SARCLISA®
(isatuximab-irfc)
Injection for IV use | 500 mg/25 mL, 100 mg/5 mL

Isatuximab-irfc Risk of Interference With Blood Compatibility Testing

Information for healthcare professionals and blood banks

Indication

SARCLISA (isatuximab-irfc) is indicated:

- In combination with pomalidomide and dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least 2 prior therapies including lenalidomide and a proteasome inhibitor
- In combination with carfilzomib and dexamethasone, for the treatment of adult patients with relapsed or refractory multiple myeloma who have received 1 to 3 prior lines of therapy

Important Safety Information

CONTRAINDICATIONS

SARCLISA is contraindicated in patients with severe hypersensitivity to isatuximab-irfc or to any of its excipients.

WARNINGS AND PRECAUTIONS

Infusion-Related Reactions

Serious infusion-related reactions (IRRs), including life-threatening anaphylactic reactions, have occurred with SARCLISA treatment. Severe signs and symptoms include cardiac arrest, hypertension, hypotension, bronchospasm, dyspnea, angioedema, and swelling.

Based on ICARIA-MM, IRRs occurred in 38% of patients treated with SARCLISA, pomalidomide, and dexamethasone (Isa-Pd). All IRRs started during the first SARCLISA infusion and resolved on the same day in 98% of the cases.

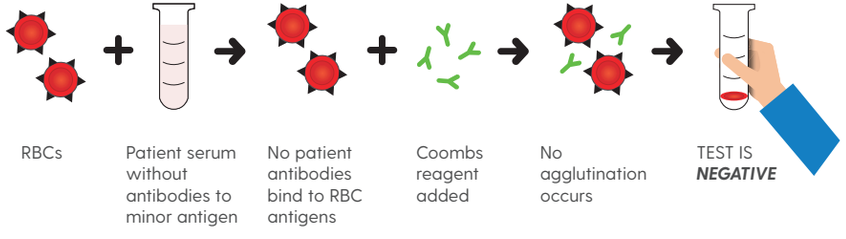
Please see additional Important Safety Information throughout, and accompanying full Prescribing Information.

How Isatuximab-irfc May Interfere With Blood Compatibility Testing

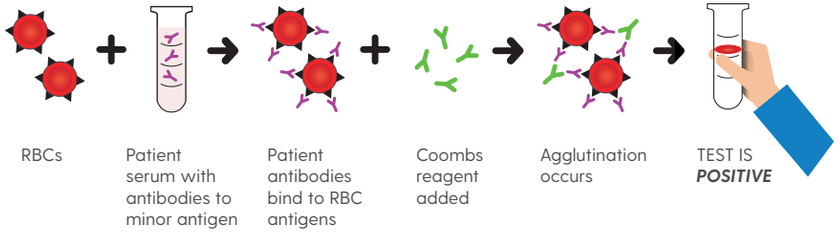
- Isatuximab-irfc is an anti-CD38 mAb used for the treatment of relapsed or refractory multiple myeloma[1]
- As an anti-CD38 mAb, isatuximab-irfc binds to RBCs and may result in a false-positive indirect antiglobulin test (indirect Coombs test)[1,2]
- The indirect antiglobulin test was positive during Isa-Pd treatment in 68% of the tested patients in the ICARIA-MM trial, and during Isa-Kd treatment in 63% of patients in the IKEMA trial. In patients with a positive indirect antiglobulin test, blood transfusions were administered without evidence of hemolysis[1]
- ABO/RhD typing is not affected by isatuximab-irfc treatment[1]

Indirect antiglobulin test (indirect Coombs test) outcomes[1-3]

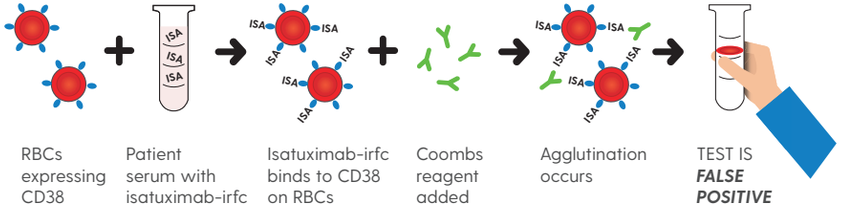
True *NEGATIVE* indirect antiglobulin test (indirect Coombs test)



True *POSITIVE* indirect antiglobulin test (indirect Coombs test)



Indirect antiglobulin test (indirect Coombs test) from an *ISATUXIMAB-IRFC–TREATED PATIENT*



= Antibodies to minor antigen = CD38 receptor = Coombs reagent **ISA** = Isatuximab-irfc = RBCs

Help Ensure Timely Transfusions

Take appropriate measures to manage isatuximab-irfc interference

Guidance for healthcare professionals

- Before the first isatuximab-irfc infusion, conduct blood type and screen tests on isatuximab-irfc–treated patients[1]
- Consider phenotyping prior to starting isatuximab-irfc treatment[1]
- If treatment with isatuximab-irfc has already started, inform the blood bank that the patient is receiving isatuximab-irfc[1]
- In the event of a planned transfusion, please notify blood transfusion centers about the risk of interference with the indirect antiglobulin test (indirect Coombs test)[1]
- Interference may persist for 2 to 6 months after the last infusion of an anti-CD38 mAb[2,3]

