



## Colony Stimulating Factors: Neupogen® (filgrastim) (Subcutaneous/Intravenous)

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### I. Length of Authorization

Coverage will be provided for four months and may be renewed.

### II. Dosing Limits

#### A. Quantity Limit (max daily dose) [Pharmacy Benefit]:

- Neupogen 300 mcg vial: 3 vials per 1 day
- Neupogen 300 mcg SingleJect: 3 syringes per 1 day
- Neupogen 480 mcg vial: 3 vials per 1 day
- Neupogen 480 mcg SingleJect: 3 syringes per 1 day

#### B. Max Units (per dose and over time) [Medical Benefit]:

*Severe Chronic Neutropenia:*

- 1380 billable units per day

*BMT or PBPC or Radiation:*

- 1200 billable units per day

*All other indications:*

- 600 billable units per day

### III. Initial Approval Criteria

Granix and Zarxio are the preferred short-acting granulocyte colony-stimulating factor products.

- Patients must have failed, or have a contraindication, or intolerance to Granix AND Zarxio prior to consideration of any other short-acting G-CSF product.

Coverage for Neupogen® (filgrastim) is provided in the following conditions:

### **Bone marrow transplant (BMT) †**

### **Peripheral Blood Progenitor Cell (PBPC) mobilization and transplant †**

### **Prophylactic use in patients with non-myeloid malignancy †**

- Patient is undergoing myelosuppressive chemotherapy with an expected incidence of febrile neutropenia of 20% or greater §; **OR**
- 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:
  - Elderly patients (age 65 or older) receiving full dose intensity chemotherapy
  - History of recurrent febrile neutropenia from chemotherapy
  - Extensive prior exposure to chemotherapy
  - Previous exposure of pelvis, or other areas of large amounts of bone marrow, to radiation
  - Pre-existing neutropenia ( $ANC \leq 1000/mm^3$ ) or bone marrow involvement with tumor
  - Patient has a condition that can potentially increase the risk of serious infection (i.e. HIV/AIDS)
  - Infection/open wounds
  - Recent surgery
  - Poor performance status
  - Poor renal function (creatinine clearance  $<50$ )
  - Liver dysfunction (elevated bilirubin  $>2.0$ )
  - Chronic immunosuppression in the post-transplant setting including organ transplant

### **Treatment of chemotherapy-induced febrile neutropenia ‡**

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

### **Patient who experienced a neutropenic complication from a prior cycle of the same chemotherapy ‡**

### **Acute Myeloid Leukemia (AML) patient following induction or consolidation chemotherapy †**

### **Bone Marrow Transplantation (BMT) failure or Engraftment Delay ‡**

### Severe chronic neutropenia †

- Patient must have an absolute neutrophil count (ANC) < 500/mm<sup>3</sup>; **AND**
- Patient must have a diagnosis of one of the following:
  - Congenital neutropenia; **OR**
  - Cyclic neutropenia; **OR**
  - Idiopathic neutropenia

### Myelodysplastic Syndrome ‡

- Endogenous serum erythropoietin level of ≤500 mUnits/mL; **AND**
- 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**
- Used for treatment of symptomatic anemia in patients without del(5q); **AND**
- Patient is receiving concurrent therapy with an Erythropoiesis Stimulating Agent (ESA); **AND**
  - 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**
  - Patient has ring sideroblasts ≥ 15%

### Patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Subsyndrome of Acute Radiation Syndrome) †

#### Management of CAR T-cell related Toxicity ‡

- Patient has been receiving therapy with CAR T-cell therapy (e.g. tisagenlecleucel (Kymriah), Axicabtagene Ciloleucel (Yescarta), etc.); **AND**
- Patient is experiencing neutropenia related to their therapy.

† FDA-labeled indication(s); ‡ Compendia recommended indication(s)

§ 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.

## IV. Renewal Criteria

Same as initial prior authorization policy criteria.

