

Administration of Subcutaneous Isatuximab-irfc (SARCLISA ESCENA™) via the CirCLIQ On-Body Delivery System

Description: The purpose of this document is to discuss clinical considerations and general management of subcutaneous isatuximab-irfc administration via the CirCLIQ™ On-Body Delivery System (OBDS) in patients with multiple myeloma

Background¹:

- Isatuximab-irfc is an IgG1-derived monoclonal antibody against CD38, a cell-surface glycoprotein expressed highly in multiple myeloma cells. Binding to CD38 elicits tumor cell apoptosis, immune-mediated cytotoxicity, antibody-dependent cellular phagocytosis, and complement dependent cytotoxicity.
- FDA approved indications
 - In combination with pomalidomide and dexamethasone for treatment of adult multiple myeloma patients with at least 1 prior line of therapy including lenalidomide and a proteasome inhibitor
 - In combination with carfilzomib and dexamethasone for treatment of adult multiple myeloma patients with 1-3 prior lines of therapy
 - In combination with bortezomib, lenalidomide, and dexamethasone for treatment of newly diagnosed, non-transplant eligible adult multiple myeloma patients
- Adverse reactions
 - Most common laboratory abnormalities ($\geq 30\%$) with subcutaneous isatuximab-irfc (SARCLISA ESCENA™) combination therapy: Decreased lymphocytes, leukocytes, platelets, neutrophils, hemoglobin; Increased alkaline phosphatase, alanine aminotransferase, creatinine; Decreased calcium, magnesium, albumin, sodium
 - Other adverse reactions occurring $\geq 20\%$: Upper respiratory tract infection, pneumonia, constipation, diarrhea, fatigue, insomnia, musculoskeletal pain, peripheral neuropathy, injection site reaction, rash, erythema, edema
 - Systemic administration reactions: Occurred in 3.2% (grade 3 in 0.2%). These occurred at first administration in 1.9% of patients, with median time to onset of 4 hours (range 12 minutes to 3 days). Most commonly, these reactions were dyspnea and pyrexia. Anaphylaxis occurred in $<1\%$.
 - Injection site reactions: Occurred in 9% (no grade 3 or higher reactions) of patients and 0.86% of injections. These reactions were mostly on day of administration (82%), with erythema, swelling, and pain as the most common symptoms

PQI Process:

- Verify indication, treatment regimen, and formulation of isatuximab-irfc (subcutaneous and intravenous are **not** interchangeable)
 - Dose: 1,400 mg administered as a subcutaneous injection via the CirCLIQ™ OBDS
 - Administered in a healthcare setting by a trained professional – not for self-administration

IMPORTANT NOTICE: NCODA has developed this Positive Quality Intervention platform. This platform is intended as an educational aid, does not provide individual medical advice, and does not substitute for the advice of a qualified healthcare professional. This platform does not cover all existing information related to the possible uses, directions, doses, precautions, warning, interactions, adverse effects, or risks associated with the medication. The materials contained in this platform do not constitute or imply endorsement, recommendation, or favoring of this medication by NCODA. NCODA does not ensure the accuracy of the information presented and assumes no liability relating to its accuracy. All decisions related to taking this medication should be made with the guidance and under the direction of a qualified healthcare professional. It is the individual's sole responsibility to seek guidance from a qualified healthcare professional. *Updated 7.16.2026 PQI-296*

- Schedule:

Table 1. Dosing Schedule

Cycles (28-day)	Frontline	Relapsed/refractory
Cycle 1	Days 1, 8, 15, 22	Days 1, 8, 15, 22
Cycles 2-12	Days 1, 15	Days 1, 15
Cycles 13+	Day 1	Days 1, 15

