



Cangene Corporation
155 Innovation Drive
Winnipeg, MB, Canada R3T 5Y3
204-275-4200

**Health Canada Endorsed Important Safety Information on WinRho[®] SDF (Rh_o (D)
Immune Globulin (Human))**

January 24, 2006

To: Hospital Chief of Medical Staff

Please distribute to the Blood Bank and to the relevant Departments of Hematology and of Internal Medicine and to other involved professional staff and POST THIS NOTICE IN YOUR INSTITUTION.

Subject: Association of WinRho[®] SDF [Rh_o (D) Immune Globulin (Human)] with Intravascular Hemolysis in the treatment of Immune Thrombocytopenic Purpura (ITP).

Cangene Corporation, in collaboration with Health Canada, is informing Blood Bank Directors and the medical community about important safety information on WinRho[®] SDF [Rh_o (D) Immune Globulin Intravenous (Human)] that has been observed in Post Marketing Safety Surveillance.

- Rare but severe and sometimes fatal, intravascular hemolysis and its potentially serious complications have been observed in patients with ITP following WinRho[®] SDF administration
- Potentially serious complications of intravascular hemolysis that have been reported include clinically compromising anemia, acute renal insufficiency or disseminated intravascular coagulation (DIC).
- Physicians should discuss the risks and benefits of WinRho[®] SDF with their ITP patients who should be monitored for signs and symptoms associated with those rare serious adverse events.

The extent of risk of intravascular hemolysis and its complications is not known but is reported to be rare (defined by the Council for International Organizations of Medical Sciences (CIOMS) as <1/1000), especially for DIC, which is very rare (defined by CIOMS as <1/10000). A total of nine (9) cases of suspected DIC have been reported internationally, one (1) of which was in Canada. 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. Analysis of these events

indicates that the etiology is complex and the potential association with anti-D is not clearly understood.

In the USA a similar Important Drug Warning was recently issued in addition to a warning about potential interference with Blood Glucose Measurement following administration of Liquid WinRho[®] SDF containing 10% Maltose. This portion of the US warning does not apply to Canada since Liquid WinRho[®] SDF containing 10% Maltose is not currently marketed here.

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.

Patients being treated for ITP should be instructed to immediately report symptoms of intravascular hemolysis (generalized weakness, lightheadedness, back pain, discolored urine, jaundice, decreased urine output, sudden weight gain, fluid retention/edema, and or shortness of breath) to their physicians.

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, microscopic urinalysis, 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).

Managing marketed health product-related adverse reactions depends on health care professionals and consumers reporting them. Reporting rates determined on the basis of spontaneously reported post-marketing adverse reactions are generally presumed to underestimate the risks associated with health product treatments. Any case of intravascular hemolysis, its complications or other serious or unexpected adverse reactions in patients receiving WinRho[®] SDF should be reported to Cangene Corporation or Health Canada at the following addresses:

Pharmacovigilance Unit
Cangene Corporation
26 Henlow Bay
Winnipeg, Manitoba
Canada R3Y 1G4
Tel: 1-800-768-2304
Fax: 1-800-768-2281

Any suspected adverse reaction can also be reported to:

Canadian Adverse Drug Reaction Monitoring Program (CADRMP)
Marketed Health Products Directorate
HEALTH CANADA

Address Locator 0701C

OTTAWA, Ontario, K1A 0K9

Tel: (613) 957-0337 or Fax: (613) 957-0335

To report an Adverse Reaction, consumers and Health Professionals may call toll free:

Tel: 1-866-234-2345

Fax: 1-866-678-6789

cadrmpp@hc-sc.gc.ca

The AR Reporting Form and the AR Guidelines can be found on the Health Canada website or in *The Canadian Compendium of Pharmaceuticals and Specialties*.

http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/form/ar-ei_form_e.html

http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/guide/ar-ei_guide-ldir_e.html

For other inquiries, please refer to contact information:

Marketed Health Products Directorate (MHPD)

MHPD_DPSC@hc-sc.gc.ca

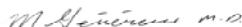
Tel: (613) 954-6522

Fax: (613) 952-7738

Your professional commitment in this regard has an important role in protecting the well being of your patients by contributing to early signal detection and informed use of drugs. Comprehensive information is important to our ability to evaluate the significance of the reported event in association with WinRho[®] SDF.

Cangene, in consultation with Health Canada, is currently in the process of updating the Product Monograph for WinRho[®] SDF. Should you have any questions regarding the use of WinRho[®] SDF, please contact Cangene Medical Affairs at 1-204-275-4368.

Sincerely,



Maurice Généreux M.D.
Medical Director
Cangene Corporation