SARCLISA ESCENA™ (isatuximab-irfc) with CirCLIQ™ and SARCLISA® (isatuximab-irfc) Distribution Guide

SARCLISA ESCENA with CirCLIQ for SC use and SARCLISA for IV use are available from the following authorized specialty distributors:

ASD Healthcare
1.800.746.6273
asdhealthcare.com
Part of AmerisourceBergen Specialty Distribution

McKesson Specialty Health
1.800.482.6700
mckesson.com/specialty/oncology

Cardinal Health Specialty Distribution
1.866.677.4844
specialtyonline.cardinalhealth.com

Morris & Dickson
1.800.388.3833
morrisdickson.com

McKesson Plasma and Biologics
1.877.625.2566
connect.mckesson.com

Oncology Supply
1.800.633.7555
oncologysupply.com
Part of AmerisourceBergen Specialty Distribution

Specialty pharmacies

SARCLISA ESCENA with CirCLIQ for SC use and SARCLISA for IV use are available for the dispensing process from the following authorized specialty pharmacies:

Biologics
1.800.850.4306
1.800.823.4506
biologics.mckesson.com

CVS Specialty
1.800.799.0251
1.855.296.0210
cvsspecialty.com

For additional details or product return inquiries, please contact your Sanofi U.S. Trade Customer Support at 1-800-372-6634.

IV, intravenous; SC, subcutaneous.

Indications for SARCLISA (isatuximab-irfc) **and SARCLISA ESCENA** (isatuximab-irfc)

- SARCLISA and SARCLISA ESCENA are indicated 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)
- SARCLISA and SARCLISA ESCENA are indicated 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
- SARCLISA 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
- SARCLISA ESCENA is indicated in combination with pomalidomide and dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least 1 prior line of therapy including lenalidomide and a proteasome inhibitor

Important Safety Information for SARCLISA and SARCLISA ESCENA

CONTRAINDICATIONS—SARCLISA AND SARCLISA ESCENA

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

Please see additional Important Safety Information on the next page, full Prescribing Information for SARCLISA and SARCLISA ESCENA.

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

SARCLISA ESCENA™ FOR USE WITH CirCLIQ™ On-Body Delivery System (isatuximab-irfc) Injection for subcutaneous use 1,400 mg/10 mL

Important Safety Information for SARCLISA and SARCLISA ESCENA (cont'd)

WARNINGS AND PRECAUTIONS—SARCLISA AND SARCLISA ESCENA

Infusion-Related Reactions—SARCLISA

SARCLISA can cause severe and/or serious infusion-related reactions including anaphylactic reactions. These reactions can be life-threatening and fatal outcomes have been reported. 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.

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.

Hypersensitivity and Other Administration Reactions—SARCLISA ESCENA

SARCLISA ESCENA can cause both systemic administration reactions (SARs), including severe or life-threatening reactions, and local injection-site reactions (ISRs).

Systemic Administration Reactions

In a pooled safety population of 411 patients with multiple myeloma who received SARCLISA ESCENA in combination with pomalidomide and dexamethasone (Pd); carfilzomib and dexamethasone (Kd); and bortezomib, lenalidomide, and dexamethasone (VRd) (IRAKLIA, IZALCO, and IsaSocut, respectively, N=411), SARs occurred in 3.2% (Grade 1: 2.2%, Grade 2: 0.7%, Grade 3: 0.2%) of patients. SARs occurred at the first administration in 1.9% of patients and at subsequent administrations in 1.5% of patients. The median time to onset was 4 hours (range: 12 minutes to 3 days). The most frequently reported symptoms of SARs (all below 1%) were pyrexia and dyspnea, and the most frequently reported Grade ≥3 symptom was dyspnea (not collected in IsaSocut study). In multiple myeloma clinical trials with intravenous isatuximab-irfc, anaphylactic reactions occurred in <1% of patients.

To decrease the risk and severity of SARs, premedicate patients prior to SARCLISA ESCENA administration with leukotriene receptor antagonists (at cycle 1 only), acetaminophen, diphenhydramine or equivalent, and dexamethasone.

In case of grade 2 SAR during SARCLISA ESCENA administration, stop current administration and do not complete it. Administer additional premedication, as needed, for subsequent SARCLISA ESCENA administration. In case of grade 3 SAR during SARCLISA ESCENA administration, stop current administration and do not complete it. SARCLISA ESCENA administration may be resumed at the next planned administration. In case of a third occurrence of a grade 3 SAR, permanently discontinue SARCLISA ESCENA treatment. In case of grade 4 SAR, permanently discontinue SARCLISA ESCENA treatment.

