Reference number(s)
4490-A

JURISDICTION SPECIFIC MEDICARE PART B

FILGRASTIM PRODUCTS
NEUPOGEN (filgrastim)
NIVESTYM (filgrastim-aafi)
RELEUKO (filgrastim-ayow)
ZARXIO (filgrastim-sndz)

POLICY

I. COVERED USES

The indications below are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. Patients with cancer receiving myelosuppressive chemotherapy and/or immunotherapy
B. Patients with acute myeloid leukemia receiving induction or consolidation chemotherapy
C. Patients with cancer receiving bone marrow transplantation
D. Patients undergoing autologous peripheral blood progenitor cell collection and therapy
E. Patients with severe chronic neutropenia (congenital, cyclic, or idiopathic)
F. Patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic syndrome of acute radiation syndrome)
G. Adjunctive treatment of neutropenia in certain conditions
H. Acute lymphocytic leukemia (ALL)
I. Hairy cell leukemia
J. Myelodysplastic syndromes (MDS) with severe neutropenia or recurrent infection
K. Dose dense therapy for adjuvant treatment of breast cancer or other malignancies
L. Drug-induced (non-chemotherapy) neutropenia
M. Glycogen storage disease type 1b
N. Neutropenia associated with human immunodeficiency virus (HIV) infection and antiretroviral therapy
O. Radiation therapy in the absence of chemotherapy
P. After hematopoietic progenitor stem cell transplant (HPCT/HSCT) to promote reconstitution
Q. After hematopoietic progenitor stem cell transplant (HPCT/HSCT) when engraftment is delayed or has failed
R. Mobilization of progenitor cells as an adjunct to peripheral blood/hematopoietic stem cell transplant (PBSCT/PHSCT)
S. Alternate or adjunct to donor leukocyte infusions (DLI) after allogenic hematopoietic stem cell transplant

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

II. DOCUMENTATION

The following documentation must be available, upon request, for all submissions:

A. The member's medical record must document the medical necessity of services performed for each date of service submitted on a claim
B. For primary or secondary prophylaxis in conjunction with cancer chemotherapy, the record must document risk factors in members receiving agents/doses uncommonly associated with myelosuppression.
C. For dose dense chemotherapy, the medical record clearly indicates the member is on a 14-day dose dense chemotherapy cycle regimen.
D. For the treatment of chronic neutropenia, the medical record must document the appropriate evaluation of the cause of neutropenia, and where appropriate, a history of recurrent fevers and/or infections. The absolute neutrophil count must be documented but does not need to be submitted with the claim.
E. For prophylaxis of chemotherapy-associated neutropenia, indicate the chemotherapy drug used in the medical record.
F. The member's medical record must clearly document the time the last dose of the cytotoxic chemotherapy cycle ended and the time the G-CSF drug was administered.
G. If filgrastim will be administered outside the timeframe specified by the FDA labeling, the reason for the exception should be clearly documented in the medical record.

III. EXCLUSIONS

Coverage will not be provided for members with any of the following exclusions:

A. Administration of filgrastim to increase chemotherapy dose intensity except as noted below
B. Continuous use of filgrastim for myelodysplastic syndrome or Felty's syndrome without infections
C. Chemosensitization of myeloid leukemias
D. Continued use if no response is seen within 28-42 days
E. Administration in members with chronic aplastic anemia

IV. CRITERIA FOR APPROVAL

A. Prevention of Febrile Neutropenia in Cancer Patients Receiving Myelosuppressive Chemotherapy and/or Immunotherapy

Authorization of 6 months may be granted for prevention of febrile neutropenia when the chemotherapeutic agents are covered by Medicare and any of the following criteria are met:

1. Filgrastim will be used for primary prophylaxis in a member whose risk of febrile neutropenia is 20% or greater based on the chemotherapy regimen
2. Filgrastim will be used for primary prophylaxis in a member whose risk of febrile neutropenia is greater than or equal to 10% and less than 20% based on the chemotherapy regimen and at least one of the following risk factors for febrile neutropenia are present:
   i. Age greater than 65 years
   ii. Poor performance status
   iii. Previous episodes of febrile neutropenia
   iv. History of previous chemotherapy or radiation therapy
   v. After completion of combined chemoradiotherapy
   vi. Bone marrow involvement by tumor producing cytopenias
   vii. Preexisting neutropenia

viii. Poor nutritional status
ix. Poor renal function
x. Liver dysfunction (i.e., elevated bilirubin)
xi. Presence of open wounds or active infections
xii. Recent surgery (within the past 12 weeks)
xiii. Advanced cancer
xiv. Other serious comorbidities

