

Medical Affairs Policy & Procedure

Title/Service: Human Granulocyte/Macrophage Colony Stimulating Factors
(filgrastim, G-CSF, sargramostim, GM-CSF, Pegfilgrastim, Neulasta, Neupogen, Leukine)

Revised	09/16/11
Reviewed	03/24/00, 10/25/02, 03/24/06, 01/23/09, 10/22/10, 04/15/11
Developed	03/24/00
Policy Committee Approval	09/16/11

Description:

Human granulocyte colony-stimulating factors are drugs used to regulate the production of neutrophils (a white blood cell) in the bone marrow. Neutrophils congregate at the site of an infection as a component of the body's immune system response. Granulocyte macrophage colony-stimulating factor is a substance used to increase bone marrow production of new white blood (macrophage) cells.

Indications of Coverage:

Human Granulocyte/Macrophage Colony Stimulating Factors are considered medically necessary for the following conditions:

- A. To decrease the incidence of infection as manifested by febrile neutropenia, for patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence (greater than 20%)* of severe neutropenia with fever.
- B. For the prevention of febrile neutropenia in individuals where any of the following are documented:
 - 1) The anti-cancer drugs proposed for use are associated with a significant incidence (greater than 20%)* of severe neutropenia with fever
 - 2) The dose of the anti-cancer drugs cannot be reduced to decrease the incidence of febrile neutropenia
 - 3) Current or expected neutropenia will cause a delay in chemotherapy treatment
 - 4) The individual is at high risk for chemotherapy-induced infectious complications. Such risk factors may include the following and must be documented in the patient record:

- a) Pre-existing neutropenia due to disease
 - b) Extensive prior chemotherapy
 - c) Previous irradiation to the pelvis or other areas containing large amounts of bone marrow
 - d) A history of recurrent febrile neutropenia while receiving earlier chemotherapy of similar or lesser dose-intensity
 - e) Conditions potentially enhancing the risk of serious infection (for example, age greater than 65 years, poor nutritional status, renal or hepatic dysfunction)
- C. For individuals with chemotherapy-induced infectious complications with febrile neutropenia requiring hospitalization. Febrile neutropenia is defined as a single oral temperature of 38.3C (101 F) or 38 C (100.4 F) for more than 1 hr, when the absolute neutrophil count (ANC) is less than 500 per cubic millimeter or less than 1000 per cubic millimeter and a predicted decline to less than 500 per cubic millimeter over the next forty eight hours.
- D. Peripheral Blood Progenitor Cell (PBPC) Collection - for the mobilization of hematopoietic progenitor cells into the peripheral blood for leukapheresis collection.
- E. Acquired immunodeficiency syndrome (AIDS) patients with neutropenia caused by the disease itself or by opportunistic infections or individuals with AIDS receiving zidovudine.
- F. Severe aplastic anemia.
- G. In individuals with Acute Myeloid Leukemia (AML) receiving induction or consolidation chemotherapy.
- H. Drug induced or congenital agranulocytosis, alloimmune neonatal neutropenia.
- In addition to the indications above, Filgrastim (Neupogen) is considered medically necessary for any of the following conditions:
- A. To reduce the duration of neutropenia and neutropenia related clinical sequelae (febrile neutropenia) for patients with non-myeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplant.
 - B. Severe chronic neutropenia: chronic administration to reduce the incidence and duration of sequelae of neutropenia (for example, fever, infections, and oropharyngeal ulcers) in symptomatic patients with congenital, cyclic or idiopathic neutropenia.
 - C. Hairy cell leukemia

D. Myelodysplastic syndrome (not recommended for routine infection prophylaxis; allowed for recurrent or resistant infections in neutropenic patients).

➤ In addition to the indications above, sargramostim (Leukine) is considered medically necessary for any of the following conditions:

- A. Acceleration of myeloid recovery in patients with non-Hodgkin's lymphoma (NHL), acute lymphoblastic leukemia (ALL) and Hodgkin's disease undergoing autologous bone marrow transplantation (BMT)
- B. Bone Marrow Transplant failure or engraftment delay. (For individuals who have undergone allogeneic or autologous BMT in whom engraftment is delayed or has failed.)
- C. The acceleration of neutrophil recovery following induction of chemotherapy in the treatment of patients over the age of 55-years old with acute myelogenous leukemia. (Safety and efficacy has not been established in AML patients less than 55 years of age.)
- D. Myeloid reconstitution after allogeneic bone marrow transplant (BMT). For acceleration of myeloid recovery in individuals undergoing allogeneic BMT from human lymphocyte antigen (HLA) matched related donors
- E. To increase white blood cell (WBC) counts in patients with myelodysplastic syndromes
- F. To decrease nadir of leukopenia secondary to myelosuppressive chemotherapy and decrease myelosuppression in preleukemic patients

* See list from the National Comprehensive Cancer Network (NCCN) Practice Guideline in Oncology for Myeloid Growth Factors (page MGF-A) available at www.nccn.org. Note that this is not an all-inclusive list. The use of myeloid growth factors for other chemotherapy regimens should be referred for pharmacy review.

Administration: Human Granulocyte/Macrophage Colony Stimulating Factor injections are self-administered unless contraindicated (for example, the individual is unable to inject themselves due to a functional limitation). One injection in the clinic for teaching is allowed for individuals who have not previously received instruction in self-administered injections. For individuals with functional limitations, home health assistance may be considered.

Limitations of Coverage:

- A. Review contract and endorsements for exclusions and prior authorization or benefit requirements.

- B. If used for a condition/diagnosis other than is listed in the Indications of Coverage, deny as experimental or investigative.
- C. If used for a condition/diagnosis that is listed in the Indications of Coverage, but the criteria are not met, deny as not medically necessary.

Documentation Required:

- Office notes
- Laboratory test results
- Prescription medication use data

Rationale:

White blood cell stimulating factors may be required to reduce the risk of severe infection for patients whose own production of cells is suppressed by circumstances such as disease or chemotherapy, or to stimulate cells prior to stem cell or bone marrow transplant. Their use may also be needed to allow certain intensive chemotherapy regimens.

References:

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3. Bayer HealthCare Pharmaceuticals. Leukine (sargramostim) package insert. Seattle, WA: Bayer HealthCare Pharmaceuticals Inc. Revised: 07/2009. Available at: www.leukine.com/~media/Files/Leukine/Leukine_PI.pdf. Accessed: 30 Aug 11.
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5. Lyman GH, Lyman CH, Agboola O. Risk models for predicting chemotherapy-induced neutropenia. Oncologist. 2005 Jun-Jul;10(6):427-37.
6. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology. Myeloid Growth Factors V.1.2011. Available at: www.nccn.org. Accessed: 30 Aug 11.

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8. Timmer-Bonte JN, Adang EM, Smit HM, Biesma B, Wilschut FA, Bootsma GP, de Boo, TM, Tjan-Heijnen VC. Cost-effectiveness of adding granulocyte-colony stimulating factor to primary prophylaxis with antibiotics in small-cell lung cancer. *J Clin Oncol* 2006; 24:2991-2997.

Approved by the Medical Director