SARCLISA ESCENA™ (isatuximab-irfc) with CirCLIQ™ Returns & Replacements Request Checklist

For Healthcare Professionals

INDICATIONS

SARCLISA ESCENA (isatuximab-irfc) is 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)
- 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 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

Purpose

This checklist is designed to support healthcare professionals when submitting a SARCLISA ESCENA with CirCLIQ replacement request for the device or vial, which are packaged separately. Providing complete and accurate information will help expedite review and minimize delays. This guide is for SARCLISA ESCENA ONLY.

Product Replacement Eligibility Criteria

A replacement request may be submitted if all of the following conditions are met:

Qualifying Circumstances

The SARCLISA ESCENA with CirCLIQ device or vial experienced one of the following:

- ☐ Mishandling, dropping, or breakage after delivery
- ☐ Improper storage or refrigeration (eg, power outage, refrigeration failure, storage outside labeled conditions)
- ☐ Error during preparation
- ☐ Product prepared but not administered due to an unforeseen patient condition or missed appointment

Additional Requirements

- ☐ No portion of the product was administered to a patient or billed to any third party
- ☐ An active SARCLISA ESCENA with CirCLIQ prescription was in place at the time of the event
- ☐ Product was prescribed for an on-label indication
- ☐ Product was purchased from a Sanofi-authorized specialty distributor or pharmacy (or acquired via **CareASSIST™ Patient Assistance Program**)

All replacement requests are subject to review and approval by Customer Relations Management.

Please note, some of the circumstances above may represent adverse events/product technical complaints and should be reported through standard Pharmacovigilance channels in accordance with regulatory requirements.

Program Limitations & Timing

One replacement request per product may be submitted at a time per healthcare provider. Device and vial require separate requests

Refrigeration-related replacements are **limited to 3 vials** within a rolling 12-month period

Replacement requests must be **submitted within 30 days** of the incident

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IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

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

Please see additional Important Safety Information throughout, and full Prescribing Information for SARCLISA ESCENA.

SARCLISA ESCENA™ (isatuximab-irfc)
Injection for subcutaneous use
1,400 mg/10 mL

FOR USE WITH CirCLIQ™ On-Body Delivery System

Required Information Checklist

Please ensure the following information is available before submitting a request:

Organization Information

- ☐ Full organization/facility name
- ☐ Department name (if applicable)
- ☐ Facility ID number (if applicable)

Shipping Information

- ☐ Complete shipping address
- ☐ Building, floor, or room number (if applicable)
- ☐ Special delivery instructions (if applicable)

Contact Information

- ☐ Primary contact name
- ☐ Primary contact title/position
- ☐ Primary contact phone number
- ☐ Primary contact email address
- ☐ Secondary/alternate contact (recommended)

Product & Incident Details

- ☐ Product serial number
- ☐ Date issue was identified
- ☐ Detailed description of the issue or malfunction

How to Submit a Replacement Request

1. Compile all required information listed above

2. Using the subject line "Replacement Request," submit the request via email to your Key Account Manager (KAM) or Regional Business Director (RBD). For PAP patients, submit to your **CareASSIST**™ Case Manager.

   Alternatively, you may call the Sanofi Medical Information Center at 1-800-633-1610 and provide the required information. Please note: during this call, you must state that you are requesting a replacement

Requests should be submitted within 24 hours of identifying the issue, when possible.
If both **device and vial** require replacements, **2 separate requests must be submitted**.

Additional Notes

- Retain the original packaging
- A return shipping label will be provided upon verification of replacement eligibility and after receipt of the affected product
- Incomplete submissions may delay processing

PAP, patient assistance program.

This guide is for SARCLISA ESCENA ONLY.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS

Hypersensitivity and Other Administration Reactions

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

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WARNINGS AND PRECAUTIONS

Hypersensitivity and Other Administration Reactions

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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.

Neutropenia

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. Monitor patients with neutropenia for signs of infection. In case of grade 4 neutropenia, delay or omit SARCLISA ESCENA dose until neutrophil count recovery to at least 1×10^9/L, and provide supportive care with growth factors, according to institutional guidelines.

Infections

SARCLISA ESCENA can cause severe, life-threatening, or fatal infections. 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 ESCENA should be closely monitored for signs of infection and appropriate standard therapy instituted.

Antibacterial and antiviral prophylaxis (such as herpes zoster prophylaxis) should be considered during treatment.

Second Primary Malignancies

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.

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IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Laboratory Test Interference

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. 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.

Embryo-Fetal Toxicity

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

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

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

The combination of 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 with SARCLISA ESCENA and for 7 months after the last dose.

Please see accompanying full Prescribing Information.

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