Filgrastim (Neupogen®), Filgrastim-sndz (Zarxio®), Filgrastim-aafi (Nivestym®), Tbo-filgrastim (Granix®)

Prior Authorization Drug Coverage Policy

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Lines of Business: Commercial
Policy type: Prior Authorization

This Drug Coverage Policy provides parameters for the coverage of Filgrastim (Neupogen®), Filgrastim-sndz (Zarxio®), Filgrastim-aafi (Nivestym®), and Tbo-filgrastim (Granix®). Consideration of medically necessary indications are based upon U.S. Food and Drug Administration (FDA) indications, recommended uses within the Centers of Medicare & Medicaid Services (CMS) five recognized compendia, including the National Comprehensive Cancer Network (NCCN) Drugs & Biologics Compendium (Category 1 or 2A recommendations), and peer-reviewed scientific literature eligible for coverage according to the CMS, Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 titled, "Off-Label Use of Anti-Cancer Drugs and Biologics." This policy evaluates whether the drug therapy is proven to be effective based on published evidence-based medicine.

Drug Description[1]

Colony-stimulating factors are glycoproteins which act on hematopoietic cells by binding to specific cell surface receptors and stimulating proliferation, differentiation commitment, and some end-cell functional activation.

FDA Indications[1]

Filgrastim (Neupogen®) is FDA indicated for the following:

- Decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever
- Reduce the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML)
- Reduce the duration of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation (BMT)

- Mobilize autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis
- Reduce the incidence and duration of sequelae of severe neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia
- Increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome)

Filgrastim-sndz (Zarxio®) and Filgrastim-aafi (Nivestym®) are FDA indicated for the following:

- Decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anticancer drugs associated with a significant incidence of severe neutropenia with fever
- Reduce the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML)
- Reduce the duration of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation (BMT)
- Reduce the incidence and duration of sequelae of severe neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia
- Mobilize autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis

Tbo-filgrastim (Granix®) is FDA indicated for the following:

- Reduction in the duration of severe neutropenia in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia

NCCN Compendium Supported Indications[6]

- Neutropenia in Myelodysplastic Syndrome

Coverage Determinations[1,2]

Filgrastim (Neupogen®), Filgrastim-sndz (Zarxio®), Filgrastim-aafi (Nivestym®) Tbo-filgrastim (Granix®) will require prior authorization. These agents are considered medically necessary for the following oncology-related indications if all criteria below are met:

Treatment Febrile Neutropenia

- The patient must have a diagnosis of febrile neutropenia **AND**
- Filgrastim (Neupogen®), Filgrastim-sndz (Zarxio®), Filgrastim-aafi (Nivestym®) and Tbo-filgrastim (Granix®) must be used in adjunct with appropriate antibiotics in high risk members

Recommended dosage: 5 mcg/kg/day once daily until neutrophil recovery

Febrile neutropenia Prophylaxis, in non-myeloid malignancies following myelosuppressive chemotherapy

- The patient is receiving myelosuppressive chemotherapy with a risk of febrile neutropenia of at least 20% **OR**
- The patient is receiving myelosuppressive chemotherapy with an intermediate risk of febrile neutropenia of 10-20% **AND** at least one of the following patient-specific risk factors including prior chemotherapy or radiation therapy, persistent neutropenia (Absolute Neutrophil Count < 500/mm^3 or < 1000/mm^3 and expected to decline to less than 500/mm^3 within the next 48 hours), bone marrow involvement by tumor, recent surgery and/or open wounds, liver dysfunction with a total bilirubin > 2 mg/dL, renal dysfunction with a creatinine clearance < 50 mL/min, age > 65 years and receiving full chemotherapy dose intensity **OR**
- The patient is receiving dose-dense myelosuppressive chemotherapy **OR**
- The patient experienced a febrile neutropenic event with prior administration of the same or similar chemotherapy regimen **AND**
- The patient has a solid tumor or a non-myeloid malignancy **AND**
- Filgrastim (Neupogen®), Filgrastim-sndz (Zarxio®), Filgrastim-aafi (Nivestym®), Tbo-filgrastim (Granix®) is administered 24-72 hours following myelosuppressive chemotherapy

Recommended dosage: 5 mcg/kg/day once daily

Febrile Neutropenia Prophylaxis, in patients with acute myeloid leukemia receiving chemotherapy

- The patient must have a diagnosis Acute Myeloid Leukemia (AML) **AND**
- The patient must be scheduled to receive either induction chemotherapy **OR** consolidation chemotherapy

