

Updating order sets with **SARCLISA ESCENA™** (isatuximab-irfc) injection, for subcutaneous use **Instructions for the Epic® EHR system**

EHR, electronic health record.

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

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

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

Please see Important Safety Information throughout
and full [Prescribing Information](#).

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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).

Please see Important Safety Information throughout and full [Prescribing Information](#).

1 Overview and limitations

This document is intended to provide health systems with instructions to update order sets with SARCLISA ESCENA™ with CirCLIQ™ in the Epic® electronic health record (EHR) system, within the approved indications and consistent with Prescribing Information.

These instructions are specific to SARCLISA ESCENA. This guide is for the Epic EHR system. This guide is not appropriate for other conditions, treatments, or therapeutic areas for any other EHR system.

The process outlined in this document is variable, and not all steps will apply to every organization. Any steps or settings that are not part of an organization's standard process should be excluded or modified accordingly. Any questions should be directed to the appropriate service provider. The organization is solely responsible for implementing, testing, monitoring, and the ongoing operation of any EHR tools.

2 Background and indications

Sanofi is providing its customers with information needed to update health system EHR order sets with SARCLISA ESCENA.

INDICATIONS

SARCLISA ESCENA (isatuximab-irfc) is a CD38-directed cytolytic antibody 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
- 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 (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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.

Please see Important Safety Information throughout and full [Prescribing Information](#).

3 Considerations

Suggested order set content

Key clinical details from the SARCLISA ESCENA™ Prescribing Information are included below and may be incorporated as part of the order set update based on steps in the *Instructions* section that follows. Details chosen here from the Prescribing Information data serve as suggestions, and it is strongly recommended that clinical and operational leadership align the order set contents with the expectations and goals of the organization. The organization may add or edit any details, as desired, to align with governing EHR policies and standards.

Please consult the most recent version of the SARCLISA ESCENA [Prescribing Information](#) for full medication details.

EHR, electronic health record.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Systemic Administration Reactions (cont'd)

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.

Please see Important Safety Information throughout and full [Prescribing Information](#).

3 Considerations (cont'd)

Dosage and administration

Recommended dosage

- Administer premedications before SARCLISA ESCENA™ administration [see *Dosage and Administration* (2.3)]
- SARCLISA ESCENA should be administered by a healthcare provider [see *Warnings and Precautions* (5.1)]
- Patients currently receiving SARCLISA® IV (isatuximab-irfc) may transition to SARCLISA ESCENA solution for injection after the completion of the first cycle

The recommended dose of SARCLISA ESCENA is 1,400 mg administered as a subcutaneous injection with the CirCLIQ™ On-Body Delivery System (OBDS) or with a syringe and injection set for manual administration, in combination with pomalidomide and dexamethasone, or in combination with carfilzomib and dexamethasone, or in combination with bortezomib, lenalidomide, and dexamethasone.

SARCLISA ESCENA is used in combination with pomalidomide and dexamethasone, or in combination with carfilzomib and dexamethasone, or in combination with bortezomib, lenalidomide, and dexamethasone.

SARCLISA ESCENA dosing schedules are provided in Tables 1 and 2 [see *Clinical Studies* (14)].

Table 1: SARCLISA ESCENA dosing schedule in combination with pomalidomide and dexamethasone or in combination with carfilzomib and dexamethasone

Cycles	Dosing schedules
Cycle 1 (28-day cycle)	Days 1, 8, 15, and 22 (weekly)
Cycle 2 and beyond (28-day cycles)	Days 1, 15 (every 2 weeks)

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Systemic Administration Reactions (cont'd)

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.

Please see Important Safety Information throughout and full [Prescribing Information](#).

