Clinical Policy: Sargramostim (Leukine)

Reference Number: ERX.SPA.60
Effective Date: 09.01.17
Last Review Date: 08.21
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Sargramostim (Leukine®) is a recombinant human granulocyte-macrophage colony stimulating factor.

FDA Approved Indication(s)
Leukine is indicated:
- To shorten time to neutrophil recovery and to reduce the incidence of severe and life-threatening infections and infections resulting in death following induction chemotherapy in adult patients 55 years and older with acute myeloid leukemia (AML);
- For the mobilization of hematopoietic progenitor cells into peripheral blood for collection by leukapheresis and autologous transplantation in adult patients;
- For the acceleration of myeloid reconstitution following autologous peripheral blood progenitor cell (PBPC) or bone marrow transplantation in adult and pediatric patients 2 years of age and older with non-Hodgkin's lymphoma (NHL), acute lymphoblastic leukemia (ALL) and Hodgkin's lymphoma (HL);
- For the acceleration of myeloid reconstitution following allogeneic bone marrow transplantation in adult and pediatric patients 2 years of age and older;
- For treatment of delayed neutrophil recovery or graft failure after autologous or allogeneic bone marrow transplantation in adult and pediatric patients 2 years of age and older;
- 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 [H-ARS]).

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Leukine is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Acute Myelogenous Leukemia (must meet all)**:**
1. Diagnosis of AML;
2. Prescribed for use following induction therapy for AML;
3. Age ≥ 55 years;
4. Failure of a formulary filgrastim or filgrastim biosimilar product, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization is required for filgrastim and filgrastim biosimilars*
5. Dose does not exceed 250 mcg/m^2 IV daily.

Approval duration: 6 months

B. Peripheral Blood Progenitor Cell Collection and Transplantation (must meet all)**:**
1. Prescribed for one of the following (a or b):
   a. Mobilization of hematopoietic progenitor cells into peripheral blood for collection by leukapheresis and autologous transplantation;

b. Following autologous PBPC transplantation in members with NHL, ALL, HL for acceleration of myeloid reconstitution;

2. Age ≥ 2 years;
3. Failure of a formulary filgrastim or filgrastim biosimilar product, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization is required for filgrastim and filgrastim biosimilars*
4. Dose does not exceed 250 mcg/m^2 IV or SC daily.

Approval duration: 6 months

C. Bone Marrow Transplantation (must meet all)**:**

1. Prescribed for use in one of the following settings (a, b, or c):
   a. Following autologous BMT in members with NHL, ALL, HL for acceleration of myeloid reconstitution;
   b. Following allogeneic BMT for acceleration of myeloid reconstitution;
   c. Following BMT where engraftment is delayed or has failed;
2. Age ≥ 2 years;
3. Failure of a formulary filgrastim or filgrastim biosimilar product, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization is required for filgrastim and filgrastim biosimilars*
4. Dose does not exceed 500 mcg/m^2 IV daily.

Approval duration: 6 months

D. Acute Radiation Syndrome (must meet all)**:**

1. Prescribed for use following suspected or confirmed acute exposure to myelosuppressive doses of radiation;
2. Failure of a formulary filgrastim or filgrastim biosimilar product, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization is required for filgrastim and filgrastim biosimilars*
3. Dose does not exceed one of the following (a, b, or c):
   a. Weight <15 kg: 12 mcg/kg SC daily;
   b. Weight 15 kg to 40 kg: 10 mcg/kg SC daily;
   c. Weight > 40 kg: 7 mcg/kg SC daily.

Approval duration: 6 months

E. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Dose does not exceed the FDA-approved maximum recommended dose for the relevant indication.