Provide patients with the Patient ID Card that alerts other healthcare professionals that they are receiving treatment with isatuximab-irfc so they are aware of the potential interference. Advise patients to keep this card with them at all times and for 6 months after they discontinue treatment with isatuximab-irfc

Guidance for blood banks

- To manage isatuximab-irfc interference with blood compatibility testing, treat reagent RBCs with DTT, a reducing agent that denatures CD38 antigen and prevents the antibody from binding[1,2]
  - Since the Kell blood group system is also sensitive to DTT treatment, patients should be transfused with Kell-negative blood unless they are confirmed to be Kell-positive[2]
- If an emergency transfusion is required, non–crossed-matched ABO/RhD-compatible RBCs can be given as per local blood bank practices[1]

DTT=dithiothreitol; Isa=isatuximab-irfc; Kd=carfilzomib and dexamethasone; mAb=monoclonal antibody; Pd=pomalidomide and dexamethasone; RBC=red blood cell.

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Important Safety Information (cont'd)

Infusion-Related Reactions (cont'd)

In IKEMA, infusion-related reactions occurred in 46% of patients treated with SARCLISA, carfilzomib, and dexamethasone (Isa-Kd). In the Isa-Kd arm, the infusion-related reactions occurred on the infusion day in 99% of episodes. In patients treated with Isa-Kd, 95% of those experiencing an infusion-related reaction experienced it during the first cycle of treatment. All infusion-related reactions resolved: within the same day in 74% of episodes, and the day after in 24% of episodes.

The most common symptoms (≥5%) of an infusion-related reaction in ICARIA-MM and IKEMA (N=329) included dyspnea, cough, nasal congestion, and nausea. Anaphylactic reactions occurred in less than 1% of patients. To decrease the risk and severity of IRRs, premedicate patients prior to SARCLISA infusion with acetaminophen, H_2 antagonists, diphenhydramine or equivalent, and dexamethasone.

Monitor vital signs frequently during the entire SARCLISA infusion. For patients with grade ≥2 reactions, interrupt SARCLISA infusion and provide appropriate medical management. For patients with grade 2 or grade 3 reactions, if symptoms improve to grade ≤1, restart SARCLISA infusion at half of the initial infusion rate, with supportive care as needed, and closely monitor patients. If symptoms do not recur after 30 minutes, the infusion rate may be increased to the initial rate, and then increased incrementally. In case symptoms do not improve to grade ≤1 after interruption of SARCLISA infusion, persist or worsen despite appropriate medications, or require hospitalization, permanently discontinue SARCLISA and institute appropriate management. Permanently discontinue SARCLISA if an anaphylactic reaction or life-threatening (grade 4) IRR occurs and institute appropriate management.

Neutropenia

SARCLISA may cause neutropenia.

In patients treated with Isa-Pd, neutropenia occurred in 96% of patients and grade 3-4 neutropenia occurred in 85% of patients. Neutropenic complications occurred in 30% of patients, including febrile neutropenia (12%) and neutropenic infections (25%), defined as infection with concurrent grade ≥3 neutropenia. The most frequent neutropenic infections included infections of the upper respiratory tract (10%), lower respiratory tract (9%), and urinary tract (3%).

In patients treated with Isa-Kd, neutropenia occurred in 55% of patients, with grade 3-4 neutropenia in 19% of patients (grade 3 in 18% and grade 4 in 1.7%). Neutropenic complications occurred in 2.8% of patients, including febrile neutropenia (1.1%) and neutropenic infections (1.7%).

Monitor complete blood cell counts periodically during treatment. Consider the use of antibacterial and antiviral prophylaxis during treatment. Monitor patients with neutropenia for signs of infection. In case of grade 4 neutropenia, delay SARCLISA dose until neutrophil count recovery to at least 1 x 10^9/L, and provide supportive care with growth factors, according to institutional guidelines. No dose reductions of SARCLISA are recommended.

Second Primary Malignancies

The incidence of second primary malignancies is increased in patients treated with SARCLISA-containing regimens. The overall incidence of second primary malignancies in all the SARCLISA-exposed patients was 4.1%.

In ICARIA-MM, at a median follow-up time of 52 months, second primary malignancies occurred in 7% of patients in the Isa-Pd arm and in 2% of patients in the Pd arm.

In the ongoing IKEMA study, at a median follow-up time of 21 months, second primary malignancies occurred in 7% of patients in the Isa-Kd arm and in 4.9% of patients in the Kd arm.

The most common (≥1%) second primary malignancies in ICARIA-MM and IKEMA (N=329) included skin cancers (5% with SARCLISA-containing regimens and 2.6% with comparative regimens) and solid tumors other than skin cancer (3% with SARCLISA-containing regimens and 1.8% with comparative regimens). All patients with non-melanoma skin cancer continued treatment after resection of the skin cancer.

