Clinical Policy: Isatuximab-irfc (Sarclisa)

Reference Number: PA.CP.PHAR.482
Effective Date: 10/2020
Last Review Date: 04/2025

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 PA Health & Wellness® 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, d or e):
   a. In combination with pomalidomide and dexamethasone, after 2 or more 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 in transplant candidates (off-label)*;
   d. In combination with Kyprolis, lenalidomide, and dexamethasone, for primary therapy (*off-label*)*;
   e. 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);

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

5. Request meets one of the following (a, b, or c):
   a. Dose does not exceed 10 mg/kg per week for the first 4 weeks, then every 2 weeks thereafter;
   b. For combination with bortezomib, lenalidomide, and dexamethasone, dose does not exceed 10 mg/kg and one of the following (i-iv):
      i. For cycle 1 (42 days) on days 1, 8, 15, 22 and 29;
      ii. For cycle 2-4 (42 days) on days 1, 15 and 29;
      iii. For cycle 5-17 (28 days) on days 1 and 15;
      iv. For cycles 18+ (28 days) on day 1;
   c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
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. 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*).

Approval duration: 12 months

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

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 – PA.CP.PMN.53

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 and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Revlimid® (lenalidomide)	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
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) • 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.	10 mg/kg/week for the first 4 weeks, then every 2 weeks thereafter

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
Policy created	10/2020
2Q 2021 annual review: no significant changes; added HCPCS code; references reviewed and updated.	04/2021
2Q 2022 annual review: 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; references reviewed and updated.	04/2022
2Q 2023 annual review: no significant changes; references reviewed and updated.	04/2023
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.	04/2024
2Q 2025 annual review: RT4: Added newly FDA-approved indication for primary therapy for MM not eligible for ASCT;.added off-label indication for primary therapy in combination with Kryprolis, lenalidomide, and dexamethasone per NCCN Compendium; references reviewed and updated.	04/2025