Leukine® (sargramostim)
(Subcutaneous/Intravenous)

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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

- Refer to initial prior authorization 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/m² subcutaneously daily for 5 doses starting 5 days prior to the day 1 of naxitamab infusion followed by sargramostim 500 mcg/m² 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/m² 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/m² 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]. Lexington, MA; Partner Therapeutics, Inc.; May 2018. Accessed February 2022.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) sargramostim. National Comprehensive Cancer Network, 2022. 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 February 2022.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Hematopoietic Growth Factors. Version 1.2022. National Comprehensive

Cancer Network, 2022. 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 February 2022.

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9. 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.
10. 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.
11. 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.
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13. Danyelza [package insert]. New York, NY; Y-mAbs Therapeutics, Inc. ; November 2020. Accessed December 2020.
14. Unituxin [package insert]. Silver Spring, MD; United Therapeutics Corp; September 2020. Accessed December 2020.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C74.90	Malignant neoplasm of unspecified part of unspecified adrenal gland
C92.00	Myeloid leukemia not having achieved remission
C92.02	Myeloid leukemia in relapse
C92.50	Acute myelomonocytic leukemia not having achieved remission
C92.52	Acute myelomonocytic leukemia in relapse
C92.60	Acute myeloid leukemia with 11q23-abnormality not having achieved remission
C92.62	Acute myeloid leukemia with 11q23-abnormality in relapse
C92.A0	Acute myeloid leukemia with multilineage dysplasia not having achieved remission
C92.A2	Acute myeloid leukemia with multilineage dysplasia in relapse
C93.00	Acute monoblastic/monocytic leukemia not having achieved remission
C93.02	Acute monoblastic/monocytic leukemia in relapse
D61.81	Pancytopenia
D70.1	Agranulocytosis secondary to cancer chemotherapy
D70.9	Neutropenia, unspecified
T45.1X5A	Adverse effect of antineoplastic and immunosuppressive drugs initial encounter
T45.1X5D	Adverse effect of antineoplastic and immunosuppressive drugs subsequent encounter
T45.1X5S	Adverse effect of antineoplastic and immunosuppressive drugs sequela
T66.XXXA	Radiation sickness, unspecified, initial encounter
T66.XXXD	Radiation sickness, unspecified, subsequent encounter
T66.XXXS	Radiation sickness, unspecified, sequela
W88.1	Exposure to radioactive isotopes
W88.8	Exposure to other ionizing radiation
Z41.8	Encounter for other procedures for purposes other than remedying health state
Z48.290	Encounter for aftercare following bone marrow transplant
Z51.11	Encounter for antineoplastic chemotherapy
Z51.12	Encounter for antineoplastic immunotherapy
Z51.89	Encounter for other specified aftercare
Z52.001	Unspecified donor, stem cells
Z52.011	Autologous donor, stem cells
Z52.091	Other blood donor, stem cells
Z76.89	Persons encountering health services in other specified circumstances
Z94.81	Bone marrow transplant status
Z94.84	Stem cells transplant status

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Articles (LCAs), and Local Coverage Determinations (LCDs)

may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/ search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCA/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC