MEDICAL MUTUAL®

Drug Policy

Policy:	**201424-MRX**	**Initial Effective Date: 10/30/2014**
Code(s):	**HCPCS J1442, Q5101, Q5110, J1447, Q5125**	**Annual Review Date: 04/20/2023**
SUBJECT:	**Colony Stimulating Factors:** Filgrastim (Neupogen®); Filgrastim-aafi (Nivestym™); **Filgrastim- sndz (Zarxio™);** Filgrastim-ayow (Releuko®); Tbo-Filgrastim (Granix®)	**Last Revised Date: 04/20/2023**

☐Subject to Site of Care

***Zarxio™ (filgrastim-sndz) is the preferred filgrastim product**

Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.

Please note this policy is subject to Medicare Part B step therapy. Please see the corporate medical policy titled **Medicare Part B Step Therapy** for a complete list of preferred therapies.

I. Length of Authorization

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

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

– 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
– Nivestym 300 mcg vial: 3 vials per 1 day – Nivestym 300 mcg prefilled syringe: 3 syringes per 1 day – Nivestym 480 mcg vial: 3 vials per 1 day – Nivestym 480 mcg prefilled syringe: 3 syringes per 1 day
– Zarxio 300 mcg prefilled syringe: 3 syringes per 1 day – Zarxio 480 mcg prefilled syringe: 3 syringes per 1 day
– Releuko 300 mcg prefilled syringe: 3 syringes per 1 day – Releuko 480 mcg prefilled syringe: 3 syringes per 1 day

– Releuko 300 mcg single-dose vial: 3 vials per 1 day – Releuko 480 mcg single-dose vial:
– Granix 300 mcg pre-filled syringe: 4 syringes per 1 day – Granix 300 mcg single-dose vial: 4 vials per 1 day – Granix 480 mcg pre-filled syringe: 3 syringes per 1 day – Granix 480 mcg single-dose vial: 3 vials per 1 day

B. Max Units (per dose and over time) [HCPCS Unit]:

Severe Chronic Neutropenia (Congenital Neutropenia):

- 1380 billable units per day

BMT or PBPC or H-ARS:

- 1200 billable units per day

All other indications:

- 600 billable units per day

III. Initial Approval Criteria [1-7,19-25]

Coverage is provided in the following conditions:

If the request is for brand name Neupogen, Nivestym, or Releuko, patient had an inadequate response or has a contraindication or intolerance to Zarxio

Bone marrow transplant (BMT) † ‡ Φ

Peripheral Blood Progenitor Cell (PBPC) mobilization and transplant [19,31,34,36-38] † ‡ Φ

Prophylactic use in patients with solid tumors or non-myeloid malignancy [1-7,9,10,12,13,15,17,28-30] † ‡

- Patient is undergoing myelosuppressive chemotherapy with an expected incidence of febrile neutropenia of greater than 20% **§**; **OR**
- Patient is undergoing myelosuppressive chemotherapy with an expected incidence of febrile neutropenia of 10% to 20% **§ AND** one or more of the following co-morbidities:
  - Age >65 years receiving full dose intensity 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 $\leq 1000/mm^3$)
  - Bone marrow involvement with tumor

- Patient has a condition that can potentially increase the risk of serious infection (i.e., HIV/AIDS with low CD4 counts)
- Recent surgery and/or open wounds
- Poor performance status
- Renal dysfunction (creatinine clearance <50 mL/min)
- Liver dysfunction (elevated bilirubin >2.0 mg/dL)
- Chronic immunosuppression in the post-transplant setting including organ transplant

Note: Dose-dense therapy, in general, requires growth factor support to maintain dose intensity and schedule. In the palliative setting, consideration should be given to dose reduction or change in regimen.

Treatment of chemotherapy-induced febrile neutropenia [1-5,6,7,9,10,12,13,15,17,28-30] ‡

- Patient has been on prophylactic therapy with filgrastim or tbo-filgrastim *(Note: therapy should not be used concomitantly with pegfilgrastim)*; **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 greater than 65 years
    - Absolute neutrophil count [ANC] less than 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 [1-7,9,10,12,13,15,17,28-30] ‡

Note: Dose-dense therapy, in general, requires growth factor support to maintain dose intensity and schedule. In the palliative setting, consideration should be given to dose reduction or change in regimen.