3 Considerations (cont'd)

Table 2: SARCLISA ESCENA™ dosing schedule in combination with bortezomib, lenalidomide, and dexamethasone

Cycles	Dosing schedules
Cycle 1 (28-day cycle)	Days 1, 8, 15, 22 (weekly)
Cycles 2 to 12 (28-day cycles)	Days 1 and 15 (every 2 weeks)
Cycles 13 and beyond (28-day cycles)	Day 1 (every 4 weeks)

Treatment is repeated until disease progression or unacceptable toxicity.

For dosing instructions of combination agents administered with SARCLISA ESCENA, see *Clinical Studies (14)* and manufacturers' Prescribing Information.

Missed SARCLISA ESCENA doses

If a planned dose of SARCLISA ESCENA is missed, administer the dose as soon as possible and adjust the treatment schedule accordingly, maintaining the treatment interval.

IV, intravenous; PO, by mouth.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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 ($\geq 1\%$) symptoms of ISR were injection site erythema (3.3%), injection site swelling (2.1%), and injection site pain (1.5%).

Please see Important Safety Information throughout and full [Prescribing Information](#).

3 Considerations (cont'd)

Recommended premedications and antimicrobial prophylaxis

Recommended premedications

Administer the following premedications 15 to 60 minutes prior to SARCLISA ESCENA™ administration to reduce the risk and severity of systemic administration reactions [see *Warnings and Precautions* (5.1)]:

- When administered in combination with SARCLISA ESCENA and pomalidomide:
Dexamethasone 40 mg PO or IV (or 20 mg PO or IV for patients 75 years of age or older)
- When administered in combination with SARCLISA ESCENA and carfilzomib: Dexamethasone 20 mg PO or IV
- When administered in combination with SARCLISA ESCENA, bortezomib, and lenalidomide:
 - Dexamethasone 20 mg PO
 - Leukotriene receptor antagonists, at Cycle 1 only (Days 1, 8, 15, and 22)
 - Acetaminophen 650 mg to 1,000 mg PO
 - Diphenhydramine 25 mg to 50 mg PO or IV (or equivalent). The IV route of diphenhydramine is preferred for at least the first 4 administrations of SARCLISA ESCENA

The recommended dose of dexamethasone (PO or IV) corresponds to the total dose to be administered before SARCLISA ESCENA administration as part of the premedication and part of the backbone treatment [see *Clinical Studies* (14)].

If no systemic administration reaction occurs during Cycle 1, assess patient-specific factors and consider omitting subsequent premedication during future treatment cycles.

Recommended antimicrobial prophylaxis

Initiate antibacterial and antiviral prophylaxis (such as herpes zoster prophylaxis) if needed based on standard guidelines [see *Warnings and Precautions* (5.2, 5.3)].

Dosage modifications for adverse reactions

No dose reduction of SARCLISA ESCENA is recommended. Dose delay or omission may be required [see *Warnings and Precautions* (5.1, 5.2)].

Preparation and administration

For complete preparation and administration instructions, see sections 2.5 and 2.6 of the SARCLISA ESCENA Prescribing Information.

IV, intravenous; PO, by mouth.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Injection Site Reactions (cont'd)

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.

Please see Important Safety Information throughout and full [Prescribing Information](#).

4 Instructions

An existing Beacon protocol may be used as the foundation for a new one. Consider modifying an existing protocol that includes SARCLISA as a starting template, while saving the original protocol.

There are 3 main steps to updating a Beacon protocol in the Epic EHR system:

Step 1: Create or update the order groups

1. Review the Regimen Category Order Group to confirm Medications, Premedications, Treatment Conditions, and Supportive Medications are values in the category list
2. Select the Order Group Builder (Admin > Beacon Admin > Order Group Builder)
3. Create the new order groups (see examples on the following page)

EHR, electronic health record.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Injection Site Reactions (cont'd)

In case SARCLISA ESCENA administration using CirCLIQ OBDS needs to be paused, refer to the OBDS [Instructions for Use](#).

Please see Important Safety Information throughout and full [Prescribing Information](#).