Injection Site Reactions

In clinical trials of SARCLISA ESCENA in combination with Pd, Kd, or VRd (IRAKLIA, IZALCO, and IsaSocut, respectively, N=411), injection site reactions (ISRs) with SARCLISA ESCENA administration were reported in 9% (8% Grade 1 and 1.5% Grade 2) of patients and in 0.86% of injections. Among the SARCLISA ESCENA injections with ISRs, 82% occurred the day of the administration and 4.2% were delayed by at least 3 days. With SARCLISA ESCENA + Pd and SARCLISA ESCENA + Kd, 5% of patients experienced symptoms of ISR (not collected in IsaSocut study). The most frequent (≥1%) symptoms of ISR were injection site erythema (3.3%), injection site swelling (2.1%), and injection site pain (1.5%).

In case of grade 2 ISR during administration of SARCLISA ESCENA, interrupt it and resume it only after recovery to grade ≤1 with pauses during the administration (if using OBDS) or a slower administration (if manual injection). If the Grade 2 ISR occurs after the administration, continue SARCLISA ESCENA treatment after recovery to grade ≤1. In case of grade 3 or 4 ISR, permanently discontinue SARCLISA ESCENA treatment.

In case SARCLISA ESCENA administration using CirCLIQ OBDS needs to be paused, refer to the OBDS Instructions for Use.

Infections—SARCLISA and SARCLISA ESCENA

SARCLISA and SARCLISA ESCENA 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%).

Please see additional Important Safety Information on the next page, full Prescribing Information for SARCLISA and SARCLISA ESCENA.

Important Safety Information for SARCLISA and SARCLISA ESCENA (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Infections—SARCLISA and SARCLISA ESCENA (cont'd)

In patients who received SARCLISA ESCENA subcutaneously in combination with Pd, Kd, or VRd (IRAKLIA, IZALCO, and IsaSocut, respectively, N=411), fatal infections occurred in 2.9% of patients, serious infections occurred in 29% of patients, and Grade ≥3 infections occurred in 29% of patients. The most commonly reported infections (≥10%) were pneumonia (21%), upper respiratory tract infection (19%), and COVID-19 (12%). The most frequent serious infection (≥5%) was pneumonia (17%).

Patients receiving SARCLISA or SARCLISA ESCENA should be closely monitored for signs and symptoms of infection prior to and during treatment and appropriate standard therapy instituted. Administer prophylactic antimicrobials according to guidelines. Antibacterial and antiviral prophylaxis (such as herpes zoster prophylaxis) should be considered during treatment.

Neutropenia—SARCLISA and SARCLISA ESCENA

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%.

Neutropenia was reported in patients receiving SARCLISA ESCENA subcutaneously in combination with Pd, Kd, or VRd. In clinical trials of SARCLISA ESCENA (IRAKLIA, IZALCO, and IsaSocut, N=411), neutropenia occurred in 86% of patients based on laboratory value. Grade 3-4 neutropenia occurred in 66% of patients based on laboratory value. Febrile neutropenia was reported in 3.4% and neutropenic infections occurred in 13% of patients.

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 or delay or omit SARCLISA ESCENA 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 are recommended.

Second Primary Malignancies—SARCLISA and SARCLISA ESCENA

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.

Second primary malignancies were reported in 3.9% of patients in clinical trials with SARCLISA ESCENA in combination with Pd, Kd, and VRd (IRAKLIA, IZALCO, and IsaSocut, respectively, N=411).

Monitor patients for the development of second primary malignancies and initiate treatment as indicated.

Laboratory Test Interference—SARCLISA AND SARCLISA ESCENA

Interference with Serological Testing (Indirect Antiglobulin Test)

Isatuximab-irfc 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 at least 6 months after the last administration of intravenous isatuximab-irfc. The indirect antiglobulin test was positive during intravenous isatuximab-irfc + Pd treatment in 68% of the tested patients, and during intravenous isatuximab-irfc + 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 intravenous isatuximab-irfc treatment.

Before the first isatuximab-irfc administration, conduct blood type and screen tests on isatuximab-treated patients. Consider phenotyping prior to starting isatuximab-irfc treatment. If treatment with isatuximab-irfc has already started, inform the blood bank that the patient is receiving isatuximab-irfc, and isatuximab-irfc 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

Isatuximab-irfc is an IgG kappa monoclonal antibody that can be incidentally detected on both serum protein electrophoresis and immunofixation assays (IFE) 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. In patients with persistent very good partial response, where interference is suspected, consider using a validated isatuximab-specific IFE assay (Sebia Hydrashift) to remove isatuximab-irfc interference and specifically visualize any remaining serum M-protein, to facilitate determination of complete response.

