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

DOSING AND ADMINISTRATION GUIDE

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 two prior therapies including lenalidomide and a proteasome inhibitor.

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

Infusion-related reactions (IRRs) have been observed in 39% of patients treated with SARCLISA. All IRRs started during the first SARCLISA infusion and resolved on the same day in 98% of the cases. The most common symptoms of an IRR included dyspnea, cough, chills, and nausea. The most common severe signs and symptoms included hypertension and dyspnea.

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

Recommended dose and schedule

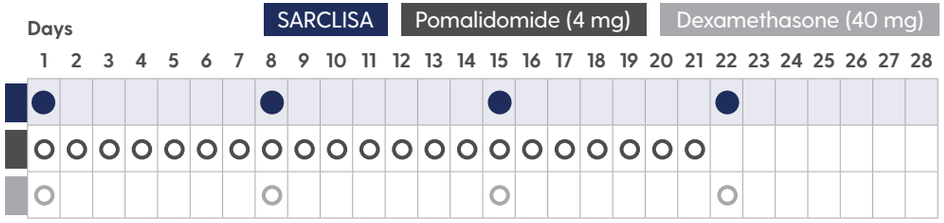
Administer preinfusion medications. The recommended dose of SARCLISA is 10 mg/kg actual body weight administered as an intravenous (IV) infusion in combination with pomalidomide and dexamethasone (Pd).[1]

- SARCLISA is given as a 250-mL fixed-volume infusion[1]
- No dose reduction of SARCLISA is recommended[1]

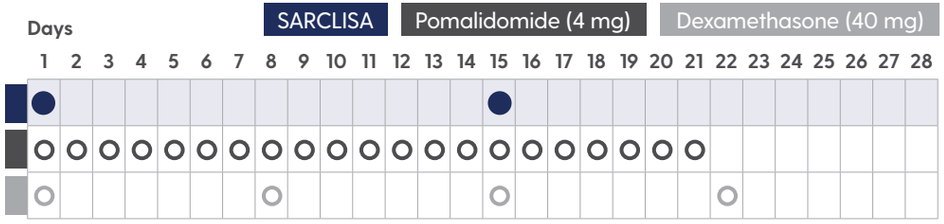
Weekly dosing for first cycle, followed by every other week for subsequent cycles[1]

SARCLISA + Pd dosing schedule[1]

Cycle 1



Cycle 2 and beyond



In the clinical trial, pomalidomide 4 mg was taken orally once daily from day 1 to day 21 of each 28-day cycle. Low-dose dexamethasone (orally or IV) 40 mg (20 mg for patients ≥75 years of age) was given on days 1, 8, 15, and 22 for each 28-day cycle.[1]

- Each treatment cycle consists of a 28-day period[1]
- Treatment is repeated until disease progression or unacceptable toxicity[1]
- If a planned dose of SARCLISA is missed, administer the dose as soon as possible and adjust the treatment schedule accordingly, maintaining the treatment interval[1]

See page 6 for information on dose modifications.

Premedication

Administer the following premedications prior to SARCLISA infusion to reduce the risk and severity of infusion-related reactions (IRRs)[1]:

- Dexamethasone 40 mg orally or IV (or 20 mg orally or IV for patients ≥75 years of age)
- Acetaminophen 650 mg to 1000 mg orally (or equivalent)
- H_2 antagonists
- Diphenhydramine 25 mg to 50 mg orally or IV (or equivalent). The IV route is preferred for at least the first 4 infusions

The above recommended dose of dexamethasone (orally or IV) corresponds to the total dose to be administered only once before infusion as part of the premedication and of the backbone treatment, before SARCLISA and pomalidomide administration.[1]

Administer the recommended premedication agents 15 to 60 minutes prior to starting a SARCLISA infusion.[1]

No post-treatment medications are required for SARCLISA

Important Safety Information (cont'd)

Infusion-Related Reactions (cont'd)

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 1 or 2 reactions, interrupt SARCLISA infusion and provide appropriate medical support. If symptoms improve, restart SARCLISA infusion at half of the initial 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 or recur after interruption, permanently discontinue SARCLISA and institute appropriate management. Permanently discontinue SARCLISA if a grade 3 or higher IRR occurs and institute appropriate emergency medical management.

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Preparation for administration

Prepare the solution for infusion using an aseptic technique as follows[1]:

- Calculate the dose (mg) of required SARCLISA based on actual patient weight (measured prior to each cycle to have the administered dose adjusted accordingly)
- More than one SARCLISA vial may be necessary to obtain the required dose for the patient
- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit
- Remove the volume of diluent from the 250-mL sodium chloride injection, USP, or 5% dextrose injection, USP, diluent bag that is equal to the required volume of SARCLISA injection
- Withdraw the necessary volume of SARCLISA injection and dilute by adding to the infusion bag of 0.9% sodium chloride injection, USP, or 5% dextrose injection, USP, to achieve the appropriate SARCLISA concentration for infusion
- The infusion bag must be made of polyolefins (PO), polyethylene (PE), polypropylene (PP), polyvinyl chloride (PVC) with di (2-ethylhexyl) phthalate (DEHP), or ethyl vinyl acetate (EVA)
- Gently homogenize the diluted solution by inverting the bag. Do not shake

