Medical Drug Clinical Criteria

Subject:	Sarclisa (isatuximab-irfc), Sarclisa Escena (isatuximab-irfc)		
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Overview

This document addresses the use of Sarclisa (isatuximab-irfc) and Sarclisa Escena. Sarclisa is the second human anti-CD38 monoclonal antibody approved by the FDA for treatment of multiple myeloma (MM), following Darzalex (daratumumab). Sarclisa Escena is a subcutaneous formulation of isatuximab-irfc that can be given via subcutaneous injection or via an on-body injector. Sarclisa Escena was shown to be non-inferior to IV Sarclisa in a phase 3 study showing similar efficacy, pharmacokinetics and safety.

Sarclisa is approved 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. Sarclisa Escena is approved in combination with pomalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy including lenalidomide and a proteasome inhibitor. Both agents are also approved for relapsed or refractory MM in combination with carfilzomib and dexamethasone in patients who have received 1 to 3 prior lines of therapy. Both agents are also indicated for use newly diagnosed multiple myeloma, in combination with bortezomib, lenalidomide, and dexamethasone, who are not eligible for autologous stem cell transplant (ASCT). The National Comprehensive Cancer Network® (NCCN) guidelines additionally recommend the use of Sarclisa as primary therapy in transplant candidates in combination with bortezomib, lenalidomide, and dexamethasone or in combination with carfilzomib, lenalidomide and dexamethasone. NCCN also recommends Sarclisa in non-transplant candidates in combination with either bortezomib, lenalidomide, and dexamethasone or in combination with lenalidomide and dexamethasone. The NCCN guidelines do not yet address Sarclisa Escena.

Sarclisa Escena was approved for multiple myeloma based in part on the IRAKLIA trial (NCT05405166) that compared Sarclisa Escena to Sarclisa IV. The enrolled population had received at least one prior therapy including lenalidomide and proteasome inhibitor. Treatment arms were either Sarclena Escena 1,400 mg fixed dose or IV Sarclesa as 10 mg/kg infusion, in combination with pomalidomide and dexamethasone. The median number of lines of therapy was 2; 30% had received only one line of therapy. Sarclisa Escena showed non-inferiority to Sarclisa IV in this population.

Definitions and Measures

Line of Therapy:

- First-line therapy: The first or primary treatment for the diagnosis, which may include surgery, chemotherapy, radiation therapy or a combination of these therapies.
- Second-line therapy: Treatment given when initial treatment (first-line therapy) is not effective or there is disease progression.
- Third-line therapy: Treatment given when both initial (first-line therapy) and subsequent treatment (second-line therapy) are not effective or there is disease progression.

Multiple myeloma: A type of cancer that begins in plasma cells (white blood cells that produce antibodies).

Proteasome inhibitors: A class of drugs used to treat multiple myeloma that work by blocking the action of proteasomes which are cellular complexes that break down proteins. Examples include bortezomib, carfilzomib and ixazomib.

Refractory Disease: Illness or disease that does not respond to treatment.

Relapse or recurrence: After a period of improvement, during which time a disease (for example, cancer) could not be detected, the return of signs and symptoms of illness or disease. For cancer, it may come back to the same place as the original (primary) tumor or to another place in the body.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Sarclisa (isatuximab-irfc)

Requests for Sarclisa (isatuximab-irfc) and Sarclisa Escena (isatuximab-irfc) may be approved if the following criteria are met:

I. Individual is under 19 years of age;

OR

II. Individual has a diagnosis of multiple myeloma; **AND**
III. Individual has relapsed or refractory disease following treatment with at least one prior line of therapy including lenalidomide and a proteasome inhibitor (for example, bortezomib, carfilzomib, or ixazomib); **AND**
IV. Individual is using in combination with pomalidomide and dexamethasone (Label, NCCN 1);

OR

V. Individual has a diagnosis of multiple myeloma; **AND**
VI. Sarclisa is used in combination with carfilzomib and dexamethasone; **AND**
VII. Individual has relapsed or refractory disease following treatment with one to three prior lines of therapy (Label, NCCN 1);