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALL: acute lymphoblastic leukemia
AML: acute myelogenous leukemia
BMT: bone marrow transplantation
FDA: Food and Drug Administration
GM-CSF: granulocyte-macrophage colony stimulating factor
H-ARS: hematopoietic syndrome of acute radiation syndrome
NHL: non-Hodgkin's lymphoma
PBPC: peripheral blood progenitor cell

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Maximum Dose
Filgrastim (Neupogen), filgrastim-sndz (Zarxio), filgrastim-aafi (Nivestym)	Chemotherapy-induced neutropenia: 5 mcg/kg SC or IV QD Dose may be increased in increments of 5 mcg/kg for each chemotherapy cycle, according to the duration and severity of the ANC nadir Do not administer 24 hours before and after chemotherapy	30 mcg/kg/day [IV] or 24 mcg/kg/day [SC]
	Chronic neutropenia: Congenital: 6 mcg/kg SC BID Idiopathic or cyclic: 5 mcg/kg SC QD	30 mcg/kg/day [IV] or 24 mcg/kg/day [SC]
	BMT: 10 mcg/kg IV or SC infusion QD	10 mcg/kg/day
	Peripheral blood progenitor cell collection: 10 mcg/kg SC bolus or continuous infusion QD	10 mcg/kg/day
	Patients acutely exposed to myelosuppressive doses of radiation: 10 mcg/kg SC QD	10 mcg/kg/day
Tbo-filgrastim (Granix)	Myelosuppressive chemotherapy: 5 mcg/kg SC or IV QD	5 mcg/kg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): history of serious allergic reactions, including anaphylaxis
- Boxed warning(s): none reported

Appendix D: General Information

- Because of potential sensitivity of rapidly dividing hematopoietic progenitor cells, Leukine should not be administered simultaneously with cytotoxic chemotherapy or radiotherapy or within 24 hours preceding or following chemotherapy or radiotherapy.
- Use Leukine with caution in patients with pre-existing fluid retention, pulmonary infiltrates, or congestive heart failure.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
AML	250 mcg/m^2/day IV over a 4 hour period approximately on day 11 or four days following the completion of induction chemotherapy	250 mcg/m^2 IV daily
Peripheral blood progenitor cell collection and transplantation	250 mcg/m^2/day administered IV over 24 hours or SC once daily	250 mcg/m^2 IV or SC daily
Myeloid reconstitution after autologous or allogeneic BMT	250 mcg/m^2/day IV over a 2 hour period beginning two to four hours after bone marrow infusion, and not less than 24 hours after the last dose of chemotherapy or radiotherapy	500 mcg/m^2 IV daily
BMT failure or engraftment delay	250 mcg/m^2/day for 14 days as a 2 hour IV infusion	500 mcg/m^2 IV daily
Acute radiation syndrome	Weight-based dose SC QD: > 40 kg: 7 mcg/kg 15 to 40 kg: 10 mcg/kg < 15 kg: 12 mcg/kg	See dosing regimen

VI. Product Availability

- Lyophilized powder: 250 mcg single-dose vial
- Solution: 500 mcg/mL multiple-dose vial

VII. References

1. Leukine Prescribing Information. Bridgewater, NJ: Sanofi-Aventis U.S., LLC.; March 2018. Available at: www.leukine.com. Accessed April 5, 2021.
2. National Comprehensive Cancer Network: Hematopoietic Growth Factors Version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/growthfactors.pdf. Accessed: April 5, 2021.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed April 5, 2021.
4. DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed April 5, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy split from ERX.SPMN.07 Colony Stimulating Factors and converted to new template. Renewal criteria added. Separated criteria by indication rather than by drug. Off-label uses are referred to the off-label use policy. Changed approval duration for peripheral blood progenitor cell collection to reflect actual duration of therapy. Post-consolidation for AML is not a labeled use so was removed.	07.17	08.17
3Q 2018 annual review: added new indication for acute radiation syndrome; removed contraindications that are no longer included in the product label; modified age restrictions consistent with label; references reviewed and updated.	05.02.18	08.18
3Q 2019 annual review: no significant changes; updated maximum dosing and route of administration consistent with the prescribing information; references reviewed and updated.	05.15.19	08.19
3Q 2020 annual review: added redirection to a formulary filgrastim or filgrastim biosimilar product; for ARS indication added weight based dosing to criteria set; references reviewed and updated.	05.04.20	08.20

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2021 annual review: no significant changes; references reviewed and updated.	04.05.21	08.21

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.