

STANDARD MEDICARE PART B MANAGEMENT

NEUPOGEN (filgrastim)
GRANIX (tbo-filgrastim)
ZARXIO (filgrastim-sndz)
NIVESTYM (filgrastim-aafi)

POLICY

I. INDICATIONS

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

A. FDA-Approved Indications

Neupogen

1. Patients with Cancer Receiving Myelosuppressive Chemotherapy
Neupogen is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever.
2. Patients with Acute Myeloid Leukemia Receiving Induction or Consolidation Chemotherapy
Neupogen is indicated for reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of adults with acute myeloid leukemia.
3. Patients with Cancer Undergoing Bone Marrow Transplantation
Neupogen is indicated to reduce the duration of neutropenia and neutropenia-related clinical sequelae, (e.g., febrile neutropenia) in patients with non-myeloid malignancies undergoing myeloablative chemotherapy followed by marrow transplantation.
4. Patients Undergoing Autologous Peripheral Blood Progenitor Cell Collection and Therapy
Neupogen is indicated for the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.
5. Patients with Severe Chronic Neutropenia
Neupogen is indicated for chronic administration to reduce the incidence and duration of sequelae of neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia.
6. Patients Acutely Exposed to Myelosuppressive Doses of Radiation (Hematopoietic Syndrome of Acute Radiation Syndrome)
Neupogen is indicated to increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome).

Nivestym

1. **Patients with Cancer Receiving Myelosuppressive Chemotherapy**
Nivestym is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever.
2. **Patients with Acute Myeloid Leukemia Receiving Induction or Consolidation Chemotherapy**
Nivestym is indicated for reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of adults with acute myeloid leukemia (AML).
3. **Patients with Cancer Undergoing Bone Marrow Transplantation (BMT)**
Nivestym is indicated to reduce the duration of neutropenia and neutropenia-related clinical sequelae, (e.g., febrile neutropenia) in patients with non-myeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation.
4. **Patients Undergoing Autologous Peripheral Blood Progenitor Cell Collection and Therapy**
Nivestym is indicated for the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.
5. **Patients with Severe Chronic Neutropenia**
Nivestym is indicated for chronic administration to reduce the incidence and duration of sequelae of neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia.

Granix

Granix is indicated to reduce the duration of severe neutropenia in adult and pediatric patients 1 month and older with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

Zarxio

1. **Patients with Cancer Receiving Myelosuppressive Chemotherapy**
Zarxio is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever.
2. **Patients with Acute Myeloid Leukemia Receiving Induction or Consolidation Chemotherapy**
Zarxio is indicated for reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of adults with acute myeloid leukemia (AML).
3. **Patients with Cancer Undergoing Bone Marrow Transplantation**
Zarxio is indicated to reduce the duration of neutropenia and neutropenia-related clinical sequelae, (e.g., febrile neutropenia) in patients with non-myeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation.
4. **Patients Undergoing Autologous Peripheral Blood Progenitor Cell Collection and Therapy**
Zarxio is indicated for the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.
5. **Patients with Severe Chronic Neutropenia**
Zarxio is indicated for chronic administration to reduce the incidence and duration of sequelae of neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia.

B. Compendial Uses (Neupogen/Granix/Zarxio/Nivestym)

1. Treatment of chemotherapy-induced febrile neutropenia in patients with non-myeloid malignancies
2. Prophylaxis for chemotherapy-induced febrile neutropenia in patients with solid tumors
3. Treatment of anemia and neutropenia in patients with myelodysplastic syndromes (MDS)
4. Stem cell transplantation-related indications
5. Agranulocytosis (non-chemotherapy drug induced)
6. Aplastic anemia
7. Neutropenia related to HIV/AIDS
8. Neutropenia related to renal transplantation
9. Acute myeloid leukemia
10. Severe chronic neutropenia (congenital, cyclic, or idiopathic)
11. Hematopoietic Subsyndrome of Acute Radiation Syndrome
12. Supportive care for neutropenic patients with CAR T-cell-related toxicities
13. Hairy Cell Leukemia
14. Chronic Myeloid Leukemia
15. Glycogen Storage Disease (GSD) Type 1
16. Reducing the instance of neonatal sepsis in infants with preeclampsia-associated neutropenia
17. Perioperative administration of filgrastim to patients with esophageal cancer undergoing esophagectomy reduced infectious complications following surgery
18. Improving the neutrophil count in Shwachman syndrome

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: For febrile neutropenia, submit member's diagnosis and chemotherapeutic regimen.

