

Corporate Medical Policy

Isatuximab-irfc (Sarclisa[®])

File Name:	isatuximab_sarclisa
Origination:	5/2020
Last CAP Review:	11/2020
Next CAP Review:	11/2021
Last Review:	11/2020

Description of Procedure or Service

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.

Multiple myeloma (MM) is a malignant neoplasm of immunoglobulin-producing plasma cells, which accumulate in the bone marrow and lead to marrow failure. Systemic effects include skeletal bone destruction and infiltration and damage to organs. Treatment is generally based on risk stratification and transplant eligibility. Newly diagnosed MM is usually responsive to cytotoxic therapy. However, there is no cure for MM, and relapsing disease is typical, requiring use of multiple lines of therapy, as well as different classes and generations of drugs.

Isatuximab-irfc (Sarclisa) is a CD38-directed cytolytic monoclonal antibody, which was approved by the U.S. Food and Drug Administration (FDA) in March 2020 for the treatment of relapsed or refractory multiple myeloma. It works by binding to CD38 expressed on the surface of hematopoietic and tumor cells, including multiple myeloma cells, and induces tumor cell apoptosis and activation of immune effector mechanisms. Isatuximab can also activate natural killer (NK) cells in the absence of CD38-positive target tumor cells and suppresses CD38-positive T-regulatory cells. Use of isatuximab and pomalidomide combined enhances antibody-dependent cell-mediated cytotoxicity and direct tumor cell killing compared to use alone.

Related Medical Policies:Carfilzomib (Kyprolis[®])Daratumumab (Darzalex[®])Elotuzumab (Empliciti[®])

Hematopoietic Cell Transplantation for Plasma Cell Dyscrasias, Including Multiple Myeloma and POEMS Syndrome

Related Pharmacy Policies:Ninlaro[®]Pomalyst[®]

*****Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

Policy

BCBSNC will provide coverage for isatuximab-irfc (Sarclisa[®]) when it is determined to be medically necessary because the medical criteria and guidelines noted below are met.

Isatuximab-irfc (Sarclisa[®])

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Isatuximab-irfc (Sarclisa) is covered

Initial Therapy

Isatuximab-irfc (Sarclisa) may be considered medically necessary for the treatment of adult patients with multiple myeloma when the following criteria are met:

- The patient has a diagnosis of multiple myeloma; and
- The patient has relapsed or refractory disease; and
- The patient has received at least two prior systemic chemotherapies, including lenalidomide and a proteasome inhibitor (i.e., bortezomib, carfilzomib, ixazomib); and
- Isatuximab is administered in combination with pomalidomide and dexamethasone

Initial authorization: 12 months

Continuation Therapy

Continuation of treatment with isatuximab-irfc (Sarclisa) beyond 12 months after initiation of therapy, and every 12 months thereafter, is considered medically necessary for the treatment of relapsed or refractory multiple myeloma when the following criteria are met:

1. The patient is currently receiving isatuximab and continues to meet initial criteria; and
2. The patient has continued clinical benefit on isatuximab therapy as demonstrated by tumor response or lack of disease progression, and an acceptable toxicity profile.

Use of isatuximab-irfc (Sarclisa) may be considered medically necessary for clinical indications not listed above when the drug is prescribed for the treatment of cancer either:

- In accordance with FDA label (when clinical benefit has been established, (see Policy Guidelines); **OR**
- In accordance with specific strong endorsement or support by nationally recognized compendia, when such recommendation is based on strong/high levels of evidence, and/or uniform consensus of clinical appropriateness has been reached.

When Isatuximab-irfc (Sarclisa) is not covered

Isatuximab-irfc (Sarclisa) is considered **investigational** and therefore not covered when the above criteria are not met.

Isatuximab-irfc (Sarclisa[®])

Isatuximab-irfc (Sarclisa) is considered investigational when used for:

1. Non-cancer indications; **OR**
2. When criteria are not met regarding FDA labeling **OR** strong endorsement/support by nationally recognized compendia, as stated under “When Isatuximab-irfc (Sarclisa) is covered.”

