Clinical Policy Title:	isatuximab-irfc
Policy Number:	RxA.640
Drug(s) Applied:	Sarclisa®
Original Policy Date:	07/05/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

Isatuximab-irfc (Sarclisa®) 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 two prior therapies including lenalidomide and a proteasome inhibitor.
- In combination with carfilzomib and dexamethasone, for the treatment of adult patients with relapsed or refractory multiple myeloma (RRMM) who have received 1 to 3 prior lines of therapy.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
isatuximab-irfc (Sarclisa®)	Progressive Multiple myeloma orRRMM	In combination with pomalidomide and dexamethasone for progressive Multiple myeloma OR carfilzomib and dexamethasone for RRMM; **Cycle 1:** 10 mg/kg Intravenous on days 1, 8, 15, and 22 of a 28-day cycle,(in combination with pomalidomide and dexamethasone or in combination with carfizomib and dexamethasone) **Cycle 2 and beyond:** 10 mg/kg Intravenous on days 1 and 15 of a 28-day cycle, (in combination with pomalidomide and dexamethasone or in combination with carfizomib and dexamethasone) continue until disease progression or unacceptable toxicity.	10 mg/kg with max infusion rates: First infusion = 150 mL/hour Second and subsequent infusions = 200 mL/hour

Dosage Forms

- Injection: 100 mg/5 mL (20 mg/mL), 500 mg/25 mL (20 mg/mL) in a single-dose vial

This clinical policy has been developed to authorize, modify, or determine coverage for individuals with similar conditions. Specific care and treatment may vary depending on individual need and benefits covered by the plan. This policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. This document may contain prescription brand name drugs that are trademarks of pharmaceutical manufacturers that are not affiliated with RxAdvance.

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Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Multiple Myeloma (must meet all):

1. Diagnosis of relapsed, refractory, or progressive multiple myeloma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Request is for one of the following (a or b):
   a. For progressive multiple myeloma, prescribed in combination with pomalidomide and dexamethasone after failure of at least two prior therapies including Revlimid® and a proteasome inhibitor such as Velcade®, Kyprolis®, Ninlaro®;
   b. For relapsed or refractory multiple myeloma, prescribed in combination with carfilzomib and dexamethasone in patients who have received 1 to 3 prior lines therapy;
5. Dose does not exceed 10 mg/kg intravenous weekly.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Multiple Myeloma (must meet all):

1. Member is currently receiving medication that has been authorized by RxAdvance, 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. Dose does not exceed 10 mg/kg intravenous weekly.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
NCCN: National Comprehensive Care Network
RRMM: Relapsed and refractory multiple myeloma

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
bortezomib (Velcade®), Revlimid®,	Examples of primary and subsequent therapy regimens:	Varies

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Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Kyprolis®, Darzalex®, Empliciti®, Ninlaro®, bendamustine (Bendeka®),	• Velcade®/Revlimid®/dexamethasone • Kyprolis®/dexamethasone • Kyprolis®/Revlimid®/dexamethasone • Darzalex®/ Velcade®/dexamethasone • Darzalex®/ Kyprolis®/dexamethasone • Darzalex®/Revlimid®/dexamethasone • Empliciti®/Revlimid®/dexamethasone • Ninlaro®/Revlimid®/dexamethasone • Bendeka®/Velcade®/dexamethasone • cyclophosphamide/Revlimid®/dexamethasone	

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

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Patients with severe hypersensitivity to isatuximab-irfc or to any of its excipients.

- Boxed Warning(s):
  - None reported.

APPENDIX D: General Information

- Infusion-Related Reactions: In case of grade ≥ 2, interrupt Sarclisa® and manage medically. Permanently discontinue for grade 4 infusion-related reactions or anaphylactic reaction.

References

1. Sarclisa® Prescribing Information. Bridgewater, NJ: Sanofi Aventis US, LLC; March 2021. Available at: https://www.sarclisa.com/. Accessed July 5, 2021.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed July 5, 2021.
3. National Comprehensive Cancer Network Guidelines. Multiple Myeloma Version 7.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Published April 26, 2021. Accessed July 5, 2021.
4. Attal M, Richardson PG, Rajkumar SV, 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 [published correction appears in Lancet. 2019 Dec 7;394(10214):2072]. Lancet. 2019;394(10214):2096-2107. doi:10.1016/S0140-6736(19)32556-5. Available at https://pubmed.ncbi.nlm.nih.gov/31735560/. Accessed July 5, 2021.
5. Sarclisa®. Lexi-Drugs. Lexicomp. Wolters Kluwer. Hudson, Oh. Available at: https://online.lexi.com. Accessed July 5, 2021.
6. Sarclisa®. Micromedex Solutions. Truven Health Analtics Inc. Greenwood Village, CO. Available at: http://www.micromedexsolutions.com. Accessed July 5, 2021.
7. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2021. Available at: http://www.clinicalpharmacology-ip.com/. Accessed July 5, 2021.

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8. IPD Analytics. [database online]. Aventura, FL: IPD Analytics LLC.; 2021. Available at: https://secure.ipdanalytics.com/User/Pharma/RxStrategy. Accessed July 5, 2021.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	07/05/2020	09/14/2020
Policy was reviewed: 1. Background was updated to include "In combination with carfilzomib and dexamethasone, for the treatment of adult patients…". 2. Dosing Information was updated to include indication "Progressive Multiple myeloma orRRMM". **3.** Dosing Information dosing regimen was updated to include "In combination with pomalidomide and dexamethasone for progressive Multiple myeloma OR carfilzomib and dexamethasone for RRMM;", "…(in combination with pomalidomide and dexamethasone or in combination with carfizomib and dexamethasone)…", and "…(in combination with pomalidomide and dexamethasone or in combination with carfizomib and dexamethasone)…". **4.** Dosing Regimen maximum dose was updated from "No max dose" to "10mg/kg". **5.** Statement about provider sample ''The provision of provider samples does not guarantee coverage…" was added to Clinical Policy. **6.** Initial Approval Criteria I.A.1 was updated to include "…relapsed, refractory, or progressive…". 7. Initial Approval Criteria I.A.4 was updated to include "Request is for one of the following (a or b)…". **8.** Initial Approval Criteria I.A.4.a was updated to include "For progressive multiple myeloma, prescribed in combination with pomalidomide…". **9.** Initial Approval Criteria I.A.4.b was updated to include "For relapsed or refractory multiple myeloma, prescribed in combination…".	07/05/2021	09/14/2021

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Review/Revision History	Review/Revision Date	P&T Approval Date
10. Continued Therapy Approval Criteria II.A was updated from “All Indications in Section I” to “Multiple Myeloma”. **11.** Continued Therapy Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". **12.** Appendix A was updated to include abbreviations FDA, NCCN, and RRMM. **13.** Therapeutic Alternatives verbiage was rephrased to "Below are suggested therapeutic alternatives based on clinical guidance..". **14.** Appendix B: Therapeutic Alternatives was updated from bullet-list format to table format. **15.** Appendix B was updated to include brand-name drug Kyprolis and its combination regimen. **16.** Statement about drug listing format in Appendix B is rephrased to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". **17.** Appendix C contraindications was updated to include “atients with severe hypersensitivity to isatuximab-irfc or to any of its excipients…”. **18.** Appendix D was updated to include “Infusion-Related Reactions: In case of grade ≥ 2, interrupt Sarclisa® and manage medically….”. **19.** References were reviewed and updated.		

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