Filgrastim (Neupogen®, Zarxio®, Nivestym™, Granix®)
EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO031

Description
Granulocyte- colony stimulating factors (G-CSF) act on the hematopoietic cells by binding to specific cell surface receptors thereby stimulating the production, maturation, and activation of neutrophils.

Length of Authorization
- Initial: Four months
- Renewal: Four months

Quantity limits

Dosage Form	Indication	Quantity Limit
Self-Administered Agents		
Neupogen (filgrastim) 300mcg/mL; 480mcg/1.6mL; 300mc/0.5mL; 480mcg/0.8mL Vial; 300mcg/0.5mL;480mcg/0.8mL Syringe	• Bone marrow transplant • Peripheral progenitor cell (PBPC) mobilization and transplant • Prophylactic use in patients with non-myeloid malignancy • Treatment of chemotherapy-induced febrile neutropenia • Neutropenic complications from prior cycle • Acute myeloid leukemia (AML) patient following induction or consolidation chemotherapy • Bone marrow transplantation failure or engraftment delay • Severe chronic neutropenia • Myelodysplastic syndrome • Exposure to myelosuppressive doses of radiation	15 prefilled syringes or 15 vials per 30-day supply
Zarxio (filgrastim-sndz)* 300mcg/0.5mL; 480/0.8mL Syringe		15 prefilled syringes or 15 vials per 30-day supply
Nivestym (filgrastim-aafi) 300mcg/mL; 480mcg/1.6mL Vial; 300mcg/0.5mL; 480/0.8mL Syringe		15 prefilled syringes or 15 vials per 30-day supply
Granix (tbo-filgrastim) 300mcg/mL; 480mcg/1.6mL Vial; 300mcg/0.5mL; 480/0.8mL Syringe		15 prefilled syringes or 15 vials per 30-day supply
Leukine (sargramostim) 250mcg; 500mcg/mL vial		15 vials per 30-day supply

**No PA required*

Initial Evaluation

I. Products may be considered medically necessary when the following criteria below are met:

Zarxio is the preferred short-acting G-CSF

- **Patients must have failed, have contraindication to, or intolerance of Zarxio prior to the consideration of any other short-acting G-CSF.**
  - There is no prior authorization required for Zarxio unless requesting above the quantity limit noted above.

A. A diagnosis of:

1. **Peripheral Blood Progenitor Cell (PBPC) mobilization and transplant**; **OR**
2. Patient who experienced a **neutropenic complication from a prior cycle of the same chemotherapy**; **OR**
3. **Bone Marrow Transplant (BMT); OR**
4. **Bone Marrow Transplantation (BMT) failure or Engraftment Delay**; **OR**
5. Patients acutely exposed to **myelosuppressive doses of radiation** (Hematopoietic Subsyndrome of Acute Radiation Syndrome); **OR**
6. **Acute Myeloid Leukemia (AML)** patient following induction or consolidation chemotherapy; **OR**
7. **Prophylactic use in patients with non-myeloid malignancy**; **AND**
   i. Patient is undergoing myelosuppressive chemotherapy with an expected incidence of febrile neutropenia of 20% or greater; **OR**
   ii. Patient is undergoing myelosuppressive chemotherapy with an expected incidence of febrile neutropenia of 10% or greater **AND** one or more of the following co-morbidities:
      a. Elderly patients (age 65 or older) receiving full dose intensity chemotherapy
      b. History of recurrent febrile neutropenia from chemotherapy
      c. Extensive prior exposure to chemotherapy
      d. Previous exposure of pelvis, or other areas of large amounts of bone marrow, to radiation
      e. Pre-existing neutropenia (ANC ≤ 1000/mm3) or bone marrow involvement with tumor
      f. Patient has a condition that can potentially increase the risk of serious infection (i.e. HIV/AIDS)
      g. Infection/open wounds
      h. Recent surgery
      i. Poor performance status
      j. Poor renal function (creatinine clearance <50)
      k. Liver dysfunction (elevated bilirubin >2.0)
      l. Chronic immunosuppression in the post-transplant setting including organ transplant; **OR**
8. **Myelodysplastic Syndrome**; **AND**
   i. Endogenous serum erythropoietin level of ≤500 mUnits/mL; **AND**

ii. Patient has lower risk disease (i.e., defined as IPSS-R [Very Low, Low, Intermediate], IPSS [Low/Intermediate-1], WPSS [Very Low, Low, Intermediate]); **AND**
iii. Used for treatment of symptomatic anemia in patients without del(5q); **AND**
iv. Patient is receiving concurrent therapy with Erythropoiesis Stimulating Agents (ESAs); **AND**
a. Patient has ring sideroblasts < 15% and will use in combination with lenalidomide following no response (despite adequate iron stores) or loss or response to an ESA alone; **OR**
b. Patient has ring sideroblasts ≥ 15%; **OR**

