Clinical Policy: Isatuximab-irfc (Sarclisa)

Reference Number: CP.PHAR.482
Effective Date: 06.01.20
Last Review Date: 05.25
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Isatuximab-irfc (Sarclisa®) is a CD38-directed cytolytic antibody

FDA Approved Indication(s)

Sarclisa is indicated

- In combination with pomalidomide and dexamethasone, for the treatment of adult patients with multiple myeloma (MM) who have received at least 2 prior therapies including lenalidomide and a proteasome inhibitor (PI)
- In combination with carfilzomib and dexamethasone, for the treatment of adult patients with relapsed or refractory MM 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 MM who are not eligible for autologous stem cell transplant (ASCT)

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Sarclisa is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Multiple Myeloma (must meet all)**:**

1. Diagnosis of MM;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Sarclisa is prescribed in one of the following ways (a, b, c, or d):
   a. In combination with pomalidomide and dexamethasone, after 2 prior therapies, including lenalidomide and a PI (e.g., bortezomib, Kyprolis®, Ninlaro®);*
   b. In combination with Kyprolis and dexamethasone, for relapsed or refractory disease after 1 to 3 prior lines of therapy;*
   c. In combination with bortezomib, lenalidomide, and dexamethasone, for primary therapy*;
   d. In combination with Kyprolis, lenalidomide, and dexamethasone, for primary therapy (*off-label*);

**Prior authorization may be required for prior therapies, including lenalidomide, bortezomib, Kyprolis and Ninlaro.*

5. Request meets one of the following (a or b):*
   a. Dose does not exceed 10 mg/kg per week for the first 4 weeks, then every 2 weeks thereafter;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Multiple Myeloma (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Sarclisa for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a, b, or c):*
   a. In combination with dexamethasone and pomalidomide or carfilzomib: New dose does not exceed 10 mg/kg every 2 weeks;
   b. In combination with dexamethasone, lenalidomide, and bortezomib: New dose does not exceed 10 mg/kg every 2 weeks, then every 4 weeks starting Cycle 18 and beyond;
   c. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):

a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
MM: multiple myeloma
PI: proteasome inhibitor

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
lenalidomide (Revlimid®)	10 mg or 25 mg PO QD; dose and frequency of administration vary based on specific use	See FDA approved dosing regimen
Ninlaro (ixazomib)	4 mg PO on days 1, 8, and 15 of every 28-day treatment cycle	See FDA approved dosing regimen
bortezomib (Velcade®)	1.3 mg/m^2 SC or IV; frequency of administration varies based on specific use	See FDA approved dosing regimen
Kyprolis (carfilzomib)	20 mg/m^2, 27 mg/m^2, and/or 56 mg/m^2 IV; frequency of administration varies based on specific use	See FDA approved dosing regimen
Pomalyst® (pomalidomide)	4 mg PO QD on days 1-21 of repeated 28-day cycles	4 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Examples of prior lines of therapy for relapsed or refractory MM: • bortezomib/lenalidomide/ dexamethasone • carfilzomib/lenalidomide/ dexamethasone • daratumumab/lenalidomide/ bortezomib/dexamethasone • ixazomib/lenalidomide/ dexamethasone • daratumumab/lenalidomide/ dexamethasone • daratumumab/bortezomib/ melphalan/prednisone • daratumumab/cyclophosphamide/ bortezomib/dexamethasone	Varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s): severe hypersensitivity to isatuximab-irfc or to any of its excipients
- Boxed warning(s): none reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
MM	10 mg/kg IV in combination with pomalidomide and dexamethasone or with carfilzomib and dexamethasone according to the dosing schedule below: • Cycle 1: Days 1, 8, 15, and 22 (weekly) • Cycle 2 and beyond: Days 1, 15 (every 2 weeks) Each treatment cycle consists of a 28-day period. Treatment is repeated until disease progression or unacceptable toxicity. 10mg/kg IV in combination with bortezomib, lenalidomide, and dexamethasone according to the dosing schedule below: • Cycle 1 (42-day cycle): Days 1, 8, 15, 22, and 29 • Cycles 2 to 4 (42-day cycles): Days 1, 15, and 29 (every 2 weeks)	10 mg/kg/week for the first 4 weeks, then every 2 weeks thereafter

Indication	Dosing Regimen	Maximum Dose
	• Cycles 5 to 17 (28-day cycles): Days 1 and 15 (every 2 weeks) • Cycles 18 and beyond (28-day cycles): Day 1 (every 4 weeks) Treatment cycles 1-4 consist of a 42-day period. Cycles 5-18 and beyond consist of a 28-day period. Treatment is repeated until disease progression or unacceptable toxicity.	

VI. Product Availability

Single-dose vial with solution for injection: 100 mg/5 mL (20 mg/mL), 500 mg/25 mL (20 mg/mL)

VII. References

1. Sarclisa Prescribing Information. Bridgewater, NJ: Sanofi; October 2024. Available at: https://products.sanofi.us/Sarclisa/sarclisa.pdf . Accessed February 14, 2025.
2. National Comprehensive Cancer Network. Multiple Myeloma Version 1.2025. Available at: https://www.nccn.org. Accessed February 14, 2025.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed February 14, 2025.
4. Attal M, Richardson P, Rajkumar V, 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). *Lancet*. 2019;394(10214):2096-2107.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9227	Injection, isatuximab-irfc, 10 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2021 annual review: no significant changes; added HCPCS code; references reviewed and updated.	02.12.21	05.21
RT4: Criteria added for FDA approved indication: combination use with carfilzomib and dexamethasone for relapsed or refractory MM after 1 to 3 prior lines of therapy; updated max dose criteria to require every 2 week dosing after the first cycle per PI; added off-label policy references for Commercial and HIM.	12.07.21	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2022 annual review: no significant changes; references reviewed and updated.	01.25.22	05.22
Template changes applied to other diagnoses/indications.	10.03.22	
2Q 2023 annual review: no significant changes; references reviewed and updated.	01.13.23	05.23
2Q 2024 annual review: added indication in transplant candidates for primary therapy in combination with bortezomib, lenalidomide, and dexamethasone per NCCN 2A recommendation; references reviewed and updated.	02.02.24	05.24
RT4: Added newly FDA-approved indication for primary therapy for MM not eligible for ASCT.	12.09.24	
2Q 2025 annual review: added off-label indication for primary therapy in combination with Kryprolis, lenalidomide, and dexamethasone per NCCN Compendium; references reviewed and updated.	02.14.25	05.25

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan

retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.