Please see additional Important Safety Information on the next page, full Prescribing Information for SARCLISA and SARCLISA ESCENA.

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

SARCLISA ESCENA™ (isatuximab-irfc) Injection for subcutaneous use 1,400 mg/10 mL FOR USE WITH CirCLIQ™ On-Body Delivery System

Important Safety Information for SARCLISA and SARCLISA ESCENA (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Embryo-Fetal Toxicity—SARCLISA and SARCLISA ESCENA

Based on its mechanism of action, isatuximab-irfc can cause fetal harm when administered to a pregnant woman. Isatuximab-irfc may cause fetal immune cell depletion and decreased bone density. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with isatuximab-irfc and for 7 months after the last dose. The combination of isatuximab-irfc 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—SARCLISA

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.

Serious adverse reactions occurred in 62% of patients receiving Isa-IV + Pd. Serious adverse reactions in >5% of patients who received Isa-IV + 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-IV + Kd. The most frequent serious adverse reactions in >5% of patients who received Isa-IV + 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-IV + 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-IV + VRd. The serious adverse reaction in >5% of patients who received Isa-IV + VRd was pneumonia (30%). Fatal adverse reactions occurred in 11% of patients with Isa-IV + VRd (those occurring in more than 1% of patients were pneumonia [5%]).

ADVERSE REACTIONS—SARCLISA ESCENA

In combination with pomalidomide and dexamethasone: The most common adverse reactions (≥20%) are upper respiratory tract infection, fatigue, pneumonia, musculoskeletal pain, and diarrhea.

In combination with carfilzomib and dexamethasone: The most common adverse reactions (≥20%) are upper respiratory tract infection and musculoskeletal pain.

In combination with bortezomib, lenalidomide, and dexamethasone: The most common adverse reactions (≥20%) are peripheral neuropathy, constipation, diarrhea, fatigue, musculoskeletal pain, upper respiratory tract infections, injection site reaction, insomnia, edema, rash, and erythema.

The most common hematology laboratory abnormalities (≥40%) with SARCLISA ESCENA combination therapies are decreased neutrophils, decreased platelets, decreased hemoglobin, decreased leukocytes, and decreased lymphocytes.

Serious adverse reactions occurred in 53% of patients receiving SARCLISA ESCENA + Pd. Serious adverse reactions in ≥5% of patients who received SARCLISA ESCENA + Pd included pneumonia (20.5%). Fatal adverse reactions occurred in 4.9% of patients who received SARCLISA ESCENA + Pd, including pneumonia (1.5%), sepsis/septic shock (1.5%), death (0.8%), COVID-19, lower respiratory tract infection, hemorrhagic stroke, and sudden death (0.4% each).

Serious adverse reactions occurred in 41% of patients receiving SARCLISA ESCENA+ Kd. Serious adverse reactions in ≥5% of patients included pneumonia (11%). Fatal adverse reactions occurred in 5.4% of patients who received SARCLISA ESCENA + Kd, including meningitis (1.4%), acute pulmonary edema (1.4%), acute respiratory distress syndrome (1.4%), and death from unknown cause (1.4%).

Serious adverse reactions occurred in 45% of patients who received SARCLISA ESCENA + VRd. Serious adverse reactions in >5% of patients included pneumonia (8%). Fatal adverse reactions occurred in 2.7% of patients who received SARCLISA ESCENA + VRd, including cardio-respiratory arrest (1.4%) and myocardial infarction (1.4%).

USE IN SPECIAL POPULATIONS—SARCLISA and SARCLISA ESCENA

Based on its mechanism of action, SARCLISA and SARCLISA ESCENA can cause fetal harm when administered to a pregnant woman. There are no available data on SARCLISA or SARCLISA ESCENA use in pregnant women to evaluate for a drug-associated risk.

The combination of SARCLISA or SARCLISA ESCENA and pomalidomide or lenalidomide is contraindicated in pregnant women because pomalidomide and lenalidomide may cause birth defects and death of the unborn child. Refer to the pomalidomide or lenalidomide prescribing information on use during pregnancy. Pomalidomide and lenalidomide are only available through a REMS program.

Because of the potential for serious adverse reactions in a breastfed child, advise patients not to breastfeed during treatment and for 7 months after the last dose.

Please see accompanying full Prescribing Information for SARCLISA and SARCLISA ESCENA.

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SARCLISA ESCENA™ (isatuximab-irfc) Injection for subcutaneous use 1,400 mg/10 mL FOR USE WITH CirCLIQ™ On-Body Delivery System