## V. Dosage/Administration

| Indication                     | Dose                              |
|--------------------------------|-----------------------------------|
| BMT/PBPC/Radiation Indications | 10 mcg/kg daily for up to 14 days |
| Congenital Neutropenia         | 6 mcg/kg twice daily              |
| All other indications          | 5 mcg/kg daily for up to 14 days  |

## VI. Billing Code/Availability Information

### JCode:

- J1442 – injection, filgrastim (g-csf), excludes biosimilars, 1 microgram: 1 billable unit = 1 microgram

### NDC:

- Neupogen 300 mcg single-dose vial: 55513-0530-xx
- Neupogen 300 mcg single-dose prefilled syringe (SingleJect): 55513-0924-xx
- Neupogen 480 mcg single-dose vial: 55513-0546-xx
- Neupogen 480 mcg single-dose prefilled syringe (SingleJect): 55513-0209-xx

## VII. References

1. Neupogen [package insert]. Thousand Oaks, CA; Amgen Inc; June 2018. Accessed March 2019.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) filgrastim. National Comprehensive Cancer Network, 2019. 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 2019.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Hematopoietic Growth Factors. Version 1.2019. National Comprehensive Cancer Network, 2019. 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 2019.
4. 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]
5. Wisconsin Physicians Service Insurance Corporation. Local Coverage Determination (LCD): Human Granulocyte/Macrophage Colony Stimulating Factors (L34699). Centers for Medicare & Medicaid Services, Inc. Updated on 01/24/2019 with effective date 02/01/2019. Accessed March 2019.
6. First Coast Service Options, Inc. Local Coverage Determination (LCD): G-CSF (Neupogen®, Granix™, Zarxio™) (L34002). Centers for Medicare & Medicaid Services, Inc. Updated on 10/12/2018 with effective date 10/01/2018. Accessed March 2019.

7. 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 01/24/2019 with effective date 02/01/2019. Accessed March 2019.
8. Palmetto GBA. Local Coverage Determination: White Cell Colony Stimulating Factors (L37176). Centers for Medicare & Medicaid Services, Inc. Updated on 02/22/2019 with effective date 01/01/2019. Accessed March 2019.

## Appendix 1 – Covered Diagnosis Codes

| ICD-10 | ICD-10 Description   |
|--------|--|
| C92.00 | Myeloid leukemia not having achieved remission                                   |
| C92.02 | Myeloid leukemia in relapse  |
| C92.50 | Acute myelomonocytic leukemia not having achieved remission                      |
| C92.52 | Acute myelomonocytic leukemia in relapse   |
| C92.60 | Acute myeloid leukemia with 11q23-abnormality not having achieved remission      |
| C92.62 | Acute myeloid leukemia with 11q23-abnormality in relapse                         |
| C92.A0 | Acute myeloid leukemia with multilineage dysplasia not having achieved remission |
| C92.A2 | Acute myeloid leukemia with multilineage dysplasia in relapse                    |
| C93.00 | Acute monoblastic/monocytic leukemia not having achieved remission               |
| C93.02 | Acute monoblastic/monocytic leukemia in relapse                                  |
| C93.10 | Chronic myelomonocytic leukemia, not having achieved remission                   |
| C94.00 | Acute erythroid leukemia not having achieved remission                           |
| C94.02 | Acute erythroid leukemia in relapse  |
| C94.20 | Acute megakaryoblastic leukemia not having achieved remission                    |
| C94.22 | Acute megakaryoblastic leukemia in relapse                                       |
| D46.0  | Refractory anemia without ring sideroblasts, so stated                           |
| D46.1  | Refractory anemia with ring sideroblasts   |
| D46.20 | Refractory anemia with excess of blasts, unspecified                             |
| D46.21 | Refractory anemia with excess of blasts 1  |
| D46.4  | Refractory anemia, unspecified   |
| D46.9  | Myelodysplastic syndrome, unspecified  |
| D46.A  | Refractory cytopenia with multilineage dysplasia                                 |
| D46.B  | Refractory cytopenia with multilineage dysplasia and ring sideroblasts           |
| D46.Z  | Other myelodysplastic syndrome   |
| D61.81 | Pancytopenia   |
| D70.0  | Congenital agranulocytosis   |