Monitor patients for the development of second primary malignancies.

Laboratory Test Interference

Interference with Serological Testing (Indirect Antiglobulin Test)

SARCLISA binds to CD38 on red blood cells (RBCs) and may result in a false-positive indirect antiglobulin test (indirect Coombs test). The indirect antiglobulin test was positive during Isa-Pd treatment in 68% of the tested patients, and during Isa-Kd treatment in 63% of 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.

Before the first SARCLISA infusion, conduct blood type and screen tests on SARCLISA-treated patients. Consider phenotyping prior to starting SARCLISA treatment. If treatment with SARCLISA has already started, inform the blood bank that the patient is receiving SARCLISA and that SARCLISA interference with blood compatibility testing can be resolved using dithiothreitol-treated RBCs. If an emergency transfusion is required, non–cross-matched ABO/RhD-compatible RBCs can be given as per local blood bank practices.

Interference with Serum Protein Electrophoresis and Immunofixation Tests

SARCLISA is an IgG kappa monoclonal antibody that can be incidentally detected on both serum protein electrophoresis and immunofixation assays used for the clinical monitoring of endogenous M-protein. This interference can impact the accuracy of the determination of complete response in some patients with IgG kappa myeloma protein.

Embryo-Fetal Toxicity

Based on the mechanism of action, SARCLISA can cause fetal harm when administered to a pregnant woman. SARCLISA may cause fetal immune cell depletion and decreased bone density. Advise pregnant women of the potential risk to a fetus. Advise females with reproductive potential to use an effective method of contraception during treatment with SARCLISA and for 5 months after the last dose. The combination of SARCLISA with pomalidomide is contraindicated in pregnant women because pomalidomide may cause birth defects and death of the unborn child. Refer to the pomalidomide prescribing information on use during pregnancy.

ADVERSE REACTIONS

In combination with pomalidomide and dexamethasone: The most common adverse reactions (≥20%) were upper respiratory tract infection, infusion-related reactions, pneumonia, and diarrhea. The most common hematology laboratory abnormalities (≥80%) were decreased hemoglobin, decreased neutrophils, decreased lymphocytes, and decreased platelets.

In combination with carfilzomib and dexamethasone: The most common adverse reactions (≥20%) were upper respiratory tract infection, infusion-related reactions, fatigue, hypertension, diarrhea, pneumonia, dyspnea, insomnia, bronchitis, cough, and back pain. The most common hematology laboratory abnormalities (≥80%) were decreased hemoglobin, decreased lymphocytes, and decreased platelets.

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Additional Resources

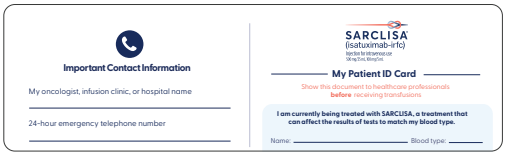
For more information about SARCLISA

Please refer to the accompanying full Prescribing Information, or contact Sanofi at 800-633-1610

Visit sarclisahcp.com to download the Patient ID Card and other helpful resources for your patients

Patient ID Card

Front



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Important Safety Information (cont'd)

ADVERSE REACTIONS (cont'd)

Serious adverse reactions occurred in 62% of patients receiving Isa-Pd. Serious adverse reactions in >5% of patients who received Isa-Pd included pneumonia (26%), upper respiratory tract infections (7%), and febrile neutropenia (7%). Fatal adverse reactions occurred in 11% of patients (those that occurred in more than 1% of patients were pneumonia and other infections [3%]).

Serious adverse reactions occurred in 59% of patients receiving Isa-Kd. The most frequent serious adverse reactions in >5% of patients who received Isa-Kd were pneumonia (25%) and upper respiratory tract infections (9%). Adverse reactions with a fatal outcome during treatment were reported in 3.4% of patients in the Isa-Kd group (those occurring in more than 1% of patients were pneumonia occurring in 1.7% and cardiac failure in 1.1% of patients).

USE IN SPECIAL POPULATIONS

Because of the potential for serious adverse reactions in the breastfed child from isatuximab-irfc administered in combination with Pd, advise lactating women not to breastfeed during treatment with SARCLISA.

Please see additional Important Safety Information throughout, and accompanying full Prescribing Information.

References: 1. SARCLISA [prescribing information]. Bridgewater, NJ: sanofi-aventis U.S. LLC. **2.** Lancman G, Arinsburg S, Jhang J, et al. Blood transfusion management for patients treated with anti-CD38 monoclonal antibodies. *Front Immunol.* 2018;9:2616. doi:10.3389/fimmu.2018.02616. **3.** van de Donk NW, Moreau P, Plesner T, et al. Clinical efficacy and management of monoclonal antibodies targeting CD38 and SLAMF7 in multiple myeloma. *Blood.* 2016;127(6):681–695. doi:10.1182/blood-2015-10-646810.

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