- Verify premedications and hypersensitivity management protocols are in place
 - Administer recommended premedications 15-60 minutes prior to each dose
 - Dexamethasone 40 mg by mouth or IV. For patients ≥ 75 years of age or when given in combination with carfilzomib or bortezomib and lenalidomide, give dexamethasone 20 mg.
 - Acetaminophen 650 or 1,000 mg by mouth
 - Diphenhydramine 25-50 mg (or equivalent) by mouth or IV (IV preferred for first 4 administrations)
 - Leukotriene receptor antagonist (e.g.: montelukast 10 mg) (days 1, 8, 15, and 22 of cycle 1 only)
 - If no systemic administration reactions occur during cycle 1, may consider omitting subsequent premedication based on patient specific factors
- Consider need for antiviral and/or antibacterial prophylaxis
 - If indicated, initiate herpes zoster infection prophylaxis within 1 week of starting therapy and continue for 3 months after completion
 - Screen for hepatitis B virus prior to initiation and monitor for reactivation or provide prophylaxis if indicated
- Verify baseline labs, treatment parameters, concomitant medications, and allergies. The on-body device contains acrylic.
- Obtain baseline blood type and screen
 - Notify blood banks as isatuximab-irfc may interfere with indirect antiglobulin testing, which may be resolved using dithiothreitol-treated RBC's
- Prior to preparation, assemble components for administration
 - CirCLIQ™ OBDS: this should contain one 10 mL injector and one filling base
 - Isatuximab-irfc vial. This is not included in the delivery system. Confirm vial labels match the intended formulation. The subcutaneous formulation vial has a green cap.
- Preparation
 - Refer to supplemental materials (page 4) for detailed instructions on preparation and storage
 - Injection must be completed within 4 hours after vial is punctured
 - The filling status can be monitored with the fill window with red fill gauge
- Administration
 - Refer to supplemental materials for detailed instructions on administration
 - Injection must be completed within 4 hours after vial is punctured
 - Choose a flat injection site on bare skin around the abdomen that belts, waistbands, or tight clothing will not disturb
 - Change (rotate) the site of each subcutaneous administration– at least 1 inch from previous injection site- with every injection to avoid accumulation of fatty tissue.
 - Do not remove the red safety tab until device is attached to the body and you are ready to inject
 - The injection status can be monitored with the fill window with red fill gauge

- Medication injection typically takes up to 20 minutes but may take up to 60 minutes. The injection button pops out when injection is complete
- Monitor for systemic administration and injection site reactions
- To pause the injection: press and hold the injection button. Delivery resumes when button is released
- If the button has not popped out after 60 minutes, slowly remove the on-body injector from skin. Do not touch the needle or any medicine that may be on the Injector. Call Sanofi at 1-800-633-1610 for further help or assistance.

Table 2. Management of Administration Adverse Reactions

Severity	Systemic Administration Reactions	Injection Site Reactions
Grade 1	Continue administration	Continue administration
Grade 2	Discontinue current administration. Administer additional premedications as needed for subsequent administration	Interrupt current administration. Resume after recovery to Grade ≤1 with pauses during administration (to pause the injection, press and hold the injection button)
Grade 3	Same as grade 2. Upon 3 rd Grade 3 occurrence, permanently discontinue	Permanently discontinue
Grade 4	Permanently discontinue	Permanently discontinue

- Additional considerations for On-Body Delivery System
 - A hands-free delivery system may reduce the physical administration effort and free up nursing staff for other tasks
 - A transfer device may reduce compounding complexity, supplies, time, and effort.
 - A thinner, hidden needle may decrease risk of patient phobia
 - An on-body device for administration may allow for more patient privacy and increased ambulation during infusion
 - Additional supplies and staff training are required to prepare, use, store, and dispose of a novel delivery system
 - Introduction of new workflows/processes may increase risk of medication error and complexity
 - Injection times with OBDS may be variable and longer compared to manual subcutaneous injections
 - There may be a risk of device failure

Patient-Centered Activities:

- Complete disease state and chemotherapy education and provide patient with [Patient Education Sheet](#)
- Review treatment schedule and supportive care medications
- Verify patient understanding of potential adverse reactions, monitoring parameters, and return/call precautions

References:

1. SARCLISA ESCENA™ (isatuximab-irfc) [package insert]. Morristown, NJ: Sanofi-Aventis U.S. LLC.; 2026.
2. CirCLIQ™ On-Body Delivery System Healthcare Provider Instructions for Use. Morristown, NJ: Sanofi-Aventis U.S. LLC.; 2026.
3. SARCLISA ESCENA™ US Preparation and Administration Guide. Morristown, NJ: Sanofi-Aventis U.S. LLC.; 2026.
4. Ocio EM, Parmar G, Mateos MV, et al. Review of the first on-body injector (OBI) for the subcutaneous delivery of an oncology drug: isatuximab in multiple myeloma. *Expert Opin Drug Deliv*. 2026;23(7):1289-1303. doi:10.1080/17425247.2026.2659263

Supplemental Information:

1. [CirCLIQ™ On-Body Delivery System Instructions for use](#)
2. [CirCLIQ Preparation and Administration Video](#)
3. [SARCLISA ESCENA Preparation and Administration Guide](#)