9. **Treatment of chemotherapy-induced febrile neutropenia**; **AND**
i. Patient has been on prophylactic therapy with filgrastim; **OR**
ii. Patient has not received prophylactic therapy with a granulocyte colony stimulating factor; **AND**
a. Patient has one or more of the following risk factors for developing infection-related complications:
i. Sepsis Syndrome
ii. Age >65
iii. Absolute neutrophil count [ANC] <100/mcL
iv. Duration of neutropenia expected to be greater than 10 days
v. Pneumonia or other clinically documented infections
vi. Invasive fungal infection
vii. Hospitalization at the time of fever
viii. Prior episode of febrile neutropenia; **OR**

10. **Severe chronic neutropenia; AND**
i. Patient must have an absolute neutrophil count (ANC) < 500/mm3; **AND**
ii. Patient must have a diagnosis of <u>one</u> of the following:
a. Congenital neutropenia
b. Cyclic neutropenia
c. Idiopathic neutropenia; **OR**

11. **Management of CAR-T related Toxicity**; **AND**
i. Patient has been receiving therapy with CAR T-cell therapy (e.g. tisangenleclecleucel (Kymriah), Axicabtagene Ciloleucel (Yescarta), etc.); **AND**
ii. Patient is experiencing neutropenia related to their therapy.

Renewal Evaluation

I. Renewal criteria
A. Same as initial prior authorization policy criteria

Supporting Evidence

I. All indications listed follow FDA labeled indications or compendia indications
II. Expected incidence of febrile neutropenia percentages for myelosuppressive chemotherapy regimens can be found in the NCCN Myeloid Growth Factors Clinical Practice Guideline at NCCN.org.

References

1. Neupogen [package insert]. Thousand Oaks, CA; Amgen Inc; June 2016. Accessed March 2018.
2. Zarxio [package insert]. Princeton, NJ; Sandoz Inc; December 2017. Accessed July 2018.
3. Nivestym [package insert]. Lake Forest, IL; Hospira Inc; July 2018. Accessed July 2018
4. Neulasta [package insert]. Thousand Oaks, CA; Amgen Inc; June 2018. Accessed July 2018
5. Fulphila [package insert]. Zurich, Switzerland; Mylan GmbH; September 2018. Accessed October 2018.
6. Udenyca [package insert]. Redwood City, California; Coherus Biosciences; November 2018. Accessed November 2018.
7. Leukine [package insert]. Bridgewater, NJ; sanofi-aventis US LLC; February 2017. Accessed March 2018.
8. Granix [package insert]. North Wales, PA; Teva Pharmaceuticals USA, Inc.; June 2017. Accessed March 2018.
9. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) filgrastim. National Comprehensive Cancer Network, 2018. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc." To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed March 2018. Moda Health Plan, Inc. Medical Necessity Criteria Page 4/6
10. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Myeloid Growth Factors. Version 1.2018. National Comprehensive Cancer Network, 2017. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc." To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed March 2018.
11. Smith TJ, Bohlke K, Lyman GH, Carson KR, Crawford J, Cross SJ, Goldberg JM, Khatcheressian JL, Leighl NB, Perkins CL, Somlo G, Wade JL, Wozniak AJ, Armitage JO. Recommendations for the use of WBC growth factors: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol. 2015 Jul 13. pii: JCO.2015.62.3488. [Epub ahead of print]
12. Wisconsin Physicians Service Insurance Corporation. Local Coverage Determination (LCD): Human Granulocyte/Macrophage Colony Stimulating Factors (L34699). Centers for Medicare & Medicaid Services, Inc. Updated on 1/23/2018 with effective date 02/1/2018. Accessed March 2018.
13. First Coast Service Options, Inc. Local Coverage Determination (LCD): G-CSF (Neupogen®, Granix™, Zarxio™) (L34002). Centers for Medicare & Medicaid Services, Inc. Updated on 6/10/2016 with effective date 7/5/2016. Accessed March 2018.
14. National Government Services, Inc. Local Coverage Article: Filgrastim, Pegfilgrastim, Tbofilgrastim, Filgrastim-sndz (e.g., Neupogen®, Neulasta™, Granix™, Zarxio™) - Related to LCD L33394 (A52408). Centers for Medicare & Medicaid Services, Inc. Updated on 9/23/2016 with effective date 10/1/2016. Accessed March 2018.
15. Palmetto GBA. Local Coverage Determination: White Cell Colony Stimulating Factors (L37176). Centers for Medicare & Medicaid Services, Inc. Updated on 12/7/2017 with effective date 2/26/2018. Accessed March 2018.

Policy Implementation/Update:

Date Created	February 2018
Date Effective	February 2017
Last Updated	December 2019
Last Reviewed	12/28/2018, 10/15/2019, 12/2019

Action and Summary of Changes	**Date**
Updated quantity level limit to allow 15 doses per 30 day supply	12/2019
Policy title change, designate Zarxio as a preferred product, add "No PA Required" to Initial Evaluation Section 1 boxed information	10/2019
Added Nivestym, biosimilar to Neupogen	10/2018
Criteria update. Zarxio is the preferred short-acting G-CSF	02/2017