Clinical Policy Title:	sargramostim
Policy Number:	RxA.199
Drug(s) Applied:	Leukine®
Original Policy Date:	02/07/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

Sargramostim (Leukine®) is a recombinant human granulocyte-macrophage colony-stimulating factor (GM-CSF). Sargramostim is indicated:

- To shorten time to neutrophil recovery and to reduce the incidence of severe, life- threatening infections or 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 with cancer;
- 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]).

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
sargramostim (Leukine®)	AML	250 mcg/m^2/day intravenous over a 4-hour period approximately on day 11 or 4 days following the completion of induction chemotherapy	250 mcg/m^2 intravenous daily
	PBPC collection and transplantation	250 mcg/m^2/day intravenous over 24 hours or subcutaneous once daily	250 mcg/m^2 intravenous or subcutaneous daily
	Myeloid reconstitution after autologous or allogeneic bone marrow transplantation	250 mcg/m^2/day intravenous 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 intravenous daily

	bone marrow transplantation failure or engraftment delay	250 mcg/m^2/day for 14 days as a 2-hour intravenous infusion	500 mcg/m^2 intravenous daily
	acute radiation syndrome	weight-based dose sub cutaneous daily: greater than 40 kg: 7 mcg/kg 15 to 40 kg: 10 mcg/kg less than15 kg: 12 mcg/kg	see dosing regimen

Dosage Forms

- Lyophilized powder: 250 mcg single-dose vial

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of prescriber samples does not guarantee coverage under the provisions of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Acute myeloid leukemia (must meet all)**:**

1. Diagnosis of acute myeloid leukemia;
2. Prescribed for use following induction therapy for acute myeloid leukemia;
3. Age 55 years or older;
4. Failure of Neupogen® or Zarxio®, unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed 250 mcg/m^2 intravenous daily.

Approval Duration
Commercial: 6 months
Medicaid: 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; or
   b. Following autologous peripheral blood progenitor cell transplantation in members with non-Hodgkin's lymphoma, acute lymphoblastic leukemia, Hodgkin's lymphoma for acceleration of myeloid reconstitution;
2. Age 2 years or older;
3. Failure of Neupogen® or Zarxio®, unless contraindicated or clinically significant adverse effects are experienced;
4. Dose does not exceed 250 mcg/m^2 intravenous or subcutaneous daily.

Approval Duration
Commercial: 6 months
Medicaid: 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 bone marrow transplantation in members with non-Hodgkin's lymphoma, acute lymphoblastic leukemia, or Hodgkin's lymphoma for acceleration of myeloid reconstitution;
   b. Following allogeneic bone marrow transplantation for acceleration of myeloid reconstitution;
   c. Following bone marrow transplantation where engraftment is delayed or has failed;
2. Age 2 years or older;
3. Failure of Neupogen® or Zarxio®, unless contraindicated or clinically significant adverse effects are experienced;
4. Dose does not exceed 500 mcg/m^2 intravenous daily.

Approval Duration
Commercial: 6 months
Medicaid: 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 Neupogen® or Zarxio®, unless contraindicated or clinically significant adverse effects are experienced;
3. Dose does not exceed 12 mcg/kg subcutaneously daily.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

E. Chemotherapy-induced febrile neutropenia (off-label) (must meet all):
1. Prescribed as prevention or treatment of neutropenia in patients receiving chemotherapy or who are at high risk for neutropenic fever;
2. Member has one or more of the following risk factors (a through k):
   a. Age 65 years of age or older;
   b. Absolute neutrophil count less than 100/mcL occurred after previous cycle of similar chemotherapy;
   c. Neutropenia is expected to last greater than 10 days in duration;
   d. Documented active clinical infection, such as pneumonia or fungal infection, open wounds or recent surgery;
   e. Bone marrow involvement by tumor resulting in cytopenia(s);
   f. Previous chemotherapy and/or radiation therapy;
   g. Poor nutritional and/or performance status;
   h. Presence of sepsis syndrome;
   i. Presence of serious comorbidities, including renal dysfunction, hepatic dysfunction, HIV infection or cardiovascular disease;
   j. Member was hospitalized at the time of the development of fever;
   k. Prior episode of febrile neutropenia.
3. Member is not receiving other colony stimulating factors within a chemotherapy regimen;
4. Dose does not exceed 250mcg/m^2 daily.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. Dose does not exceed the Food and Drug Administration-approved maximum recommended dose for the relevant indication.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

III. Appendices

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
NCCN: National comprehensive cancer network
NHL: Non-Hodgkin's lymphoma
PBPC: Peripheral blood progenitor cell

APPENDIX B: Therapeutic Alternatives

Not applicable

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Patients with a history of serious allergic reactions, including anaphylaxis to human granulocyte-macrophage colony stimulating factor such as sargramostim, yeast-derived products, or any component of the product.

- Boxed Warning(s):
  - None reported

APPENDIX D: General Information

- NCCN lists the use of granulocyte colony-stimulating factors for the prevention of chemotherapy-induced febrile neutropenia as a category 2A recommendation.

References

1. Leukine® Prescribing Information. Lexington, MA: Partner Therapeutics, Inc.; May 2018. Available at: https://www.leukine.com/#. Accessed March 01, 2021.
2. National Comprehensive Cancer Network: Hematopoietic Growth Factors Version 1.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/growthfactors.pdf . Accessed March 01, 2021.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed March 01, 2021.
4. Sargramostim. Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI; 2020, May 8. Accessed with subscription at: http://www.micromedexsolutions.com. Accessed March 01, 2021.

5. Clinical Pharmacology [database online] powered by ClinicalKey. Tampa, FL: Elsevier, 2020. Accessed with subscription at: http://www.clinicalkey.com. Updated January 14, 2020. Accessed March 01, 2021.
6. Sargramostim, Lexi-Drug. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed with subscription at: http://online.lexi.com. Accessed March 01, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
1. Clinical Policy Title was updated. 2. Drug(s) Applied was updated. 3. Line of Business Policy Applies to was update to all lines of business. 4. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 5. Initial Approval criteria: Commercial and Medicaid approval duration were updated from member's renewal date to 6 months. 6. Continued Approval criteria: Commercial and Medicaid approval duration were updated from length of benefit to 12 months. 7. References were updated.	08/03/2020	09/14/2020
Policy was reviewed: 1. Dosage forms was updated: [DSC] was updated for Solution: 500 mcg/mL. 2. APPENDIX B: Therapeutic Alternatives was added. 3. References were updated.	03/01/2021	06/10/2021