Recommended dosage: 5 mcg/kg/day once daily

Febrile Neutropenia Prophylaxis, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation (BMT)

Recommended dosage: 10 mcg/kg/day given as an IV infusion no longer than 24 hours

Mobilize hematopoietic progenitor cells for a hematopoietic cell transplant in either one of the following:

- The autologous setting as a single agent or following combination chemotherapy **OR**
- In combination with plerixafor in the autologous setting for patients with non-Hodgkin lymphoma or multiple myeloma **OR**
- For donor hematopoietic progenitor cells or for granulocyte transfusion in the allogeneic setting

Recommended dosage: 10 mcg/kg/day for at least four days before first leukapheresis procedure and continued until last leukapheresis

Neutropenia in Myelodysplastic Syndromes

- The patient must have a diagnosis of neutropenia associated with myelodysplastic syndrome OR
- In combination with an Erythropoiesis-stimulating agent in order to diminish or eliminate transfusions

Recommended dosage: 5 mcg/kg/day once daily

All indications:

- Filgrastim (Neupogen®), Filgrastim-sndz (Zarxio®), Filgrastim-aafi (Nivestym®), and Tbo-filgrastim (Granix®) will be approved through clinical review for up to a 12-month duration

Coverage Limitations

Treatment with Filgrastim (Neupogen®), Filgrastim-sndz (Zarxio®), Filgrastim-aafi (Nivestym®), and Tbo-filgrastim (Granix®) is not considered medically necessary for members with the following concomitant conditions:

- Concomitant use with filgrastim, biosimilar filgrastim, sargramostim (unless part of the stem cell mobilization protocol), pegfilgrastim (within seven days of pegfilgrastim dose), or biosimilar pegfilgrastim (within seven days of biosimilar pegfilgrastim dose).
- Same day administration with myelosuppressive chemotherapy or therapeutic radiation.
- As prophylaxis in members without significant risk, less than 10%, of febrile neutropenia or in members that are not receiving myelosuppressive chemotherapy.
- Indications not supported by NCCN category 2A or higher recommendations may not be considered medically necessary.

Contraindications/Warnings/Precautions[1]

- History of serious allergic reactions to human granulocyte colony-stimulating factors such as filgrastim or pegfilgrastim
- Warnings/precautions:
    - Fatal splenic rupture
    - Acute respiratory distress syndrome
    - Serious allergic reactions
    - Fatal sickle cell crisis
    - Glomerulonephritis
    - Capillary leak syndrome

For specific recommendations on contraindications, warnings and precautions, patient monitoring, and on dose adjustments and discontinuation, please refer to the current prescribing information.

Billing

- **Description**: inj., filgrastim, 1 mcg
    - HCPCS: J1442
- **Description**: inj., filgrastim-sndz, 1 mcg
    - HCPCS: Q5101
- **Description**: inj., filgrastim-aafi, 1 mcg
    - HCPCS: Q5110
- **Description**: inj., tbo-filgrastim, 1 mcg
    - HCPCS: J1447

Disclaimer

Drug Coverage Policies are developed as needed, regularly reviewed, updated at least annually, and are subject to change. Other policies and coverage determination guidelines may apply. Federal and state regulatory requirements and member specific benefit plan documents, if applicable, must be reviewed prior to this Drug Coverage Policy. This Drug Coverage Policy is for informational purposes only and does not constitute medical advice or dictate how providers should practice medicine. This policy should not be reproduced, stored in a retrieval system, or altered from its original form without written permission from Oncology Analytics, Inc.

References

1. Neupogen [package insert]. Thousand Oaks, CA: Amgen Inc.; Available at: https://www.pi.amgen.com/~/media/amgen/repositorysites/pi-amgen-com/neupogen/neupogen_pi_hcp_english.pdf

2. Granix [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; Available at: https://www.granixhcp.com/globalassets/granix-hcp/prescribing-information.pdf
3. Zarxio [package insert]. Princeton, NJ: Sandoz Inc.; Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=c0d1c22b-566b-4776-bdbf-00f96dad0cae
4. Nivestym [package insert]. Lake Forest, IL: Hospira, Inc.; Available at: http://labeling.pfizer.com/ShowLabeling.aspx?id=10899
5. Lexicomp Online®, Hudson, Ohio: Lexi-Comp, Inc. 2020.
6. Filgrastim. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. Available at: https://www.nccn.org/professionals/drug_compendium/content/