3. Filgrastim will be used as secondary prophylaxis when both of the following conditions are met:
   i. The member has documented febrile neutropenia from a prior chemotherapy cycle (for which primary prophylaxis was not received)
   ii. A reduction in dosage of the chemotherapeutic agent or delay in treatment may compromise disease-free or overall survival or treatment outcome

B. Adjunctive Treatment of Neutropenia

Authorization of 6 months may be granted for adjunctive treatment of neutropenia when any of the conditions below are present:

1. Expected prolonged (greater than 10 days) and profound (less than 0.1 x 10^9/L) neutropenia
2. Age greater than 65 years
3. Uncontrolled primary disease
4. Pneumonia
5. Hypotension and multiorgan dysfunction (sepsis syndrome)
6. Invasive fungal infection
7. Hospitalization at the time of the development of fever

C. Acute Myeloid Leukemia

Authorization of 6 months may be granted to reduce the time to neutrophil recovery and the duration of fever following induction or consolidation chemotherapy treatment of members with acute myeloid leukemia

D. Bone Marrow Transplantation

Authorization of 6 months may be granted to reduce the duration of neutropenia and neutropenia-related clinical sequelae (e.g., febrile neutropenia) in members with non-myeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation.

E. Other Indications

Authorization of 6 months may be granted for treatment of any of the following conditions:

1. Mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis
2. Acute exposure to myelosuppressive doses of radiation
3. After completion of the first few days of initial induction chemotherapy or for first post-remission course of chemotherapy for the treatment of acute lymphocytic leukemia (ALL)
4. Adult members with AML shortly after the completion of induction or repeat induction chemotherapy, or after the completion of consolidation therapy for AML
5. Treatment of severe neutropenia in individuals with hairy cell leukemia
6. Myelodysplastic syndrome when either of the following criteria is met:
   i. Absolute neutrophil count (ANC) less than or equal to 500/mm^3
   ii. Member is experiencing recurrent infection
7. Dose dense chemotherapy (treatment given more frequently, such as every two weeks instead of every three weeks) for adjuvant treatment of breast cancer or other malignancies for which dose dense chemotherapy is an accepted treatment option

8. Chronic administration to reduce the incidence and duration of sequelae (e.g., fever, infections, oropharyngeal ulcers) in symptomatic individuals with congenital neutropenia, cyclic neutropenia or idiopathic neutropenia
9. Treatment of (non-chemotherapy) drug-induced neutropenia
10. Treatment of low neutrophil counts in members with glycogen storage disease type 1b
11. Treatment for neutropenia associated with human immunodeficiency virus (HIV) infection and antiretroviral therapy
12. Member receiving radiation therapy in the absence of chemotherapy if prolonged delays due to neutropenia are expected
13. After hematopoietic progenitor stem cell transplant (HPCT/HSCT) for any of the following conditions:
    i. To promote myeloid reconstitution
    ii. When engraftment is delayed or has failed
    iii. Mobilization of progenitor cells into peripheral blood for collection by leukapheresis, as an adjunct to peripheral blood/hematopoietic stem cell transplantation (PBSCT/PHSCT)
    iv. As an alternate or adjunct to donor leukocyte infusions (DLI) in members with leukemic relapse after an allogenic hematopoietic stem cell transplant

V. DOSAGE AND ADMINISTRATION

Services performed for excessive frequency are not medically necessary. Frequency is considered excessive when services are performed more frequently than generally accepted by peers and the reason for additional services is not justified by documentation. Filgrastim will be covered when administered under direct supervision in the office setting. When administered by the member or caregiver, the drug will be considered self-administered and not payable.

VI. REFERENCES

1. White Cell Colony Stimulating Factors LCD (L37176) Version R15. Available at: https://www.cms.gov/medicare-coverage-database/indexes/national-and-local-indexes.aspx. Accessed January 26, 2023.
2. Billing and Coding: White Cell Colony Stimulating Factors (A56748) Version R9. Available at: https://www.cms.gov/medicare-coverage-database/indexes/national-and-local-indexes.aspx. Accessed October 6, 2022.
3. Neupogen [package insert]. Thousand Oaks, CA: Amgen, Inc.; February 2021.
4. Nivestym [package insert]. Lake Forest, IL: Hospira Inc.; November 2021.
5. Releuko [package insert]. Piscataway, NJ: Kashiv Biosciences, LLC; February 2022.
6. Zarxio [package insert]. Princeton, NJ: Sandoz, Inc.; March 2021.