 Approved Revision: Do Not Implement until 8/31/21

Sargramostim (Leukine®)

NDC CODE(S) 71837-5843-XX LEUKINE 250MCG Solution Reconstituted (PARTNER THERAPEUTICS)

DESCRIPTION

Sargramostim is a recombinant human granulocyte-macrophage colony stimulating factor (rGM-CSF) produced by recombinant DNA technology in a yeast (S. cerevisiae) expression system. Like endogenous GM-CSF, rGM-CSF is a hematopoietic growth factor which stimulates proliferation and differentiation of hematopoietic progenitor cells in the granulocyte-macrophage pathways which include neutrophils, monocytes/macrophages and myeloid-derived dendritic cells. It is also capable of activating mature granulocytes and macrophages. Various cellular responses such as division, maturation and activation are induced by GM-CSF binding to specific receptors expressed on the cell surface of target cells.

POLICY

- Sargramostim for the treatment of the following is considered ***medically necessary:***
  - Acute myelogenous leukemia following induction or consolidation chemotherapy
  - Bone Marrow Transplantation (BMT) failure or Engraftment Delay
  - Individuals acutely exposed to myelosuppressive doses of radiation (Hematopoietic Subsyndrome of Acute Radiation Syndrome [H-ARS])
  - Myeloid reconstitution after autologous or allogeneic bone marrow transplant (BMT)
  - Peripheral Blood Progenitor Cell (PBPC) mobilization and transplant
- Sargramostim for the treatment of chemotherapy-induced febrile neutropenia is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**
- Sargramostim for the treatment of other conditions/diseases is considered ***investigational.***

MEDICAL APPROPRIATENESS

INITIAL APPROVAL CRITERIA

Myeloid reconstitution after autologous or allogeneic bone marrow transplant (BMT)

Peripheral Blood Progenitor Cell (PBPC) mobilization and transplant

Acute Myeloid Leukemia (AML) following induction or consolidation chemotherapy

Bone Marrow Transplantation (BMT) failure or Engraftment Delay

Treatment of chemotherapy-induced febrile neutropenia

- Used for the treatment of chemotherapy induced febrile neutropenia in patients who have not received prophylactic therapy with a granulocyte colony stimulating factor; **AND**
- Patient has one or more of the following risk factors for developing infection-related complications:
  - Sepsis Syndrome
  - Age greater than 65 years
  - Absolute neutrophil count [ANC] less than 100/mcL
  - Duration of neutropenia expected to be greater than 10 days
  - Pneumonia or other clinically documented infections
  - Invasive fungal infection

- Hospitalization at the time of fever
- Prior episode of febrile neutropenia

Patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Subsyndrome of Acute Radiation Syndrome [H-ARS])

High-Risk Neuroblastoma

- Used in combination with GD2-binding monoclonal antibodies (i.e., naxitamab, dinutuximab, etc.) for the treatment of high-risk neuroblastoma

RENEWAL CRITERIA

High-Risk Neuroblastoma

- Use in combination with dinutuximab may not be renewed.
- Used in combination with naxitamab; **AND**
  - Patient continues to meet indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in the Initial Approval Criteria; **AND**
  - Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include severe hypersensitivity reactions, severe effusions and capillary leak syndrome, severe supraventricular arrythmias, etc.

All Other Indications

- Same as the Initial Approval Criteria
- Absence of toxicity or adverse reactions, including serious allergic or anaphylactic reaction to recombinant protein.

DOSAGE/ADMINISTRATION

INDICATION	DOSE
Acute Exposure to Myelosuppressive Doses of Radiation	• 7 mcg/kg in adult and pediatric patients weighing greater than 40 kg • 10 mcg/kg in pediatric patients weighing 15 kg to 40 kg • 12 mcg/kg in pediatric patients weighing less than 15 kg ▫ *Administer Leukine as soon as possible after suspected or confirmed exposure to radiation doses greater than 2 gray (Gy).*
High-Risk Neuroblastoma	**In combination with naxitamab** 250 mcg/m^2 subcutaneously daily for 5 doses starting 5 days prior to the day 1 of naxitamab infusion followed by sargramostim 500 mcg/m^2 subcutaneously daily on days 1, 2, 3, 4, and 5 repeated each cycle in combination with naxitamab. *Note: Treatment cycles are repeated every 4 weeks until complete or partial response, followed by 5 additional cycles (every 4 weeks). Subsequent cycles may be repeated every 8 weeks. Discontinue (naxitamab and GM-CSF) with disease progression or unacceptable toxicity.* **In combination with dinutuximab** 250 mcg/m^2 daily on days 1 through 14 of cycles 1, 3 and 5 (cycle length is 24 days) for a maximum of 5 cycles only
All other indications	250 mcg/m^2 daily for up to 14 days

LENGTH OF AUTHORIZATION

High Risk Neuroblastoma:
- When used in combination with dinutuximab, coverage will be provided for five months and may not be renewed.
- When used in combination with naxitamab, coverage will be provided for six months and may be renewed.

All other indications: Coverage will be provided for four months and may be renewed

DOSING LIMITS

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

- 15 billable units per day (acute radiation syndrome)
- 10 billable units per day on days 1 through 14 of cycles 1, 3 and 5 (cycle length is 24 days) for a maximum of 5 cycles only (high-risk neuroblastoma in combination with dinutuximab)
- 10 billable units per day for 10 days of each 28-day cycle for six cycles followed by subsequent cycles every 8 weeks thereafter (high-risk neuroblastoma in combination with naxitamab)
- 10 billable units per day (all other indications)

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

1. Leukine [package insert]. Bridgewater, NJ; Sanofi-Aventis U.S. LLC; March 2018. Accessed March 2021.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) sargramostim. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN

GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed March 2021.

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11. Rowe JN, Andersen JW, Mazza JJ et al. A randomized placebo-controlled phase III study of granulocyte-macrophage colony-stimulating factor in adult patients (> 55 to 70 years of age) with acute myelogenous leukemia: a study of the Eastern Cooperative Oncology Group (E1490). Blood. 1995;86:457-62.
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EFFECTIVE DATE 8/31/2021

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