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5.85.008

Section:	Prescription Drugs	**Effective Date:**	July 1, 2024
Subsection:	Hematological Agents	**Original Policy Date:**	December 7, 2011
Subject:	Leukine	**Page:**	1 of 6

Last Review Date: June 13, 2024

Leukine

Description

Leukine (sargramostim)

Background
Leukine (sargramostim) is a man-made form of granulocyte-macrophage colony-stimulating factor (GM-CSF) which is a type of protein that your body produces to help increase the number of white blood cells (WBCs). Some cancer treatments, including chemotherapy, can kill healthy cells like WBCs in addition to killing cancer cells. Leukine is used to help increase the number and function of white blood cells after bone marrow transplantation, in cases of bone marrow transplantation failure or engraftment delay, before and after peripheral blood stem cell transplantation, and following induction chemotherapy in older patients with acute myelogenous leukemia (1).

Leukine may treat other conditions such as neutropenia that is HIV associated, chemotherapy associated, or hepatitis C treatment associated and in the treatment of severe chronic, congenital neutropenia (1-2).

Regulatory Status
FDA-approved indications: Leukine is a leukocyte growth factor indicated: (1)

1. 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)
2. For the mobilization of hematopoietic progenitor cells into peripheral blood for collection by leukapheresis and autologous transplantation in adult patients

3. For the acceleration of myeloid reconstitution following autologous bone marrow or peripheral blood progenitor cell transplantation in adult and pediatric patients 2 years of age and older
4. For the acceleration of myeloid reconstitution following allogeneic bone marrow transplantation in adult and pediatric patients 2 years of age and older
5. 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
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 [H-ARS])

Off-Label Uses: (2-3)

1. Neutropenia
    a. Prophylaxis and treatment of chemotherapy-induced febrile neutropenia in non-myeloid malignancies
    b. Chemotherapy associated
    c. Neutropenia related to HIV/AIDS
    d. Hepatitis C therapy associated
    e. Chronic congenital (Kostmann's Syndrome)
2. Acute myelogenous leukemia following induction or consolidation chemotherapy in pediatrics and adults
3. Mobilization and following transplantation of autologous peripheral blood progenitor cells in pediatric patients
4. Agranulocytosis
5. Aplastic anemia
6. Stem cell transplantation-related indications

Leukine use is contraindicated 24 hours before and after administration of myelosuppressive chemotherapy or radiation (1).

Related policies

Neulasta, Neupogen, Rolvedon

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Leukine may be considered **medically necessary** if the conditions indicated below are met.

Leukine may be considered **investigational** for all other indications.

Prior-Approval Requirements

Diagnoses

Patient must have **ONE** of the following:

1. Acute myeloid leukemia (AML)
2. Hematopoietic stem cell transplantation
3. Peripheral blood progenitor cell (PBPC) collection
4. Umbilical cord stem cell transplantation
5. Myelodysplastic syndrome in neutropenic patients with recurrent or resistant infections
6. Neutropenia
    a. AIDS associated
    b. Chemotherapy associated; prophylaxis in patients at intermediate to high risk for febrile neutropenia following chemotherapy with solid or non-myeloid malignancies
    c. Hepatitis C therapy associated (ANC<750/mm^3)
    d. Chronic congenital (Kostmann's Syndrome)
7. Autologous peripheral blood progenitor cell (PBPC) mobilization and following transplantation
8. Agranulocytosis
9. Aplastic anemia
10. Hematopoietic Syndrome of Acute Radiation Syndrome [H-ARS]

AND the following

1. **NOT** used in combination with granulocyte colony-stimulating factor (G-CSF) medications

Prior – Approval *Renewal* Requirements

Same as above

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 6 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Leukine (sargramostim) is a recombinant human granulocyte-macrophage colony-stimulating factor (GM-CSF) that facilitates the proliferation and differentiation of cells including neutrophils and macrophages. Leukine prevents the growth of tumor cells and increases activity against cancer cells. Leukine use is contraindicated 24 hours before and after administration of myelosuppressive chemotherapy or radiation (1-3).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Leukine while maintaining optimal therapeutic outcomes.

References

1. Leukine [package insert]. Lexington, MA: Partner Therapeutics, Inc.; August 2023.
2. NCCN Drugs & Biologics Compendium® Sargramostim 2024. National Comprehensive Cancer Network, Inc. Accessed on April 17, 2024.
3. Smith TJ, Bohlke K, Lyman GH, et al. Recommendations for the use of white blood cell growth factors: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol. 2015;33(28):3199-3212.

