not use WinRho SDF in patients with autoimmune hemolytic anemia
  - Do not used WinRho SDF in patients with pre-existing hemolysis or in patients at high risk for hemolysis
  - Do not use WinRho SDF in patients who are IgA deficient with antibodies against IgA …

- The **WARNINGS** section has been revised to describe the signs and symptoms of IVH and its complications including clinically compromising anemia, acute renal insufficiency, and Disseminated Intravascular Coagulation (DIC).

  INTRAVASCULAR HEMOLYSIS (IVH)

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

  IVH can lead to clinically compromising anemia and multi-system organ failure including acute respiratory distress symdrome (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 health care setting for at least eight hours after administration. Perform a dipstick urinalysis at baseline, 2 hours, 4 hours after administration 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 hematuria. Absence of theses 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 administration, post-treatment laboratory tests should be performed including plasma haemoglobin.

- **The Laboratory Tests** subsection of the **PRECAUTIONS** section of the labeling has been revised to provide direction to the healthcare provider to perform dipstick urinalysis at baseline, 2 hours, 4 hours after administration and prior to the end of the monitoring period. Periodic monitoring of renal function and urine output is particularly important in patients judged to be at increased risk of developing acute renal failure.

  Important changes have also been made to this section to clarify the risk associated with the treatment of ITP by incorporating the class specific subsections of Renal Failure, Thrombotic Events, Hemolysis, and Transfusion-related Acute Lung Injury (TRALI).

  The subsection, Geriatric Use, has been added to include the following:

… Other reported clinical experience suggests that patients of advanced age (age over 65) with co-morbid conditions such as active infection (including HCV), hematological malignancies (including non-Hodgkin's lymphoma, Hodgkin's disease or Chronic Lymphocytic Leukemia), autoimmune disorders (SLE, antiphosholipid syndrome, and autoimmune hemolytic anemia) may be at an increased risk of developing acute haemolytic reactions such as IVH. Patients receiving doses in excess of 300 IU/kg of WinRho 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.

- The **DOSAGE AND ADMINISTRATION** section has been modified to advise clinicians to seek alternative treatments in patients with hemoglobin levels that are less than 8g/dL due to the risk of increasing the severity of the anemia.

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

Maurice Genereux, M.D.
Medical Director

Baxter Healthcare Corporation

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