SANOFI GENZYME

September 8, 2020

Dear Blood Bank Director/Staff Member,

SARCLISA™ (ISATUXIMAB) IS ASSOCIATED WITH RISK OF INTERFERENCE WITH BLOOD COMPATIBILITY TESTS.

Summary:

- Sarclisa (isatuximab) is a monoclonal antibody that binds to CD38 and is used in the treatment of multiple myeloma
- Sarclisa binds to CD38 on red blood cells (RBCs) and may interfere with routine blood compatibility tests with **potential false positive reactions in indirect antiglobulin tests**.
- This interference is limited to the minor blood groups and does not affect the determination of a patient's ABO and Rh blood type.
- Sarclisa interference mitigation methods include treating reagent RBCs with dithiothreitol (DTT) to disrupt Sarclisa binding or other locally validated methods.
- If an emergency transfusion is required, you can give non-cross-matched ABO/RhD-compatible RBCs as per local blood bank practices.
- Sarclisa mediated positive indirect antiglobulin tests may persist for approximately 6 months after the last infusion.

Risk Management Plan:

To ensure appropriate use of Sarclisa, a Risk Management Plan (RMP) has been implemented in Canada. Sanofi-aventis Canada Inc. has developed an educational material (HEALTHCARE PROFESSIONALS AND BLOOD BANKS BROCHURE) as part of the Sarclisa RMP approved by Health Canada. This brochure is intended for healthcare professionals (HCPs) who are expected to prescribe and dispense isatuximab (e.g. oncologists, hematologists, nurses etc.) and Blood banks/transfusion centers.

Please take careful note of the important safety information regarding Sarclisa and the risk of "***interference with indirect antiglobulin test (IAT) (indirect Coombs test) and possible resulting adverse clinical consequences for the patient (transfusion delay, transfusion hemolysis)".*** The accompanying Sarclisa "HCPs AND BLOOD BANKS BROCHURE" includes more detailed information and addresses how to manage and minimize this risk.

Background:

Sarclisa (isatuximab) is a monoclonal antibody that binds to a specific extracellular epitope of CD38 and is being used in the treatment of multiple myeloma[1]. CD38 protein is expressed on the surface of red blood cells (RBCs). Sarclisa, an anti-CD38 antibody, binds to CD38 on RBCs and may interfere with blood bank serologic tests with potential false positive reactions in indirect antiglobulin tests (indirect Coombs tests), antibody detection (screening) tests, antibody identification panels, and antihuman globulin (AHG) crossmatches in patients treated with Sarclisa. ABO/RhD typing was not affected by Sarclisa treatment.

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To avoid potential problems with RBC transfusion, patients being treated with Sarclisa should have blood type and screen tests performed prior to the first Sarclisa infusion. Phenotyping may be considered prior to starting Sarclisa treatment as per local practice. If treatment with Sarclisa has already started, the blood bank should be informed that the patient is receiving Sarclisa and Sarclisa interference with blood compatibility testing can be resolved using dithiothreitol (DTT)-treated RBCs. If an emergency transfusion is required, non-cross-matched ABO/RhD-compatible RBCs can be given as per local blood bank practices[1]. There is currently no available information regarding how long the interference with the indirect antiglobulin test may persist after the last infusion of Sarclisa. Based on the half-life of Sarclisa, it is anticipated that Sarclisa mediated positive indirect antiglobulin tests may persist for approximately 6 months after the last infusion.

In the ICARIA-MM clinical study, the indirect antiglobulin test was positive during isatuximab combination treatment in 67.7% of the tested patients. In patients with a positive indirect antiglobulin test, blood transfusions were administered without evidence of hemolysis. ABO/RhD typing was not affected by Sarclisa treatment.[1]

REPORTING OF SUSPECTED ADVERSE REACTIONS

We ask that any suspected adverse reactions are reported via the following:

Health Canada
Website: http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php

Contact Sanofi by calling 1-800-589-6215 or emailing at canada.pharmacovigilance@sanofi.com

ADDITIONAL RESOURCES

For additional information on Sarclisa, **please refer to the full product monograph** or contact Sanofi by using one of the following methods:

Phone: 1-800-589-6215

Email: SanofiMedInfoCA@sanofi.com

Website: www.sanofi.ca

Sincerely,

Mark Surka, PhD
Head, Medical Affairs, Oncology
Sanofi Genzyme Canada

References
1. SARCLISA Product Monograph. Sanofi Genzyme. April 29, 2020.