Policy History

Date	Action
July 2010	ICD-9 code was removed for myelosuppressive chemotherapy, to decrease the incidence of infection as manifested by febrile neutropenia (various), bone marrow transplantation (996.85), peripheral blood progenitor cell collection (various), acceleration of myeloid recovery in

	patients with non-Hodgkin's lymphoma, ALL or Hodgkin's disease undergoing bone marrow transplantation (various), induction chemotherapy in acute myelogenous leukemia (various), mobilization and following transplantation of autologous PBPC (various), myeloid reconstitution after allogenic bone marrow transplantation (various), severe chronic neutropenia (various) and bone marrow transplantation failure or engraftment delay (996.0-996.5). ICD-9 code was updated for bone marrow transplantation failure or engraftment delay (996.82). ICD-10 code was added for bone marrow transplantation failure or engraftment delay (T86.02).
December 2010	Simplify criterion; listing approved diagnoses in a bullet point style which is easier to read with associated lab values supported in the FDA approved packaging. Removal of Neulasta from the colony stimulating agents PA criteria due to different FDA approved indications (1). Removal of remaining ICD-9 codes due to various codes used to indicate these diagnoses.
September 2011	Separating the colony stimulating agent criterion into individual agents; adding coverage for drug (non-chemotherapy) associated neutropenia for Hepatitis C treatment. Hepatitis C virus (HCV) therapy-induced neutropenia; defined as absolute neutrophil count (ANC) below 750 cells/µL. ANC typically decreases by 30-50% from normal with HCV therapy. Therefore, neutropenia is a common reason for dose reduction or withdrawal from HCV therapy (1). Treatment for neutropenia is granulocyte colony stimulating factors (GM-CSF) such as Leukine. Several studies have shown that administration of GM-CSF is effective in increasing neutrophil count and reducing dose reduction or withdrawal from HCV therapy, which leads to increased sustained virological response (SVR) (2,3). Not having to modify the dose of HCV therapy and an increased SVR means an improvement in the quality of life of the patient (3). Current criterion allows for treatment of AIDS associated neutropenia with Leukine which is supported by USP Drug Information (4). Also treatment of chemotherapy associated neutropenia with Leukine is supported by National Comprehensive Cancer Network (NCCN) (5). Although not FDA approved, treatment of Myelodysplastic syndrome is supported by the American Society of Clinical Oncology (ASCO) and the National Comprehensive Cancer Network (NCCN) (5,6).
November 2011	There has been a clarification of rationale statement. The difference between FDA approved and other approvable criteria was defined. The criteria of myelodysplastic syndrome, AIDS associated and congenital neutropenia were referenced.
November 2011	Added further requirements to the diagnosis of AML in order to align with both Leukine prescribing information and NCCN guidelines which state that efficacy and safety have not been studied in patients <55 years old.

	Further, Leukine treatment should be not be initiated post-induction if there are >5% residual blasts due to the risk of disease progression (1,6,10). Clarified use in autologous bone marrow transplants to align with the prescribing information (1). Removed Hematopoietic stem cell transplantation and added it to the diagnosis of peripheral blood progenitor cell mobilization. Clarified use in chemotherapy-associated neutropenia to align with NCCN guidelines which state that GM-CSF should only be used in patients with solid or non-myeloid malignancies at high- or intermediate-risk for developing febrile neutropenia (11).
December 2011	Annual review and update
December 2012	Annual review and update
March 2014	Annual review and reference update
June 201	Annual editorial review and reference updat
December 2016	Annual review and reference update Policy Code changed from 5.10.08 to 5.85.08
September 2017	Annual editorial review and reference update
April 2018	Addition of indications: agranulocytosis, aplastic anemia, or hematopoietic syndrome of acute radiation syndrome [H-ARS] Remove of “in patients >55 years old following induction chemotherapy if bone marrow demonstrates <5% blasts” from AML
June 2018	Annual review Addition of no dual therapy of granulocyte colony-stimulating factor (G-CSF) medications
September 2018	Annual editorial review and reference update
November 2018	Annual review
March 2019	Annual review and reference update
March 2020	Annual review and reference update
March 2021	Annual editorial review
June 2021	Annual review and reference update
June 2022	Annual review and reference update
March 2023	Annual review and reference update. Changed policy number to 5.85.008
June 2023	Annual review and reference update. Per SME, updated approval durations to 6 months from 12 months for consistency
June 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 13, 2024 and is effective on July 1, 2024.