Acute Myeloid Leukemia (AML) [1-5,8,14,36] † ‡ **Φ**

- Used in patients receiving induction/consolidation or re-induction chemotherapy; **OR**
- Used for relapsed or refractory disease

Bone Marrow Transplantation (BMT) failure or Engraftment Delay [6,7,26,27,31,34,36-38] † ‡

Severe chronic neutropenia [11] † ‡ **Φ**

- Patient must have an absolute neutrophil count (ANC) < 500/mm^3; **AND**

- Patient must have a diagnosis of one of the following:
  - Congenital neutropenia; **OR**
  - Cyclic neutropenia; **OR**
  - Idiopathic neutropenia

Myelodysplastic Syndrome [6] ‡

- Endogenous serum erythropoietin level of ≤500 mUnits/mL; **AND**
- Patient has lower risk disease (*i.e., defined as IPSS-R [Very Low, Low, Intermediate]*); **AND**
- Used for treatment of symptomatic anemia with no del(5q) mutation; **AND**
- Patient is receiving concurrent therapy with an Erythropoiesis Stimulating Agent (ESA)

Patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Subsyndrome of Acute Radiation Syndrome [H-ARS]) [1-5,18] † ‡ Φ

Management of CAR T-cell related Toxicity [6] ‡

- Patient has been receiving therapy with CAR T-cell therapy (e.g., tisangenleclecleucel, axicabtagene ciloleucel, brexucabtagene autoleucel, lisocabtagene maraleucel, etc.); **AND**
- Patient is experiencing neutropenia related to their therapy

Wilms Tumor (Nephroblastoma) [6] ‡

- Patient has favorable histology disease; **AND**
- Used in combination with a cyclophosphamide-based chemotherapy regimen (i.e., Regimen M or I only)

† FDA-labeled indication(s); ‡ Compendia recommended indication(s); **Φ** Orphan Drug

***Febrile neutropenia is defined as:**
– Temperature: a single temperature ≥38.3 °C orally or ≥38.0 °C over 1 hour; **AND** – Neutropenia: <500 neutrophils/mcL or <1,000 neutrophils/mcL and a predicted decline to ≤500 neutrophils/mcL over the next 48 hours
§ Expected incidence of febrile neutropenia percentages for myelosuppressive chemotherapy regimens can be found in the NCCN Hematopoietic Growth Factors Clinical Practice Guideline at NCCN.org [7]

IV. Renewal Criteria

Coverage may be renewed based upon the following criteria:

If the request is for brand name Neupogen, Nivestym, or Releuko, patient had an inadequate response or has a contraindication or intolerance to Zarxio

- Patient continues to meet indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: splenic rupture, acute respiratory distress syndrome (ARDS), serious allergic reactions/anaphylaxis, sickle cell crisis, glomerulonephritis, leukocytosis, capillary leak syndrome, potential for tumor growth stimulation of malignant cells, aortitis, alveolar hemorrhage and hemoptysis, thrombocytopenia, cutaneous vasculitis, MDS/AML *(when used for congenital neutropenia)*, etc.

V. Dosage/Administration

Indication	Dose
BMT/PBPC/H-ARS	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

HCPCS Code:

- J1442 – Injection, filgrastim (Neupogen), excludes biosimilars, 1 mcg: 1 billable unit = 1 mcg
- Q5110 – Injection, filgrastim-aafi, biosimilar, (Nivestym), 1 mcg: 1 billable unit = 1 mcg
- Q5101 – Injection, filgrastim-sndz, biosimilar, (Zarxio), 1 mcg: 1 billable unit = 1 mcg
- J1447 – Injection, tbo-filgrastim (Granix), 1 mcg: 1 billable unit = 1 mcg
- J3590 – Unclassified biologics *(Releuko only) (Discontinue use on 10/01/2022)*
- C9096 – Injection, filgrastim-ayow, biosimilar, (releuko), 1 mcg; 1 billable unit = 1 mcg *(Discontinue use on 10/01/2022)*
- Q5125 – Injection, filgrastim-ayow, biosimilar, (releuko), 1 mcg; 1 billable unit = 1 mcg *(Effective 10/01/2022)*

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

• Nivestym 300 mcg vial: 00069-0293-xx • Nivestym 300 mcg prefilled syringe: 00069-0291-xx • Nivestym 480 mcg vial: 00069-0294-xx • Nivestym 480 mcg prefilled syringe: 00069-0292-xx
• Zarxio 300 mcg single-dose prefilled syringe: 61314-0318-xx • Zarxio 480 mcg single-dose prefilled syringe: 61314-0326-xx
• Releuko 300 mcg single-dose prefilled syringe: 70121-1568-xx • Releuko 480 mcg single-dose prefilled syringe: 70121-1570-xx • Releuko 300 mcg single-dose vial: 70121-1569-xx • Releuko 480 mcg single-dose vial: 70121-1571-xx
• Granix 300 mcg single-dose prefilled syringe: 63459-0910-xx • Granix 480 mcg single-dose prefilled syringe: 63459-0912-xx • Granix 300 mcg single-dose vial: 63459-0918-xx • Granix 480 mcg single-dose vial: 63459-0920-xx

VII. References

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6. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) filgrastim. National Comprehensive Cancer Network, 2022. 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 2022.
7. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Hematopoietic Growth Factors. Version 1.2022. National Comprehensive Cancer Network, 2022. 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 2022.

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Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drugs provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

FOR MEDICAL BENEFIT COVERAGE REQUESTS:

Prior approval is required for HCPCS Codes J1442, Q5101, Q5110, J1447, Q5125