Policy Guidelines

Dosing and Administration

The recommended dose of Sarclisa is 10 mg/kg given as an intravenous infusion, in combination with pomalidomide and dexamethasone, every week for 4 weeks followed by every 2 weeks (28-day treatment cycles) until disease progression or unacceptable toxicity. Sarclisa should be administered by a healthcare professional with immediate access to emergency equipment and appropriate medical support to manage possible occurrence of infusion-related reactions. To reduce the risk and severity of infusion-related reactions, patients should be premedicated with dexamethasone, acetaminophen, H2 antagonists, and diphenhydramine prior to administration of Sarclisa and pomalidomide.

According to the manufacturer’s safety information for Sarclisa, the most common adverse reactions ($\geq 20\%$ incidence) include neutropenia, infusion-related reactions, pneumonia, upper respiratory tract infection, and diarrhea.

Evidence Summary

The efficacy of isatuximab-irfc (Sarclisa) in combination with pomalidomide and low-dose dexamethasone was evaluated in a randomized, open-label, multicenter phase 3 clinical trial, in which 307 patients with relapsed and refractory multiple myeloma received pomalidomide and dexamethasone, with or without concurrent isatuximab (ICARIA-MM trial; NCT02990338). Patients had received at least two previous lines of therapy, including lenalidomide and a proteasome inhibitor. Randomization was stratified by number of previous lines of treatment and patient age. Treatment continued until disease progression, unacceptable toxicity or withdrawal. At a median follow-up of 11.6 months, the median progression free survival was 11.5 months (95% confidence interval [CI] 8.9-13.9) in the group that received isatuximab versus 6.5 months (95% CI 4.5-8.3) in the group that did not. Deaths due to treatment-related adverse events were reported with similar frequency in both groups.

Drugs prescribed for treatment of cancer in accordance with FDA label may be considered medically necessary when clinical benefit has been established and should not be determined to be investigational as defined in Corporate Medical Policy (CMP), “Investigational (Experimental) Services.”

Please refer to CMP “Investigational (Experimental) Services” for a summary of evidence standards from nationally recognized compendia.

Billing/Coding/Physician Documentation Information

Isatuximab-irfc (Sarclisa[®])

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: C9399, J9227, J9999, S0353, S0354

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

Sanofi-Aventis U.S. LLC. Sarclisa (isatuximab-irfc) injection for intravenous use. Highlights of prescribing information. March 2020. Available at: <http://products.sanofi.us/Sarclisa/sarclisa.pdf>. Last accessed May 2020.

U.S. Food and Drug Administration. FDA approves new therapy for patients with previously treated multiple myeloma. March 2020. Available at: <https://www.fda.gov/news-events/press-announcements/fda-approves-new-therapy-patients-previously-treated-multiple-myeloma>. Last accessed May 2020.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Multiple Myeloma, version 3.2020. Revised March 10, 2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Last accessed May 2020.

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 randomized, multicenter, open-label, phase 3 study. *Lancet* 2019;394:2096-2107.

Medical Director review 5/2020

Specialty Matched Consultant Advisory Panel review 11/2020

Policy Implementation/Update Information

- 5/26/20 New policy developed. Sarclisa is considered medically necessary for the treatment of adult patients with multiple myeloma when specified medical criteria and guidelines are met. Added HCPCS codes C9399, J3490, J3590, J9999, S0353, and S0354 to Billing/Coding section. References added. Medical Director review 5/2020. (krc)
- 10/1/20 Added HCPCS code J9227 to Billing/Coding section effective 10/1/2020 and deleted codes J3490, J3590 termed 9/30/2020. (krc)
- 12/31/20 Specialty Matched Consultant Advisory Panel review 11/18/2020. No change to policy statements. (krc)

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Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.