

**Clinical Policy: Filgrastim, Filgrastim-sndz, Tbo-filgrastim**

Reference Number: CP.PHAR.297

Effective Date: 12/16

Last Review Date: 10/16

[Coding Implications](#)[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

**Description**

The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for Filgrastim (Neupogen® injection, for subcutaneous or intravenous use), Filgrastim-sndz (Zarxio® injection, for subcutaneous or intravenous use), and Tbo-filgrastim (Granix® injection, for subcutaneous use).

**Policy/Criteria**

It is the policy of health plans affiliated with Centene Corporation® that Neupogen, Zarxio, and Granix are **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria****A. Non-Myeloid Malignancy – Febrile Neutropenia Prophylaxis** (must meet all):

1. If request is for Neupogen or Granix, member has a contraindication or intolerance to Zarxio;
2. The prescribed drug is for use following myelosuppressive chemotherapy for non-myeloid cancer;
3. Member is at risk for febrile neutropenia due to the chemotherapy regimen or patient-related risk factors;
4. Member has no known history of serious allergic reaction to filgrastim or pegfilgrastim.

**Approval duration: 6 months**

**B. Acute Myeloid Leukemia** (must meet all):

1. If the request is for Neupogen or Granix, member has a contraindication or intolerance to Zarxio;
2. The prescribed drug is for use following induction and/or consolidation chemotherapy for acute myeloid leukemia (AML);
3. Member has no known history of serious allergic reaction to filgrastim or pegfilgrastim.

**Approval duration: 6 months**

**C. Bone Marrow Transplantation** (must meet all):

1. If the request is for Neupogen or Granix, member has a contraindication or intolerance to Zarxio;
2. The prescribed drug is for use following bone marrow transplantation (BMT) following myeloablative chemotherapy for a non-myeloid cancer;
3. Prescribed frequency/route is once daily by intravenous infusion;

4. Member has no known history of serious allergic reaction to filgrastim or pegfilgrastim.

**Approval duration: 6 months**

**D. Peripheral Blood Progenitor Cell Collection** (must meet all):

1. If the request is for Neupogen or Granix, member has a contraindication or intolerance to Zarxio;
2. The prescribed drug is for the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis;
3. The prescribed drug will be initiated before leukapheresis (e.g., prescribed for 6 to 7 days with leukapheresis on days 5, 6 and 7);
4. Member has no known history of serious allergic reaction to filgrastim or pegfilgrastim.

**Approval duration: 6 months**

**E. Chronic Neutropenia** (must meet all):

1. If the request is for Neupogen or Granix, member has a contraindication or intolerance to Zarxio;
2. The prescribed drug is for use in symptomatic (e.g., fever, infections, oropharyngeal ulcers) severe chronic neutropenia caused by congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia;
3. Member has no known history of serious allergic reaction to filgrastim or pegfilgrastim.

**Approval duration: 6 months**

**F. Acute Radiation Syndrome** (must meet all):

1. Agent is prescribed for use following suspected or confirmed acute exposure to myelosuppressive doses of radiation (>2 gray [Gy]);
2. Member has no known history of serious allergic reaction to filgrastim or pegfilgrastim.

**Approval duration: 6 months**

**G. Other diagnoses/indications:** Refer to CP.PHAR.57 - Global Biopharm Policy.

1. Off-label NCCN recommended uses:
  - a. If request is for Neupogen or Granix, member has contraindication or intolerance to Zarxio:
    - i. Treatment of chemotherapy-induced febrile neutropenia associated with myelosuppressive chemotherapy for non-myeloid cancer if pegfilgrastim (Neulasta) has not been administered in the same chemotherapy cycle;
    - ii. Mobilization of donor hematopoietic progenitor cells;
    - iii. Mobilization of autologous hematopoietic progenitor cells;
    - iv. Granulocyte transfusion in the allogeneic setting;

**Filgrastim, Filgrastim-sndz, Tbo-filgrastim**

- v. Supportive care in the post-hematopoietic cell transplant setting if not covered elsewhere in the policy;
  - vi. Neutropenia or anemia associated with myelodysplastic syndromes;
  - vii. Agranulocytosis;
  - viii. Aplastic anemia;
  - ix. Neutropenia associated with HIV/AIDS;
  - x. Neutropenia associated with pre-eclampsia;
2. Member has no known history of serious allergic reaction to filgrastim or pegfilgrastim.

**Approval duration: 6 months****Background***Description/Mechanism of Action:*

Granix (tbo-filgrastim), Neupogen (filgrastim) and Zarxio (filgrastim-sndz) are human granulocyte colony-stimulating factors (G-CSF) manufactured by recombinant DNA technology using Escherichia coli (E coli) bacteria. 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.