OR

VIII. Individual has a diagnosis of multiple myeloma; **AND**
IX. Individual is using as primary therapy; **AND**
X. Individual is eligible for stem cell transplant; **AND**
XI. Individual is using in combination with one of the following:
    A. Carfilzomib, lenalidomide, and dexamethasone (NCCN 2A); **OR**
    B. Bortezomib, lenalidomide, and dexamethasone (NCCN 1, DrugDex BIIa);

OR

XII. Individual has a diagnosis of multiple myeloma; **AND**
XIII. Individual is using as primary therapy; **AND**
XIV. Individual is not eligible for autologous stem cell transplant (ASCT) or stem cell transplant is deferred; **AND**
XV. Individual is using in combination with one of the following:
    A. Lenalidomide and dexamethasone (NCCN 2A); **OR**
    B. Bortezomib, lenalidomide, and dexamethasone (Label, NCCN 1).

Requests for Sarclisa (isatuximab-irfc) may not be approved when the above criteria are not met and for all other indications.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

C9399	Unclassified drugs or biologicals [when specified as Sarclisa Escena (isatuximab-irfc, subcutaneous)]

J9227	Injection, isatuximab-irfc, 10 mg (Effective 10/1/2020)
J9999	Not otherwise classified, antineoplastic drugs [when specified as Sarclisa Escena (isatuximab-irfc, subcutaneous)]

ICD-10 Diagnosis

C90.00-C90.32	Multiple myeloma and malignant plasma cell neoplasms

Document History

Revised: 08/14/2026
Document History:

- 08/14/2026 – Select Review: Added Sarclisa Escena to Sarclisa criteria; updated criteria to allow for Sarclisa IV in previously treated multiple myeloma after one prior therapy in combination with pomalidomide and dexamethasone to align Sarclisa and Sarclisa Escena; wording and formatting change. Coding Reviewed: Added HCPCS NOC C9399, J9999 for Sarclisa Escena. Added ICD-10-CM C90.10-C90.32 to existing range C90.00-C90.02 and updated description.
- 11/14/2025 – Annual Review: Updated therapy and references for primary therapy in individuals eligible for transplant per NCCN; updated therapy and references for primary therapy in individuals not eligible for transplant per NCCN. Administrative update for age. Coding Reviewed: No changes.
- 11/15/2024 – Select Review: Update existing criteria and add FDA indication for use in primary therapy for multiple myeloma in those not eligible for transplant when using Sarclisa in combination with bortezomib, lenalidomide, and dexamethasone. Coding Reviewed: No changes.
- 02/23/2024 – Annual Review: Add use as primary therapy in combination with bortezomib, lenalidomide, and dexamethasone per NCCN. Coding Reviewed: No changes.
- 02/24/2023 – Annual Review: Remove language excluding prior use of anti-CD38 agents. Coding Reviewed: No changes.
- 05/20/2022 – Annual Review: No changes. Coding Reviewed: No changes.
- 05/21/2021 – Annual Review: Update criteria to include new indication in combination with carfilzomib and dexamethasone. Coding Reviewed: No changes.
- 05/15/2020 – Annual Review: No changes. Coding Review: No changes. Effective 10/1/2020 Added HCPCS J9227, Added ICD-10-CM C90.00-C90.02, Delete 9/30/2020-C9399, J3490, J3590, J9999.
- 03/16/2020 – Select Review: Add clinical criteria document for new FDA approval Sarclisa (isatuximab-irfc). Coding reviewed: Added C9399, J3490, J3590, J9999. All diagnosis.

References

1. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: October 9, 2025.
2. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
3. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2025; Updated periodically.
4. NCCN Clinical Practice Guidelines in Oncology™. © 2025 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed October 9, 2025.
    a. Multiple Myeloma. V2.2026. Revised July 16, 2025.

Federal and state laws or requirements, contract language, and Plan utilization management programs or policies may take precedence over the application of this clinical criteria.

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