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Pr SARCLISA™
(isatuximab)

— IMPORTANT INFORMATION —

SARCLISA™ (ISATUXIMAB) IS ASSOCIATED WITH RISK OF INTERFERENCE WITH BLOOD COMPATIBILITY TESTS

HEALTHCARE PROFESSIONALS AND BLOOD BANKS BROCHURE

SARCLISA (isatuximab) is indicated, in combination with pomalidomide and dexamethasone, for the treatment of patients with relapsed and refractory multiple myeloma, who have received at least two prior therapies, including lenalidomide and a proteasome inhibitor.

WARNING FOR HEALTHCARE PROFESSIONALS

APPROPRIATE MEASURES TO MANAGE ISATUXIMAB INTERFERENCE WITH BLOOD COMPATIBILITY TESTING AND AVOID POSSIBLE RESULTING ADVERSE CLINICAL CONSEQUENCES

- Conduct blood type and screen tests on your patient prior to the first infusion of isatuximab.
- Consider phenotyping prior to starting isatuximab treatment as per local practice.
- In the event of a planned transfusion, inform the blood bank that the patient is receiving isatuximab and the risk of isatuximab interference with indirect antiglobulin tests.
- Give your patient the latest version of the **Patient Alert Card**.
- There is currently no available information with regard to how long the interference with the indirect Coombs test may persist after the last infusion of isatuximab. Based on the half-life of isatuximab, it is anticipated that isatuximab mediated positive indirect Coombs tests may persist for approximately 6 months after the last infusion. Therefore, please advise your patient to carry the Patient Alert Card at all times and until **6 months** after the last dose of isatuximab.
- It is important you always advise your patients to consult Part III of the product monograph for further information on isatuximab, and to present their Patient Alert Card to all of their healthcare professionals.

REPORTING OF SUSPECTED ADVERSE REACTIONS

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  Website: http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php
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For additional information on isatuximab, **please refer to the full product monograph** or contact Sanofi by using one of the following methods:

- **Phone:** 1-800-589-6215
- **Email:** SanofiMedInfoCA@sanofi.com
- **Website:** https://www.sanofi.ca/en/products-and-resources/prescription-products

WARNING FOR BLOOD BANKS

- Isatuximab binds to CD38 on red blood cells (RBCs) and may mask the detection of antibodies to minor antigens in the patient's serum. Thus, isatuximab may interfere with routine blood compatibility tests with **potential false positive reactions in indirect antiglobulin tests (indirect Coombs test)**.
- This interference is limited to the minor blood groups and does not affect the determination of a patient's ABO and Rh blood type.
- Isatuximab interference mitigation methods include treating reagent RBCs with dithiothreitol (DTT) to disrupt isatuximab binding or other locally validated methods.
- **If an emergency transfusion is required, you can give non-cross-matched ABO/RhD-compatible RBCs as per local blood bank practices.**

True Negative Indirect Coombs Test

Reagent RBCs with known minor antigen → Patient serum without antibodies to minor antigen → No patient antibodies to bind RBC antigens → Coombs reagent added → No agglutination occurs → TEST IS NEGATIVE

True Positive Indirect Coombs Test

Reagent RBCs with known minor antigen → Patient serum with antibodies to minor antigen → Patient antibodies bind RBC antigens → Coombs reagent added → Agglutination occurs → TEST IS POSITIVE

Indirect Coombs Test From An Isatuximab-treated Patient

RBCs → Patient serum with isatuximab → Isatuximab binds to CD38 on RBCs → Coombs reagent added → Agglutination occurs → TEST IS FALSE POSITIVE

ISA = Isatuximab = Coombs reagent = CD38 receptor = Red blood cells = Antibodies to minor antigen

FOR TIMELY TRANSFUSIONS

REMINDER FOR HEALTHCARE PROFESSIONALS

Conduct blood type and screen tests on your patient prior to the first infusion of isatuximab. Inform the blood bank that your patient has been treated with isatuximab, which interferes with indirect antiglobulin tests (indirect Coombs test).

Verify standing orders for transfusions to determine if your patient received isatuximab within the last year.

In the event of a planned transfusion, notify blood transfusion centres about the risk of interference with indirect antiglobulin tests. Provide your patient's pre-isatuximab compatibility profile, if available, to the blood bank.

Give your patient a Patient Alert Card to be carried at all times and until **6 months** after the last dose of isatuximab.

Ask your patients to tell their other healthcare professionals that they have received isatuximab, particularly before a transfusion, and to show them their Patient Alert Card.

REMINDER FOR BLOOD BLANKS

Identify the blood sample of your patient as containing isatuximab.

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SANOFI GENZYME

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