4 Instructions (cont'd)

1A: SARCLISA ESCENA™

1. Review the Regimen Category Order Group to confirm Medications is a value in the category list
2. Select the Order Group Builder (Admin > Beacon Admin > Order Group Builder)
3. Create a new order group named “SARCLISA ESCENA”
4. Set the default category to Medications
5. Add the details for SARCLISA ESCENA™ to the order group:
 - Right click in the empty field at the bottom of the window
 - Select Add Orders > Choose SARCLISA ESCENA
 - Complete the medication details for SARCLISA ESCENA [see *Dosage and Administration* (2) or *Recommended Dosage* (2.2)]

1B: SARCLISA ESCENA premedications

1. Review the Regimen Category Order Group to confirm Medications is a value in the category list
2. Select the Order Group Builder (Admin > Beacon Admin > Order Group Builder)
3. Create a new order group named “SARCLISA ESCENA Premedications”
4. Set the default category to Premedications
5. Add the details for SARCLISA ESCENA premedications to the order group:
 - Right click in the empty field at the bottom of the window
 - Select Add Orders > Choose the premedications the organization wants to include in the order group
 - Enter the desired premedication details for SARCLISA ESCENA [see *Recommended Premedications and Antimicrobial Prophylaxis* (2.3)]
6. Once all the desired information is added, release and publish the order group

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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.

Please see Important Safety Information throughout and full [Prescribing Information](#).

4 Instructions (cont'd)

1C: SARCLISA ESCENA™ antimicrobial prophylaxis

1. Review the Regimen Category Order Group to confirm Medications is a value in the category list
2. Select the Order Group Builder (Admin > Beacon Admin > Order Group Builder)
3. Create a new order group named “SARCLISA ESCENA Antimicrobial Prophylaxis”
4. Set the default category to Antimicrobial Prophylaxis
5. Add the details for SARCLISA ESCENA Antimicrobial Prophylaxis to the order group:
 - Right click in the empty field at the bottom of the window
 - Select Add Orders > Choose the antimicrobial prophylaxis medication the organization wants to include in the order group
 - Enter the desired premedication details for SARCLISA ESCENA [see *Recommended Premedications and Antimicrobial Prophylaxis* (2.3)]
6. Once all the desired information is added, release and publish the order group

Additional order groups

- Add the other desired order groups for SARCLISA ESCENA. Consider the Prescribing Information below for other order groups:
 - No dose reduction of SARCLISA ESCENA is recommended. Dose delay or omission may be required [see *Warning and Precautions* (5.1, 5.2)]
 - For warnings and precautions, see Section 5 of the Prescribing Information
 - For adverse reactions, see Section 6 of the Prescribing Information

SARCLISA ESCENA - Therapy Protocol Builder

Open Save Save As Restore Test Release Release Publish Retro

Sarclisa Test

Add a new order + Order Add a new order group + Order Group Edit Interval Show IDs

	Interval	Defer Until	Duration	
☐ SARCLISA ESCENA				Move Up RZ Sort
☐ Isatuximab-irfc (SARCLISA ESCENA) injection 1,400 mg 1,400 mg, Subcutaneous, ONCE, 1 dose	Treatments: 1	S	Until discontinued	X
☐ Nursing Communication The recommended dose of SARCLISA ESCENA is 1,400 mg administered as subcutaneous injection with the CirqLIO OBD3 or with a syringe and infusion set for manual administration, in combination with pomalidomide and dexamethasone, or in combination with carfilzomib and dexamethasone, or in combination with bortezomib, lenalidomide, and dexamethasone	Treatments: 1	S	Until discontinued	X
Premedications and Antimicrobial Prophylaxis When administered in combination with SARCLISA ESCENA and pomalidomide: Dexamethasone 40 mg orally or intravenously (or 20 mg orally or intravenously for patients ≥75 years of age) • When administered in combination with SARCLISA ESCENA and carfilzomib: Dexamethasone 20 mg orally or intravenously • When administered in combination with SARCLISA ESCENA, bortezomib, and lenalidomide: - Dexamethasone 20 mg orally - Leukotriene receptor antagonists, at cycle 1 only - Acetaminophen 650 mg to 1,000 mg orally (or equivalent) - Diphenhydramine 25 mg to 50 mg orally or intravenously (or equivalent). The intravenous route of diphenhydramine is preferred for at least the first 4 administrations of SARCLISA ESCENA	Treatments: 1	S	Until discontinued	X

