

Positive Quality Intervention: Isatuximab-irfc (Sarclisa®) In Patients with Relapsed Refractory Multiple Myeloma

Description: The purpose of this PQI is to discuss the option of using isatuximab-irfc for multiple myeloma patients who have been refractory to one to three prior lines of therapy or have had two prior treatment therapies including treatment with lenalidomide and a proteasome inhibitor.

Background: Isatuximab-irfc is an *intravenous infused* monoclonal antibody which selectively binds to the CD38 glycoprotein found on the surface of malignant plasma cells. Isatuximab-irfc has multiple mechanisms of action. ICARIA-MM was a phase 3 trial which compared the regimen of isatuximab-irfc plus pomalidomide and low dose dexamethasone to pomalidomide plus low dose dexamethasone alone in patients who received two or more prior therapies including lenalidomide and a proteasome inhibitor.³ The triplet therapy of isatuximab-irfc plus pomalidomide and low dose dexamethasone reduced the risk of disease progression or death by 40% compared to pomalidomide plus dexamethasone alone.⁴ In the IKEMA study, isatuximab-irfc plus carfilzomib and dexamethasone was compared to carfilzomib and dexamethasone alone. This combination reduced the risk of disease progression or death by 45% compared to carfilzomib and dexamethasone alone.⁷

PQI Process:

- Pre-medication is recommended to reduce risk of infusion related reactions⁵
 - Dexamethasone 40 mg either oral or IV x 1 dose. If patient is ≥ 75 years then give 20 mg
 - Acetaminophen 650 mg-1000 mg x 1 dose
 - H2 antagonist x 1 dose (ex: famotidine 20 mg)
 - Diphenhydramine 25 mg-50 mg orally or IV. Note: IV route is preferred for the first four infusions
 - Review institutional policy to consider using montelukast (usage not required)
- Verify dosing of isatuximab-irfc is 10 mg/kg intravenous infusion every week for 4 weeks (induction) followed by every 2 weeks in combination with pomalidomide and dexamethasone or carfilzomib and dexamethasone until disease progression or unacceptable toxicity
 - Dosing is based on patient's actual body weight at the beginning of each cycle
- Isatuximab-irfc is available in 100mg/5ml vials and 500mg/25 ml vials
- Preparation: isatuximab-irfc is compatible with 0.9% Sodium Chloride (NS) and 5% Dextrose (D5W)
- The infusion bag may be gently swirled to create a homogenous mixture. **Do Not Shake**
- Binding of isatuximab-irfc to CD38 of red blood cells may result in a false positive indirect coombs test

Table 1: Rate of infusion for isatuximab-irfc⁵

	Volume	Initial rate	No infusion reaction	Rate Increment	Maximum Rate
First infusion	250 ml	25 ml/hr	For 60 minutes	25 ml/hr every 30 minutes	150 ml/hr
Second Infusion	250 ml	50 ml/hr	For 30 minutes	50 ml/hr for 30 minutes then increase by 100ml/hr every 30 minutes	200 ml/hr
Subsequent Infusions	250 ml	200 ml/hr	-	-	200 ml/hr

Important notice: NCODA has developed this Positive Quality Intervention platform. This platform represents a brief summary of medication uses and therapy options derived from information provided by the drug manufacturer and other resources. This platform is intended as an educational aid and 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 discussed in the platform and is not intended as a substitute for the advice of a qualified healthcare professional. The materials contained in this platform are for informational purposes only and do not constitute or imply endorsement, recommendation, or favoring of this medication by NCODA, which assumes no liability for and does not ensure the accuracy of the information presented. NCODA does not make any representations with respect to the medications whatsoever, and any and all decisions, with respect to such medications, are at the sole risk of the individual consuming the medication. All decisions related to taking this medication should be made with the guidance and under the direction of a qualified healthcare professional.



Patient Centered Activities:

- Patient Education
 - Infusion related reactions may occur (38-46%)^{3, 7} with the administration of isatuximab-irfc. These usually occur with the first infusion and in most cases, resolve on the same day. Infusion reactions may include difficulty breathing, cough, chills and nausea and should counsel patient to report symptoms⁴
 - Coordinate with patient and outside pharmacy (if needed) filling of oral medication(s)
 - Discuss diarrhea management
 - See [Oncolytic Induced Diarrhea](#) PQI
 - Patient should report any symptoms of low grade fever, chills, sweating, sore throat, cough/shortness of breath, and increases in blood pressure
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- Monitoring
 - Monitor blood counts and blood pressure
 - Monitor for symptoms of low grade fever, chills, sweating, sore throat, cough/shortness of breath

Supplemental Information:

Sanofi CareASSIST Program⁶

- Patient's with commercial or private insurance may be eligible for \$0 copay; No income requirement
- Copay covers any product-specific copay, coinsurance, and insurance deductibles up to \$25,000 in assistance per year
- Patient's are responsible for costs which exceed the \$25,000/year maximum benefit
- CareASSIST not available for Medicare, Medicaid, Veterans Affairs/Department of Defense, TRICARE, or similar federal or state programs

References:

1. Trudel, Suzanne. "Incorporating Isatuximab in the Treatment of Multiple Myeloma." *The Lancet*, vol. 394, 7 Dec. 2019, pp. 2045–2046.
2. Moreno, Laura, et al. "The Mechanism of Action of the Anti-CD38 Monoclonal Antibody Isatuximab in Multiple Myeloma." *Clinical Cancer Research*, vol. 25, no. 10, 15 May 2019.
3. Martin, Thomas, et al. "Therapeutic Opportunities with Pharmacological Inhibition of CD38 with Isatuximab." *Cells*, vol. 8, no. 1522, 26 Nov. 2019.
4. Attal, Prof. Michael, et al. "Isatuximab plus Pomalidomide and Low-Dose Dexamethasone versus Pomalidomide and Low-Dose Dexamethasone in Patients with Relapsed and Refractory Multiple Myeloma (ICARIA-MM): a Randomised, Multicentre, Open-Label, Phase 3 Study." *The Lancet*, vol. 394, no. 10214, 7 Dec. 2019, pp. 2096–2107.
5. Sarclisa®(isatuximab-irfc) Package Insert Revised: 3/2021.
6. "CareASSIST Copay Program." Hcp, www.sanoficareassist.com/hcp/sarclisa/copay.
7. Moreau P (2020) Isatuximab plus carfilzomib and dexamethasone vs carfilzomib and dexamethasone in relapsed/refractory multiple myeloma (IKEMA): Interim analysis of a phase 3, randomized, open label study. (#LB2603) EHA25 Virtual, June 14th 2020.

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