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
- In combination with bortezomib, lenalidomide, and dexamethasone, for the treatment of adult patients with newly diagnosed multiple myeloma who are not eligible for autologous stem cell transplant (ASCT)

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.

In clinical trials (ICARIA-MM, IKEMA, and IMROZ), in patients treated with SARCLISA (N=592), infusion-related reactions occurred in 206 patients (35%). Among these 206 patients, 92% experienced infusion-related reactions during the first infusion and 12% after the first cycle.

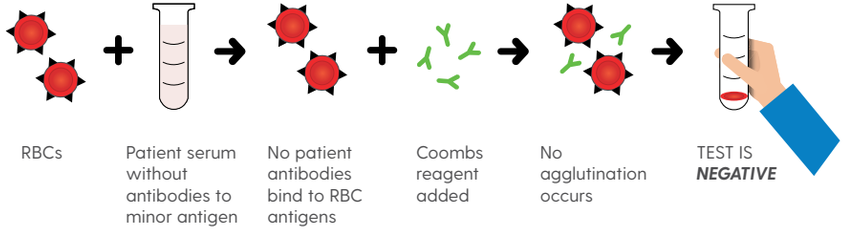
Please see additional Important Safety Information throughout, and accompanying full Prescribing Information.

How Isatuximab-irfc May Interfere With Blood Compatibility Testing

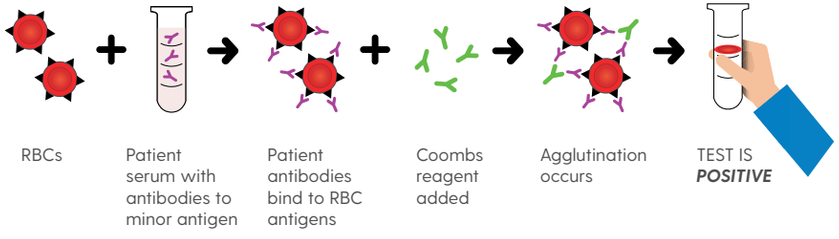
- Isatuximab-irfc is an anti-CD38 mAb used for the treatment of relapsed or refractory multiple myeloma[1]
- As an anti-CD38 mAb, isatuximab-irfc binds to RBCs and may result in a false-positive indirect antiglobulin test (indirect Coombs test). This interference with the indirect Coombs test may persist for approximately 6 months after the last infusion of isatuximab-irfc.[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 was not affected by isatuximab-irfc treatment[1]

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

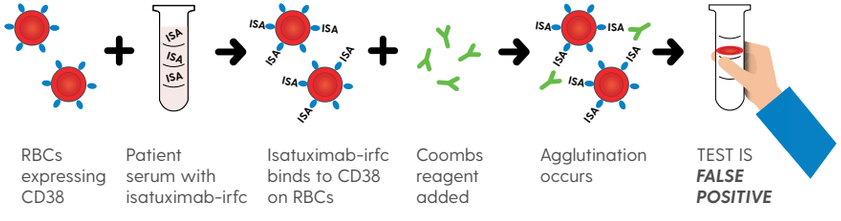
True *NEGATIVE* indirect antiglobulin test (indirect Coombs test)



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 with the indirect Coombs test may persist for approximately 6 months after the last infusion of isatuximab-irfc.[1]

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)

The most common symptoms (≥5%) of an infusion-related reaction included dyspnea and cough. Grade 1 infusion-related reactions were reported in 6% of patients, grade 2 in 28%, and grade 3 or 4 in 1.2%. Anaphylactic reactions occurred in less than 1% of patients. The total incidence of SARCLISA infusion interruptions was less than 1% and the incidence of patients with at least one SARCLISA infusion interruption due to infusion-related reactions was 26%. The median time to first SARCLISA infusion interruption was 61 minutes (range 4 to 240 minutes). SARCLISA was discontinued in 1% of patients due to infusion-related reactions. 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.

Infections

SARCLISA can cause severe, life-threatening, or fatal infections. In patients who received SARCLISA at the recommended dose in ICARIA-MM, IKEMA, and IMROZ (N=592), serious infections, including opportunistic infections, occurred in 46%, grade 3 or 4 infections occurred in 43%, and fatal infections occurred in 4.7%. The most common serious infection reported was pneumonia (32%).