III. CRITERIA FOR INITIAL APPROVAL**A. Neutropenia in cancer patients receiving myelosuppressive chemotherapy**

Authorization of 6 months may be granted for prevention or treatment of febrile neutropenia when the member will not be receiving chemotherapy and radiation therapy at the same time.

B. Other indications

Authorization of 6 months may be granted for members with any of the following indications:

1. Myelodysplastic syndrome (anemia or neutropenia)
2. Stem cell transplantation-related indications
3. Agranulocytosis (non-chemotherapy drug induced)
4. Aplastic anemia
5. Neutropenia related to HIV/AIDS
6. Neutropenia related to renal transplantation
7. Acute myeloid leukemia
8. Severe chronic neutropenia (congenital, cyclic, or idiopathic)
9. Hematopoietic Subsyndrome of Acute Radiation Syndrome

- Treatment for radiation-induced myelosuppression following a radiological/nuclear incident
10. CAR T-cell-related toxicities
Supportive care for neutropenic patients with CAR T-cell-related toxicities
 11. Hairy Cell Leukemia
Members with hairy cell leukemia with neutropenic fever following chemotherapy
 12. Chronic Myeloid Leukemia
Members with chronic myeloid leukemia (CML) for treatment of persistent neutropenia due to tyrosine kinase inhibitor therapy
 13. Glycogen Storage Disease (GSD) Type 1
Individuals with GSD Type 1 for treatment of low neutrophil counts
 14. Reducing the instance of neonatal sepsis in infants with preeclampsia-associated neutropenia
 15. Perioperative administration of filgrastim to patients with esophageal cancer undergoing esophagectomy to reduce infectious complications following surgery
 16. Improving the neutrophil count in Shwachman syndrome

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

- A. Authorization for 6 months may be granted for the treatment of chronic myeloid leukemia when all of the following criteria are met:
 1. The member is currently receiving therapy with the requested medication.
 2. The member is receiving benefit from therapy. Benefit is defined as:
 - i. No evidence of unacceptable toxicity while on the current regimen
 - ii. No evidence of disease progression while on the current regimen
- B. For all other diagnoses, all members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

1. Neupogen [package insert]. Thousand Oaks, CA: Amgen Inc.;February 2021.
2. Nivestym [package insert]. Lake Forest, IL: Pfizer Inc.;April 2021.
3. Granix [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; March 2019.
4. Zarxio [package insert]. Princeton, NJ: Sandoz Inc.;March 2021.
5. The NCCN Drugs & Biologics Compendium® © 2020 National Comprehensive Cancer Network, Inc. Available at: <https://www.nccn.org>. Accessed June 10, 2021.
6. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Hematopoietic Growth Factors. Version 2.2020. https://www.nccn.org/professionals/physician_gls/pdf/growthfactors.pdf. Accessed: June 10, 2021.
7. IBM Micromedex® DRUGDEX® (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at <https://www.micromedexsolutions.com>. (Accessed:06/10/2021).
8. Lexicomp Online, AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc.; Accessed June 10,2021.
9. Aapro MS, Bohlius J, Cameron DA, et al. 2010 update of EORTC guidelines for the use of granulocyte-colony stimulating factor to reduce the incidence of chemotherapy-induced febrile neutropenia in adult patients with lymphoproliferative disorders and solid tumors. *Eur J Cancer*. 2011;47(1):8-32.

Reference number(s)
4758-A

10. 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.
11. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Hairy Cell Leukemia. Version 1.2020. https://www.nccn.org/professionals/physician_gls/pdf/hairy_cell.pdf Accessed June 10,2021.
12. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Chronic Myeloid Leukemia. Version 3.2020. https://www.nccn.org/professionals/physician_gls/pdf/cml.pdf Accessed June 11, 2020.
13. Smith TJ, Khatcheressian J, Lyman GH, et al. 2006 update of recommendations for the use of white blood cell growth factors: an evidence-based clinical practice guideline. *J Clin Oncol*. 2006;24(19):3187-3205.