*Formulations:*

Injectable solution for subcutaneous and intravenous use:

- Vials:
  - Neupogen: filgrastim 300 mcg/mL (1 mL); filgrastim 480 mcg/1.6 mL (1.6 mL)
- Prefilled syringes:
  - Neupogen: filgrastim 300 mcg/0.5 mL (0.5 mL); filgrastim 480 mcg/0.8 mL (0.8 mL)
  - Zarxio: filgrastim-sndz 300 mcg/0.5 mL (0.5 mL); filgrastim-sndz 480 mcg/0.8 mL (0.8 mL)

Injectable solution for subcutaneous use:

- Prefilled syringes:
  - Granix: tbo-filgrastim 300 mcg/0.5 mL (0.5 mL); tbo-filgrastim 480 mcg/0.8 mL (0.8 mL)

*FDA Approved Indications:*

Granix (subcutaneous formulation) and Neupogen/Zarxio (subcutaneous and intravenous formulations) are leukocyte growth factors with the following indications:

Granix, Neupogen, Zarxio

- Patients with cancer receiving myelosuppressive chemotherapy:
  - 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.

Neupogen, Zarxio

- Patients with AML receiving induction or consolidation chemotherapy:

**CLINICAL POLICY**

**Filgrastim, Filgrastim-sndz, Tbo-filgrastim**

- To reduce the time to neutrophil recovery and the duration of fever following induction or consolidation chemotherapy treatment of patients with AML.
- Patients with cancer undergoing BMT:
  - 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 BMT.
- Patients undergoing autologous peripheral blood progenitor cell collection and therapy;
  - To mobilize autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.
- Patients with severe chronic neutropenia:
  - Chronic administration to reduce the incidence and duration of sequelae of neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with severe, chronic neutropenia due to congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia.

**Neupogen:**

- Patients with hematopoietic syndrome of acute radiation syndrome:
  - To increase survival in patients acutely exposed to myelosuppressive doses of radiation.

**Appendices**

**Appendix A: Abbreviation Key**

AML: acute myeloid/myelogenous leukemia  
 BMT: bone marrow transplantation  
 G-CSF: granulocyte colony stimulating factor  
 Gy: gray

**Coding Implications**

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J1442	Injection, filgrastim (G-CSF), excludes biosimilars, 1 microgram
J1447	Injection, tbo-filgrastim, 1 microgram
Q5101	Injection, filgrastim (G-CSF), biosimilar, 1 microgram

Reviews, Revisions, and Approvals	Date	Approval Date
Granix, Neupogen, Zarxio are split from CP.PHAR.26.Colony Stimulating Factors 2015, and converted to a new template. Contraindications added per PIs. Under the labeled indication, “BMT,” added “and bone marrow infusion.” “PBPC collection” (section I.D), removed approval for use in	10/16	12/16

Reviews, Revisions, and Approvals	Date	Approval Date
subsequent transplant after collection; however, subsequent transplant will fall under off-label use, “supportive care in the post-hematopoietic cell transplant setting”. Under sections I.A, B and C, 24-hour use restriction before and after chemotherapy is removed. Added oncology off-label uses per NCCN.		

**References**

1. Granix Prescribing Information. North Wales, PA: Teva Pharmaceuticals USA.; December 2014. Available at <http://www.granixhcp.com/Pdf/prescribing-information.pdf>. Accessed October 26, 2016.
2. Neupogen Prescribing Information. Thousand Oaks, CA: Amgen, Inc.; June 2016. Available at [http://pi.amgen.com/united\\_states/neupogen/neupogen\\_pi\\_hcp\\_english.pdf](http://pi.amgen.com/united_states/neupogen/neupogen_pi_hcp_english.pdf). Accessed October 26, 2016.
3. Zarxio Prescribing Information. Princeton, NJ: Sandoz, Inc.; April 2016. Available at <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=fe707775-a0ae-41b5-a744-28c41889fce8&type=display>. Accessed October 26, 2016.
4. Myeloid growth factors (Version 2.2016). In: National Comprehensive Cancer Network Guidelines. Available at NCCN.org. Accessed October 26, 2016.
5. Myelodysplastic syndromes (Version 1.2017 – August 18, 2016). In: National Comprehensive Cancer Network Guidelines. Available at NCCN.org. Accessed October 26, 2016.
6. Filgrastim. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at NCCN.org. Accessed October 26, 2016.
7. Filgrastim-sndz. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at NCCN.org. Accessed October 26, 2016.
8. Tbo-filgrastim. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at NCCN.org. Accessed October 26, 2016.
9. Filgrastim. In: Micromedex. Ann Arbor, MI: Truven Health Analytics; 2016. Available from: [www.micromedexsolutions.com](http://www.micromedexsolutions.com). Accessed October 26, 2016.
10. Filgrastim-sndz. In: Micromedex. Ann Arbor, MI: Truven Health Analytics; 2016. Available from: [www.micromedexsolutions.com](http://www.micromedexsolutions.com). Accessed October 26, 2016.

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health

## CLINICAL POLICY

### Filgrastim, Filgrastim-sndz, Tbo-filgrastim



plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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**Note: For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

**Note: For Medicare members**, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at <http://www.cms.gov> for additional information.

## CLINICAL POLICY

### Filgrastim, Filgrastim-sndz, Tbo-filgrastim



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