Monitor patients for signs and symptoms of infection prior to and during treatment with SARCLISA and treat appropriately. Administer prophylactic antimicrobials according to guidelines.

Neutropenia

SARCLISA may cause neutropenia.

In clinical trials (ICARIA-MM, IKEMA, and IMROZ), in patients treated with SARCLISA (N=592), neutropenia based on laboratory values occurred in 81%, with grade 3 or 4 occurring in 52%. Neutropenic infections occurred in 12% of patients, with grade 3 or 4 in 4.9%, and febrile neutropenia in 4%.

Monitor complete blood cell counts periodically during treatment. If needed, use 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, during treatment and post-treatment, is increased in patients treated with SARCLISA-containing regimens. In clinical trials (ICARIA-MM, IKEMA, and IMROZ), in patients treated with SARCLISA (N=592), second primary malignancies occurred in 71 patients (12%).

In ICARIA-MM, at a median follow-up time of 52 months, second primary malignancies occurred in 7% of patients treated with SARCLISA, pomalidomide, and dexamethasone (Isa-Pd) and in 2% of patients treated with Pd.

In IKEMA study, at a median follow-up time of 57 months, second primary malignancies occurred in 10% of patients treated with SARCLISA, carfilzomib, and dexamethasone (Isa-Kd) and in 8% of patients treated with Kd.

In IMROZ study, at a median follow-up time of 60 months, second primary malignancies occurred in 16% of patients treated with SARCLISA, bortezomib, lenalidomide, and dexamethasone (Isa-VRd) and in 9% of patients treated with VRd.

The most common (≥1%) second primary malignancies in ICARIA-MM, IKEMA, and IMROZ (N=592) included skin cancers (7% with SARCLISA-containing regimens and 3.1% with comparative regimens) and solid tumors other than skin cancer (4.6% with SARCLISA-containing regimens and 2.9% with comparative regimens). Patients with non-melanoma skin cancer continued treatment after resection of the skin cancer, except 2 patients in the Isa-VRd arm and 1 patient in the VRd arm of the IMROZ study. 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). This interference with the indirect Coombs test may persist for approximately 6 months after the last infusion of SARCLISA. 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 or lenalidomide is contraindicated in pregnant women because pomalidomide or lenalidomide may cause birth defects and death of the unborn child. Refer to the pomalidomide or lenalidomide 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.

In combination with bortezomib, lenalidomide, and dexamethasone: The most common adverse reactions (≥20%) were upper respiratory tract infections, diarrhea, fatigue, peripheral sensory neuropathy, pneumonia, musculoskeletal pain, cataract, constipation, peripheral edema, rash, infusion-related reaction, insomnia, and COVID-19. The most common hematologic laboratory abnormalities (≥80%) were decreased hemoglobin, decreased leukocytes, decreased lymphocytes, decreased platelets, and decreased neutrophils.

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Additional Resources

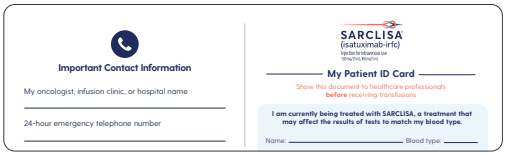
For more information about SARCLISA

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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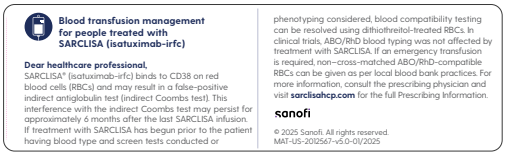

Important Safety Information (cont'd)

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).

Serious adverse reactions occurred in 71% of patients receiving Isa-VRd. The serious adverse reaction in >5% of patients who received Isa-VRd was pneumonia (30%). Fatal adverse reactions occurred in 11% of patients with Isa-VRd (those occurring in more than 1% of patients were pneumonia [5%]).

USE IN SPECIAL POPULATIONS

Because of the potential for serious adverse reactions in the breastfed child from isatuximab-irfc administered in combination with pomalidomide or lenalidomide and dexamethasone, 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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