MEDICAL MUTUAL®

Drug Policy

Policy:	**201826 MRx** **V4-21**	**Initial Effective Date: 10/30/2014** **Annual Review Date: 05/18/2023** **Last Revised Date: 05/18/2023**
Code(s):	**HCPCS J2820**	
SUBJECT:	**Colony Stimulating Factors** - **Leukine® (Sargramostim)**	

Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.

Policy Statement
This policy involves the use of Leukine. Prior authorization is recommended for medical benefit coverage of Leukine. Approval is recommended for those who meet the conditions of coverage in the **Initial Approval and Renewal Criteria, Preferred Drug (when applicable), Dosing/Administration, Length of Authorization, and Site of Care (when applicable)** for the diagnosis provided. The requirement that the patient meet the Criteria and Preferred Drug for coverage of the requested medication applies to the initial authorization only. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy.

I. 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.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Leukine 250 mcg vial: 28 vials per 14 days
- Leukine 500 mcg vial: 14 vials per 14 days

B. 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)

III. Initial Approval Criteria[1-11]

Coverage is provided in the following conditions:

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 † Φ

Bone Marrow Transplantation (BMT) failure or Engraftment Delay † Φ

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]) † Φ

High-Risk Neuroblastoma † [12,13]

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

† FDA-labeled indication(s); ‡ Compendia recommended indication(s); **Φ** Orphan Drug

IV. Renewal Criteria [1,12,13]

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 section III; **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 initial prior authorization policy criteria.

V. Dosage/Administration[1-13]

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 combinations 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

VI. Billing Code/Availability Information

HCPCS Code:

- J2820 – Injection, sargramostim (GM-CSF), 50 mcg: 1 billable unit = 50 mcg

NDC:

- Leukine 250 mcg vial– 00024-5843-xx
- Leukine 500 mcg vial– 00024-5844-xx

VII. References

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.
3. Arora M, Burns LJ, Barker JN, et al. Randomized comparison of granulocyte colony-stimulating factor versus granulocyte-macrophage colony-stimulating factor plus intensive chemotherapy for peripheral blood stem cell mobilization and autologous transplantation in multiple myeloma. Biol Blood Marrow Transplant. 2004;10(6):395-404.
4. Berghmans T, Paesmans M, Lafitte JJ, et al. Therapeutic use of granulocyte and granulocyte-macrophage colony-stimulating factors in febrile neutropenic cancer patients. A systematic review of the literature with meta-analysis. Support Care Cancer. 2002;10(3):181-188.
5. Dubois RW, Pinto LA, Bernal M, et al. Benefits of GM-CSF versus placebo or G-CSF in reducing chemotherapy-induced complications: A systematic review of the literature. Support Cancer Ther. 2004;2(1):34-41.
6. Nemunaitis J, Rosenfeld CS, Ash R, et al. Phase III randomized, double-blind placebo-controlled trial of rhGM-CSF following allogeneic bone marrow transplantation. Bone Marrow Transplant. 1995;15(6):949-954.
7. Nemunaitis J, Singer JW, Buckner CD, et al. Use of recombinant human granulocyte-macrophage colony-stimulating factor in graft failure after bone marrow transplantation. Blood. 1990;76(1):245-253.
8. Nemunaitis J, Buckner CD, Appelbaum FR et al. Phase I/II trial of recombinant human granulocyte-macrophage colony-stimulating factor following allogeneic bone marrow transplantation. Blood. 1991;77:2065-71.
9. Nemunaitis J, Rabinowe SN, Singer JW et al. Recombinant granulocyte-macrophage colony-stimulating factor after autologous bone marrow transplantation for lymphoid cancer. N Engl J Med. 1991;324:1773-8.
10. Rabinowe SN, Neuberg D, Bierman PJ et al. Long-term follow-up of a phase III study of recombinant human granulocyte-macrophage colony-stimulating factor after autologous bone marrow transplantation for lymphoid malignancies. Blood. 1993;81:1903-8.

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.
12. Danyelza [package insert]. New York, NY; Y-mAbs Therapeutics, Inc. ; November 2020. Accessed December 2020.
13. Unituxin [package insert]. Silver Spring, MD; United Therapeutics Corp; September 2020. Accessed December 2020.
14. Palmetto GBA. Local Coverage Determination (LCD): White Cell Colony Stimulating Factors (A56748). Centers for Medicare & Medicaid Services, Inc. Updated on 02/05/2021 with effective date 01/01/2021. Accessed March 2021.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

FOR MEDICAL BENEFIT COVERAGE REQUESTS:

Prior approval is required for HCPCS Codes J2820