This image is intended for illustrative purposes only

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Neutropenia (cont'd)

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 $1 \times 10^9/L$, and provide supportive care with growth factors, according to institutional guidelines.

Please see Important Safety Information throughout and full [Prescribing Information](#).

4 Instructions (cont'd)

Step 2: Add links for the Prescribing Information and other resources

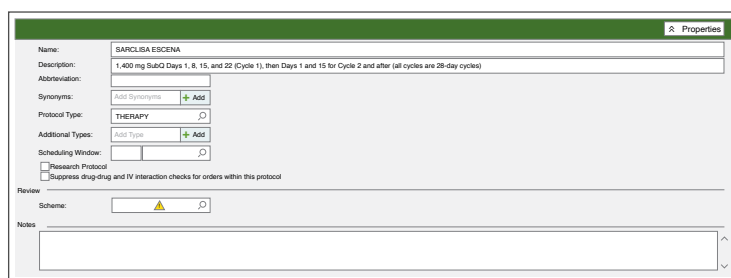
1. Log in to the Medication Master File (ERX) with authorized user credentials
2. Use the search feature in the Medication Master File to search for and select the desired SARCLISA ESCENA™ product
3. Select the Patient Medication References screen and create 2 new rows:
 - i. Row 1: For Display Name, enter “SARCLISA ESCENA Prescribing Information.” In the Text field, enter “See URL for additional SARCLISA ESCENA Prescribing Information.” In the URL field, enter this hyperlink: <https://products.sanofi.us/sarclisa-escena/sarclisa-escena.pdf>
 - ii. Row 2: For Display Name, enter “Additional Resources for HCPs and Patients.” In the Text field, enter “See URL for additional resources for HCPs and patients.” In the URL field, enter this hyperlink: <https://pro.campus.sanofi/us/products/sarclisa/clinical-access-resources>
4. Save the medication record
5. Release the record to the production environment after completing testing

Step 3: Add the order groups created in Step 1 to the new Beacon protocol

1. Click the Epic logo > Admin > Beacon Admin > Protocol Builder
2. Search for Beacon protocols using the search query and enter search terms specific to each indication. Note that an existing SARCLISA protocol may be available to optimize

Note: The existing Beacon protocol will only serve as a template for the new SARCLISA ESCENA with CirCLIQ™ protocol.

If the original protocol used to create the new SARCLISA ESCENA with CirCLIQ protocol includes SARCLISA ESCENA with CirCLIQ, confirm it is retired or removed from the EHR production system according to the organization's EHR governing principles

The image shows a screenshot of the 'Properties' window for a Beacon protocol in the Epic system. The window has a green header bar with the title 'Properties'. Below the header, there are several input fields and checkboxes. The 'Name' field contains 'SARCLISA ESCENA'. The 'Description' field contains '1,400 mg SubQ Days 1, 8, 15, and 22 (Cycle 1), then Days 1 and 15 for Cycle 2 and after (all cycles are 28-day cycles)'. There are 'Add Synonyms' and 'Add' buttons next to the 'Synonyms' field. The 'Protocol Type' is set to 'THERAPY'. There are 'Add Type' and 'Add' buttons next to the 'Additional Types' field. The 'Scheduling Window' field is empty. There are checkboxes for 'Research Protocol' and 'Suppress drug-drug and IV interaction checks for orders within this protocol'. The 'Reviewer' field is empty. The 'Scheme' field has a dropdown menu with a yellow triangle icon. The 'Notes' field is a large text area at the bottom.

