Clinical Policy: Filgrastim (Neupogen), Filgrastim-sndz (Zarxio), Tbo-filgrastim (Granix)

Reference Number: PA.CP.PHAR.297
Effective Date: 01/18
Last Review Date: 07/17/19

Coding Implications
Revision Log

Description
The intent of the criteria is to ensure that patients follow selection elements established by Pennsylvania Health and Wellness clinical policy for
Filgrastim (Neupogen®) and its biosimilars, filgrastim-sndz (Zarxio®) and tbo-filgrastim (Granix®), are human granulocyte colony-stimulating factors.

FDA Approved Indication(s)
Granix is indicated for reduction in the duration of severe neutropenia in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia (FN).

Neupogen and Zarxio are indicated to:

- Decrease the incidence of infection, as manifested by FN, 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., FN, 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

Neupogen is also indicated to increase survival in patients acutely exposed to myelosuppressive doses of radiation (hematopoietic syndrome of acute radiation syndrome).

Policy/Criteria
It is the policy of Pennsylvania Health and Wellness® that Neupogen, Zarxio, and Granix are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Chemotherapy-Induced Neutropenia (must meet all)**:**

1. Diagnosis of non-myeloid malignancy or AML;
2. Prescribed for use following myelosuppressive chemotherapy;
3. For Neupogen or Granix requests, failure of Zarxio, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization is (or may be) required for Zarxio*
4. Dose does not exceed 30 mcg/kg/day [IV] or 24 mcg/kg/day [SC].

Approval duration: 6 months

Approval duration: 6 months

B. Bone Marrow Transplantation (must meet all)**:**
1. Diagnosis of non-myeloid malignancy;
2. Member is undergoing myeloablative chemotherapy followed by BMT;
3. For Neupogen or Granix requests, failure of Zarxio, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization is (or may be) required for Zarxio*
4. Dose does not exceed 10 mg/kg/day.

Approval duration: 6 months

C. Peripheral Blood Progenitor Cell Collection (must meet all)**:**
1. Prescribed for the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis;
2. The prescribed drug will be initiated before leukapheresis (e.g., prescribed for 6 to 7 days with leukapheresis on days 5, 6 and 7);
3. For Neupogen or Granix requests, failure of Zarxio, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization is (or may be) required for Zarxio*
4. Dose does not exceed 10 mcg/kg/day.

Approved duration: 1 month

D. Chronic Neutropenia (must meet all)**:**
1. Prescribed for use in symptomatic (e.g., fever, infections, oropharyngeal ulcers) severe chronic neutropenia caused by congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia;
2. For Neupogen or Granix requests, failure of Zarxio, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization is (or may be) required for Zarxio*
3. Dose does not exceed: 30 mcg/kg/day [IV] or 24 mcg/kg/day [SC].

Approved duration: 6 months

E. Acute Radiation Syndrome (must meet all)**:**
1. Prescribed for use following suspected or confirmed acute exposure to myelosuppressive doses of radiation;
2. Dose does not exceed 10 mcg/kg/day.

Approved duration: 6 months

F. Myelodysplastic Syndrome (off-label) (must meet all)**:**
1. Diagnosis of myelodysplastic syndrome with symptomatic anemia without del (5q) abnormality;
2. Current (within the past 30 days) serum erythropoietin level ≤ 500 mU/mL;
3. For Neupogen or Granix requests, failure of Zarxio, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization is (or may be) required for Zarxio*

4. Request meets one of the following (a or b):
   a. Dose does not exceed 5 mcg/kg/day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approved duration: 6 months

G. Other diagnoses/indications

1. Refer to CP.PMN.53.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. Dose does not exceed the FDA-approved maximum recommended dose for the relevant indication.

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.

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
Revised max dosing for chemotherapy-induced neutropenia and chronic neutropenia per Clinical Pharmacology; removed radiation exposure requirement; added off-label use in myelodysplastic syndrome per NCCN Compendium; references reviewed and updated.	05.18	
3Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	07/17/19	

References

i. Granix Prescribing Information. North Wales, PA: Teva Pharmaceuticals USA; June 2017. Available at: http://granixhcp.com/. Accessed May 2, 2018.
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iii. Zarxio Prescribing Information. Princeton, NJ: Sandoz, Inc.; February 2017. Available at: www.zarxio.com. Accessed May 2, 2018.
iv. National Comprehensive Cancer Network. Myeloid Growth Factors Version 1.2018. Available at: http://www.nccn.org/professionals/physician_gls/pdf/myeloid_growth.pdf. Accessed: May 2, 2018.
v. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed May 2, 2018.
vi. DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Healthcare, Updated periodically. Accessed May 2, 2018.
vii. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: http://www.clinicalpharmacology-ip.com/. Accessed May 2, 2018.