Calculating the dose of SARCLISA based on actual patient weight[1]

Dose × Weight		Required dose	Withdrawal amount (20 mg/mL)
10 mg/kg	60 kg	**600 mg** 	**30 mL**
10 mg/kg	80 kg	**800 mg** 	**40 mL**
10 mg/kg	100 kg	**1000 mg** 	**50 mL**

Important Safety Information (cont'd)

Neutropenia

SARCLISA may cause neutropenia. Neutropenia (reported as laboratory abnormality) occurred in 96% of patients and grade 3-4 neutropenia occurred in 85% of patients treated with SARCLISA, pomalidomide, and dexamethasone (Isa-Pd). Febrile neutropenia occurred in 12% of patients, and neutropenic infections, defined as infection with concurrent grade ≥3 neutropenia, occurred in 25% of patients treated with Isa-Pd. The most frequent neutropenic infections included those of upper respiratory tract (10%), lower respiratory tract (9%), and urinary tract (3%).

Infusion rates of SARCLISA administration

Incremental escalation of the infusion rate should be considered only in the absence of IRRs. Refer to the following page for dose modifications.[1]

	Dilution volume	Initial rate	Absence of IRR	Rate increment	Maximum rate	Total time (if no rate adjustments)
First infusion	250 mL	25 mL/h	For 60 min	25 mL/h every 30 min	150 mL/h	**3 h 20 min**
Second infusion	250 mL	50 mL/h	For 30 min	50 mL/h for 30 min, then increase by 100 mL/h every 30 min	200 mL/h	**1 h 53 min**
Subsequent infusions	250 mL	200 mL/h	–	–	200 mL/h	**75 min**

SARCLISA should be administered by a healthcare professional, with immediate access to emergency equipment and appropriate medical support to manage IRRs if they occur.[1]

75-minute infusion time starting after the second infusion in the absence of IRRs[1]

Administering SARCLISA[1]

- Administer the infusion solution by IV infusion using an IV tubing infusion set (in PE, PVC with or without DEHP, polybutadiene [PBD], or polyurethane [PU]) with a 0.22-micron in-line filter (polyethersulfone [PES], polysulfone, or nylon)
- The infusion solution should be administered for a period of time that will depend on the infusion rate. Use prepared SARCLISA infusion solution within 48 hours when stored refrigerated at 36°F to 46°F (2°C to 8°C), followed by 8 hours (including the infusion time) at room temperature
- Do not administer SARCLISA infusion solution concomitantly in the same IV line with other agents

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Dose modifications

No dose reduction of SARCLISA is recommended. Dose delay may be required to allow recovery of blood counts in the event of hematological toxicity. For information concerning drugs given in combination with SARCLISA, see manufacturer's Prescribing Information.[1]

For other medicinal products that are administered with SARCLISA, refer to the respective current Prescribing Information.[1]

Important Safety Information (cont'd)

Neutropenia (cont'd)
Monitor complete blood cell counts periodically during treatment. Consider the use of antibiotics 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 1.0 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
Second primary malignancies were reported in 3.9% of patients in the SARCLISA, pomalidomide, and dexamethasone (Isa-Pd) arm and in 0.7% of patients in the pomalidomide and dexamethasone (Pd) arm, and consisted of skin squamous cell carcinoma (2.6% of patients in the Isa-Pd arm and in 0.7% of patients in the Pd arm), breast angiosarcoma (0.7% of patients in the Isa-Pd arm), and myelodysplastic syndrome (0.7% of patients in the Isa-Pd arm). With the exception of the patient with myelodysplastic syndrome, patients were able to continue SARCLISA treatment. 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). In ICARIA-multiple myeloma (MM), the indirect antiglobulin test was positive during SARCLISA 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. 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 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.

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

Storage and handling

SARCLISA injection is a clear to slightly opalescent, colorless to slightly yellow solution, essentially free of visible particulates, supplied as follows[1]:

- One 100 mg/5 mL single-dose vial in a carton: NDC 0024-0654-01
- One 500 mg/25 mL single-dose vial in a carton: NDC 0024-0656-01

Storage requirements[1]

- Store SARCLISA in a refrigerator at 36°F to 46°F (2°C to 8°C) in the original carton to protect from light
- Do not freeze
- Do not shake

Handling and disposal[1]

Discard unused portion of solution. All materials that have been utilized for dilution and administration should be disposed of according to standard procedures.

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Important Safety Information (cont'd)

Laboratory Test Interference (cont'd)

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 at least 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

The most common adverse reactions (≥20%) were neutropenia (laboratory abnormality, 96% Isa-Pd vs 92% Pd), infusion-related reactions (38% Isa-Pd vs 0% Pd), pneumonia (31% Isa-Pd vs 23% Pd), upper respiratory tract infection (57% Isa-Pd vs 42% Pd), and diarrhea (26% with Isa-Pd vs 19% Pd). Serious adverse reactions occurred in 62% of patients receiving SARCLISA. 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.

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 Important Safety Information throughout, and full Prescribing Information.

Reference: 1. SARCLISA [prescribing information]. Bridgewater, NJ: sanofi-aventis U.S. LLC.

SANOFI GENZYME

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