

**POLICY:** Colony Stimulating Factors – Leukine<sup>®</sup> (sargramostim injection – Partner)

**APPROVAL DATE:** 08/21/2019

### OVERVIEW

Leukine is a recombinant human granulocyte macrophage colony stimulating factor (rhu GM-CSF) and is a hematopoietic growth factor which stimulates proliferation and differentiation of hematopoietic progenitor cells.<sup>1</sup> GM-CSF induces partially committed progenitor cells to divide and differentiate in the granulocyte-macrophage pathways which include neutrophils, monocytes/macrophages, and myeloid-derived dendritic cells. Leukine is indicated for the following: 1) to shorten the time to neutrophil recovery and to reduce the incidence of severe, life-threatening, or fatal infections following induction chemotherapy in adult patients  $\geq 55$  years of age older adult patients with acute myelogenous leukemia (AML); 2) in adult patients with cancer undergoing autologous hematopoietic stem cell transplantation for the mobilization of hematopoietic progenitor cells into peripheral blood for collection by leukapheresis; 3) for the acceleration of myeloid reconstitution after autologous peripheral blood progenitor cell or bone marrow transplantation in adult and pediatric patients 2 years of age and older with non-Hodgkin's lymphoma, acute lymphoblastic leukemia, and Hodgkin's lymphoma; 4) for acceleration of myeloid reconstitution in adult and pediatric patients  $\geq 2$  years of age undergoing allogeneic bone marrow transplantation from HLA-matched related donors; 5) for the treatment of adult and pediatric patients  $\geq 2$  years of age who have undergone allogeneic or autologous bone marrow transplantation in whom neutrophil recovery is delayed or failed; and 6) to increase survival in adult and pediatric patients from birth to 17 years of age acutely exposed to myelosuppressive doses of radiation (hematopoietic syndrome of acute radiation syndrome).<sup>1</sup> Leukine is given as a subcutaneous or intravenous injection.

### Guidelines

The National Comprehensive Cancer Network (NCCN) guidelines for hematopoietic growth factors (version 2.2019 – March 27, 2019), recommends use of CSFs in various scenarios in patients with cancer receiving myelosuppressive chemotherapy.<sup>2</sup> It is notable that Leukine has been removed from the list of prophylactic options based on limited use. These guidelines also note that Leukine is recommended in some clinical scenarios for mobilization and post hematopoietic cell transplantation. Use concurrently with filgrastim products have also been noted.

### Dosing

For most circumstances, Leukine therapy would be given in Cycles 1, 3, and 5 for 14 days of 28 day cycles for a total of six cycles for use with Unituxin in patients with high-risk neuroblastoma.<sup>3</sup>

### POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of Leukine. Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Leukine as well as the monitoring required for adverse events and long-term efficacy, approval for some conditions requires Leukine to be prescribed by or in consultation with a physician who specializes in the condition being treated.

### RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Leukine is recommended in those who meet one of the following criteria:

#### FDA-APPROVED INDICATIONS

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- 1. Acute Myeloid Leukemia (AML).** Approve for 6 months if the patient is prescribed by or in consultation with an oncologist or a hematologist.

**Dosing.** Approve up to 250 mcg/m<sup>2</sup> per day by intravenous or subcutaneous injection.

- 2. Peripheral Blood Progenitor Cell (PBPC) Collection and Therapy.** Approve for up to 14 days if the agent is prescribed by or in consultation with an oncologist, a hematologist, or a physician who specializes in transplantation.

**Dosing.** Approve one of the following (A or B):

A) Up to 500 mcg/m<sup>2</sup> per day given by intravenous or subcutaneous injection; OR

B) Up to 7.5 mcg/kg per day by subcutaneous injection.

- 3. Bone Marrow Transplantation (BMT).** Approve for 1 month if prescribed by or in consultation with a hematologist, an oncologist, or a physician who specializes in transplantation.

**Dosing.** Approve up to 250 mcg/m<sup>2</sup> per day by intravenous injection.

- 4. Radiation Syndrome (Hematopoietic Syndrome of Acute Radiation Syndrome).** Approve for 1 month if the agent is prescribed by or in consultation with a physician who has expertise in treating acute radiation syndrome.

**Dosing.** Approve up to 12 mcg/kg per day as a subcutaneous injection.

#### Other Uses with Supportive Evidence

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- 5. Neuroblastoma.** Approve for 6 months if the patient meets ~~both of the~~ following criteria (A, B, and C):

A) The patient is < 18 years of age; AND

B) The agent is prescribed by, or in consultation with, an oncologist; AND

C) The patient is receiving Leukine in a regimen with Unituxin™ (dinutuximab injection for intravenous use).

**Dosing.** Approve up to 250 mcg/m<sup>2</sup> per day by intravenous or subcutaneous injection.

#### CONDITIONS NOT RECOMMENDED FOR APPROVAL

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Leukine has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-

coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.

1. Coverage is not recommended for circumstances *not* listed in the *Recommended Authorization Criteria*. Criteria will be updated as new published data are available.

**REFERENCES**

1. Leukine® injection for intravenous or subcutaneous use [prescribing information]. Lexington, MA: Partner Therapeutics; May 2018.
2. The NCCN Hematopoietic Growth Factors Clinical Practice Guidelines in Oncology (Version 2.2019 – March 27, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on August 21, 2019.
3. Unituxin™ injection for intravenous use [prescribing information]. Silver Springs, MD: United Therapeutic Corporation; March 2017.

**HISTORY**

Type of Revision	Summary of Changes	Approval Date
Annual revision	For the criteria regarding patients with cancer receiving myelosuppressive therapy in the criteria that reference a colony stimulating factor, the terminology of filgrastim and pegfilgrastim products were added, along with the listing of the individual products, which included adding Fulphila and Nivestym. For the criteria regarding patients with cancer receiving myelosuppressive Criteria for radiation syndrome (Hematopoietic Syndrome of Acute Radiation Syndrome) moved from other “Other Uses with Supportive Evidence Section) to the FDA-approval section. The dosing for this indication was changed to reflect the FDA-approved dosing	08/01/2018
Annual revision	For all conditions, the Dosing sections were revised to provide for the maximum range of dosing (see Policy). Additionally, the following sections were removed: initial/extended approval, duration of therapy, and labs/diagnostics. The waste management section was also deleted. Additional changes per the specific indications were as follows: <ol style="list-style-type: none"> <li>1. <b>Bone Marrow Transplant.</b> Criteria were added that approves Leukine for 1 month if prescribed by or in consultation with a hematologist, an oncologist, or a physician who specializes in transplantation. Previously, criterion directed to a Medical Director and this criterion was removed.</li> <li>2. <b>Cancer in Patients Receiving Myelosuppressive Chemotherapy:</b> This indication for use, and related criteria, were removed.</li> <li>3. <b>Myelodysplastic syndrome:</b> This indication for use was deleted.</li> <li>4. <b>Neuroblastoma:</b> Criteria were added that the patient is &lt; 18 years of age and the phrase “Pediatric Patients with High Risk” was removed from the cited condition of approval.</li> </ol>	08/21/2019