Medical Policy:
Sarclisa (isatuximab)

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.215	January 8, 2024	June 3, 2020

Definitions

Sarclisa (isatuximab) is an IgG1-derived monoclonal antibody that binds to CD38 expressed on the surface of hematopoietic and tumor cells, including multiple myeloma cells. Isatuximab-irfc induces apoptosis of tumor cells and activation of immune effector mechanisms including antibody-dependent cell-mediated cytotoxicity (ADCC), antibody-dependent cellular phagocytosis (ADCP), and complement dependent cytotoxicity (CDC) and inhibits the ADP-ribosyl cyclase activity of CD38. Isatuximab-irfc can activate natural killer (NK) cells in the absence of the CD38-positive target tumor cells and suppresses CD38-positive T-regulatory cells. The combination of isatuximab plus pomalidomide enhanced antibody-dependent, cell-mediated cytotoxicity activity and direct tumor cell killing compared to isatuximab alone (in vitro) and enhanced antitumor activity compared to isatuximab or pomalidomide activities alone in animal models.

Length of Authorization

Coverage will be provided for 6 months and may be renewed.

Dosing Limits

Max Units (per dose and over time) [HCPCS Unit]:

- Cycle 1 every week x 4 doses, followed by Cycle 2, and beyond, every 2 weeks
- 110 billable units per dose

Guideline

I. Initial Approval Criteria

Sarclisa *may be considered medically necessary if one of the below conditions are met* ***AND*** *use is consistent with the medical necessity criteria that follows:*

1. **Multiple Myeloma**

   A. Patient has a diagnosis of relapsed, refractory, or progressive disease; **AND**

   B. Used in combination with Pomalyst® (pomalidomide) and dexamethasone after at least two prior therapies including lenalidomide and a proteasome inhibitor (e.g., bortezomib, carfilzomib, ixazomib, etc.); **OR**

   C. Used in combination with carfilzomib and dexamethasone in patients who have received 1 to 3 prior lines therapy

Limitations/Exclusions

Sarclisa (Isatuximab) is not considered medically necessary for when any of the following selection criteria is met:

1. Disease progression while on Sarclisa.
2. Dosing exceeds single dose limit of 10 mg/kg body weight.
3. The patient must be 18 years of age and older
4. Indications not supported by CMS recognized Compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable.

II. Renewal Criteria

Coverage can be renewed based upon the following criteria:

1. Patient continues to meet criteria identified in Initial Approval Criteria
2. Stabilization of disease and/or absence of progression of disease; **AND**
3. Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: severe infusion reactions, neutropenia, thrombocytopenia, etc.

Dosage/Administration

Indication	Dose
Multiple Myeloma	Combination therapy with pomalidomide and dexamethasone OR carfilzomib and dexamethasone: 10 mg/kg of actual body weight given as an intravenous infusion: • Weekly Cycle 1 (four doses total; Days 1, 8, 15, & 22) • Every two weeks Cycle 2 and beyond (two doses per cycle; Days 1 & 15) **Each treatment cycle consists of a 28-day period. Treatment is repeated until disease progression or unacceptable toxicity*

The following medications are infused 15 to 60 minutes prior to administration of Sarclisa infusion to reduce the risk of an infusion reaction

- *Dexamethasone 40 mg orally or intravenously (or 20 mg orally or intravenously for patients ≥75 years of age).*
- *Acetaminophen 650 mg to 1000 mg orally (or equivalent).*
- *H2 antagonists.*

- *Diphenhydramine 25 mg to 50 mg orally or intravenously (or equivalent). The intravenous route is preferred for at least the first 4 infusions.*

Applicable Procedure Codes

Code	Description
J9227	Injection, isatuximab-irfc, 10 mg (Sarclisa). J-Code effective date: 10/01/2020

Applicable NDCs

Code	Description
00024-0654-01	Sarclisa 100 mg (5 ml) single use vial
00024-0656-01	Sarclisa 500 mg (25 ml) single use vial

ICD-10 Diagnoses

Code	Description
C90.00	Multiple myeloma not having achieved remission
C90.02	Multiple myeloma, in relapse
C90.10	Plasma cell leukemia not having achieved remission
C90.12	Plasma cell leukemia in relapse
C90.20	Extramedullary plasmacytoma not having achieved remission
C90.22	Extramedullary plasmacytoma in relapse
C90.30	Solitary plasmacytoma not having achieved remission
C90.32	Solitary plasmacytoma in relapse
Z85.79	Personal history of other malignant neoplasms of lymphoid, hematopoietic and related tissues

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	1/8/2024	Annual Review: Added dosing limits, updated dosage chart
EmblemHealth & ConnectiCare	5/9/2023	Annual Review: Multiple Myeloma Initial Criteria: Removed "Patient has a diagnosis of relapsed or progressive disease. i. Used in combination with Pomalyst® (pomalidomide) and dexamethasone; AND ii. Failure of at least two prior therapies, including Revlimid® (lenalidomide) and a proteasome inhibitor (i.e. bortezomib, ixazomib, or carfilzomib)" Added "A. Patient has a diagnosis of relapsed, refractory, or progressive disease; AND B. Used in combination with Pomalyst® (pomalidomide) and dexamethasone after at least two prior therapies including lenalidomide

		and a proteasome inhibitor (e.g., bortezomib, carfilzomib, ixazomib, etc.); OR C. Used in combination with carfilzomib and dexamethasone in patients who have received 1 to 3 prior lines therapy " Exclusion Criteria Multiple Myeloma- Removed "Members with Known Human immunodeficiency virus (HIV) infection or active Hepatitis A, B, or C infection"
EmblemHealth & ConnectiCare	1/12/2023	Transfer to New Template
EmblemHealth & ConnectiCare	9/11/2020	Added J-Code (J9227) Injection, isatuximab-irfc, 10 mg (Sarclisa). J-Code effective date: 10/01/2020
EmblemHealth & ConnectiCare	6/3/2020	New Policy

References

1. Mikhael J, Richardson P, Usmani SZ, et al. A phase 1b study of isatuximab plus pomalidomide/dexamethasone in relapsed/refractory multiple myeloma. *Blood*. 2019;134(2):123–133. doi:10.1182/blood-2019-02-895193
2. Sarclisa (isatuximab) [prescribing information]. Bridgewater, NJ: Sanofi-aventis US LLC; March 2020.
3. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines. Multiple Myeloma. Version 3.2020. Accessed March 24, 2020.
4. National Comprehensive Cancer Network (NCCN) Compendia. Sarclisa. Accessed March, 31, 2020.
5. FDA Approves New Therapy for Patients with Previously Treated Multiple Myeloma. *FDA News Release*. March 2, 2020. Available at: https://www.fda.gov/news-events/press-announcements/fda-approves-new-therapy-patients-previously-treated-multiple-myeloma.