| ICD-10   | ICD-10 Description  |
|----------|---|
| D70.1    | Agranulocytosis secondary to cancer chemotherapy                                  |
| D70.2    | Other drug-induced agranulocytosis  |
| D70.4    | Cyclic neutropenia  |
| D70.9    | Neutropenia, unspecified  |
| T45.1X5A | Adverse effect of antineoplastic and immunosuppressive drugs initial encounter    |
| T45.1X5D | Adverse effect of antineoplastic and immunosuppressive drugs subsequent encounter |
| T45.1X5S | Adverse effect of antineoplastic and immunosuppressive drugs sequela              |
| T66.XXXA | Radiation sickness, unspecified, initial encounter                                |
| T66.XXXD | Radiation sickness, unspecified, subsequent encounter                             |
| T66.XXXS | Radiation sickness, unspecified, sequela  |
| W88.1    | Exposure to radioactive isotopes  |
| W88.8    | Exposure to other ionizing radiation  |
| Z41.8    | Encounter for other procedures for purposes other than remedying health state     |
| Z48.290  | Encounter for aftercare following bone marrow transplant                          |
| Z51.11   | Encounter for antineoplastic chemotherapy   |
| Z51.12   | Encounter for antineoplastic immunotherapy  |
| Z51.89   | Encounter for other specified aftercare   |
| Z52.001  | Unspecified donor, stem cells   |
| Z52.011  | Autologous donor, stem cells  |
| Z52.091  | Other blood donor, stem cells   |
| Z76.89   | Persons encountering health services in other specified circumstances             |
| Z94.81   | Bone marrow transplant status   |
| Z94.84   | Stem cells transplant status  |

## Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: <http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD):

|                             |                                     |
|-----------------------------|-------------------------------------|
| <b>Jurisdiction(s):</b> 5,8 | <b>NCD/LCD Document (s):</b> L34699 |
|-----------------------------|-------------------------------------|

<https://www.cms.gov/medicare-coverage-database/search/lcd-date-search.aspx?DocID=L34699&bc=gAAAAAAAAAAAA>

**Jurisdiction(s):** N

**NCD/LCD Document (s):** L34002

<https://www.cms.gov/medicare-coverage-database/search/document-id-search-results.aspx?DocID=L34002&bc=gAAAAAAAAAAAA&>

**Jurisdiction(s):** 6, K

**NCD/LCD Document (s):** A52408

<https://www.cms.gov/medicare-coverage-database/search/document-id-search-results.aspx?DocID=A52408&bc=gAAAAAAAAAAAA&>

**Jurisdiction(s):** J, M

**NCD/LCD Document (s):** L37176

<https://www.cms.gov/medicare-coverage-database/search/lcd-date-search.aspx?DocID=L37176&bc=gAAAAAAAAAAAA>

### Medicare Part B Administrative Contractor (MAC) Jurisdictions

| Jurisdiction | Applicable State/US Territory   | Contractor  |
|--------------|---|---|
| E (1)        | CA, HI, NV, AS, GU, CNMI  | Noridian Healthcare Solutions, LLC                |
| F (2 & 3)    | AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ  | Noridian Healthcare Solutions, LLC                |
| 5            | KS, NE, IA, MO  | Wisconsin Physicians Service Insurance Corp (WPS) |
| 6            | MN, WI, IL  | National Government Services, Inc. (NGS)          |
| H (4 & 7)    | LA, AR, MS, TX, OK, CO, NM  | Novitas Solutions, Inc.                           |
| 8            | MI, IN  | Wisconsin Physicians Service Insurance Corp (WPS) |
| N (9)        | FL, PR, VI  | First Coast Service Options, Inc.                 |
| J (10)       | TN, GA, AL  | Palmetto GBA, LLC                                 |
| M (11)       | NC, SC, WV, VA (excluding below)  | Palmetto GBA, LLC                                 |
| L (12)       | DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA) | Novitas Solutions, Inc.                           |
| K (13 & 14)  | NY, CT, MA, RI, VT, ME, NH  | National Government Services, Inc. (NGS)          |
| 15           | KY, OH  | CGS Administrators, LLC                           |