This image is intended for illustrative purposes only

EHR, electronic health record; HCP, healthcare provider.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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%).

Please see Important Safety Information throughout and full [Prescribing Information](#).

4 Instructions (cont'd)

3. In the Treatment Regimen Calendar, select 28 for the number of days in each cycle (4-week cycle)
4. Add all the newly created order groups from Step 1 to the treatment regimen (order groups with SARCLISA ESCENA™ with CirCLIQ™, the premedications, and other order groups) to the treatment calendar and protocol [see *Tables 1 and 2 in Recommended Dosage (2.2) and Recommended Premedications and Antimicrobial Prophylaxis (2.3)*]

5. Update the Beacon treatment plan name as desired, for example:

- a. “2L MM with SARCLISA ESCENA in combination with pomalidomide and dexamethasone (Isa-Pd)”
- b. “2L RRMM with SARCLISA ESCENA in combination with carfilzomib and dexamethasone (Isa-Kd)”
- c. “1L NDMM, not eligible for ASCT, with SARCLISA ESCENA in combination with bortezomib, lenalidomide, and dexamethasone (Isa-VRd)”

6. Update the Beacon treatment plan description as desired
7. Add any desired synonyms to the treatment plan to help ease the search process for providers when searching for appropriate treatment plans
8. Click “Save”
9. Release the Beacon protocol to the production environment after completing testing

This image is intended for illustrative purposes only

1L, first line; 2L, second line; ASCT, autologous stem cell transplant; MM, multiple myeloma; NDMM, newly diagnosed multiple myeloma; RRMM, relapsed/refractory multiple myeloma.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Infections (cont'd)

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.

Please see Important Safety Information throughout and full [Prescribing Information](#).

5 Notes

- The customer (eg, physician, medical group, integrated delivery network) shall be solely responsible for the implementation, testing, and monitoring of the instructions to ensure proper orientation in each customer's EHR system
- Capabilities, functionality, and setup (customization) for each EHR system may vary. Sanofi shall not be responsible for revising the implementation instructions it provides to any customer if the customer modifies or changes its software or the configuration of its EHR system after such time as the implementation instructions have been initially provided by Sanofi
- While Sanofi tests its implementation instructions on multiple EHR systems, the instructions are not guaranteed to work for all available EHR systems, and Sanofi shall have no liability thereto
- While EHRs may assist providers in identifying appropriate patients for consideration of assessment, treatment, and referral, the decision and action should ultimately be decided by a provider in consultation with the patient, after a review of the patient's records to determine eligibility, and Sanofi shall have no liability thereto
- The instructions have not been designed for, and are not tools and/or solutions for, meeting Advancing Care Information and/or any other quality/accreditation requirement
- All products are trademarks of their respective holders, all rights reserved. Reference to these products is not intended to imply affiliation with or sponsorship of Sanofi and/or its affiliates

EHR, electronic health record.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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.

Please see Important Safety Information throughout and full [Prescribing Information](#).

6 Important Safety Information

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

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

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

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).

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.

Please see Important Safety Information throughout and full [Prescribing Information](#).

6 Important Safety Information (cont'd)

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 ($\geq 1\%$) 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 $1 \times 10^9/L$, 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 ($\geq 10\%$) were pneumonia (21%), upper respiratory tract infection (19%), and COVID-19 (12%). The most frequent serious infection ($\geq 5\%$) 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.

6 Important Safety Information (cont'd)

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.

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.

Please see Important Safety Information throughout and full [Prescribing Information](#).

6 Important Safety Information (cont'd)

ADVERSE REACTIONS

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

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

In combination with bortezomib, lenalidomide, and dexamethasone: The most common adverse reactions ($\geq 20\%$) 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 ($\geq 40\%$) 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 $\geq 5\%$ 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 $\geq 5\%$ 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 full [Prescribing Information](#).

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

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