Policy Title:	Colony Stimulating Factors: Nivestym (filgrastim-aafi), Neupogen (filgrastim), Granix (tbo-filgrastim)		
		Department:	PHA
Effective Date:	01/01/2020		
Review Date:	04/19/2019, 09/18/2019, 12/13/2019		
Revision Date:	04/19/2019, 09/18/2019, 12/13/2019		

Purpose: To support safe, effective and appropriate use of short-acting Colony Stimulating Factors.

Scope: Medicaid, Exchange, Medicare-Medicaid Plan (MMP)

Policy Statement:

Colony Stimulating Factors are covered under the Medical Benefit when used within the following guidelines. Use outside of these guidelines may result in non-payment unless approved under an exception process. Zarxio (filgrastim-sndz) is the preferred short-acting Colony Stimulating Factor.

Procedure:

Coverage of short-acting Colony Stimulating Factors will be reviewed prospectively via the prior authorization process based on criteria below.

Initial Criteria:

- Patient has one of the following conditions:
  - Bone marrow transplant (BMT); OR
  - Peripheral Blood Progenitor Cell (PBPC) mobilization and transplant (Nivestym/Neupogen-ONLY); OR Peripheral Blood Stem Cell (PBSC) mobilization and transplant (Granix-ONLY); OR
  - Prophylactic use in patients with non-myeloid malignancy:
    - Patient is undergoing myelosuppressive chemotherapy and/or radiotherapy 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 ≤ 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

- 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;

- Acute Myeloid Leukemia (AML) patient following induction or consolidation chemotherapy (Nivestym/Neupogen- ONLY); OR
- Patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Subsyndrome of Acute Radiation Syndrome); OR
- Severe chronic neutropenia (Nivestym/Neupogen- ONLY);:
  - 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;
- Patient who experienced a neutropenic complication from a prior cycle of the same chemotherapy; OR

- Bone Marrow Transplantation (BMT) failure or Engraftment Delay; OR
- Myelodysplastic Syndrome (MDS):
  - Endogenous serum erythropoietin level of ≤500 mUnits/mL;
  - Patient is receiving concurrent therapy with Erythropoiesis Stimulating Agents (ESAs);AND

- Patients must have a documented failure, contraindication, or intolerance to Zarxio (filgrastim-sndz) OR for patients that are currently on treatment with Nivestym (filgrastim-aafi), Neupogen (filgrastim), or Granix (tbo-filgrastim) can remain on treatment.

Coverage Duration: 4 months

*** Requests will also be reviewed to National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) if applicable. ***

Dosage/Administration:

Drug	**Dose**	**Maximum dose (1 billable unit = 1 mcg)**
Nivestym	• 10mcg/kg daily for up to 14 days for BMT/PBPC/Radiation indications • 6mcg/kg twice daily for Severe Congenital Neutropenia • 5mcg/kg daily for up to 14 days for all other indications	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
Granix	• 5 mcg/kg daily for up to 14 days for febrile neutropenia • 10 mcg/kg daily for up to 14 days for PBPC/BMT • 5 mcg/kg daily for up to 14 days for all other indications	BMT or PBSC: • 1200 billable units per day All Other indications: • 600 billable units per day
Neupogen	• 5mcg/kg daily for up to 14 days for non-BMT/PBPC indications • 10mcg/kg daily for up to 14 days for BMT/PBPC/Radiation indications • 6mcg/kg twice daily for Severe Congenital Neutropenia	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

***** 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.

Investigational use: All therapies are considered investigational when used at a dose or for a condition other than those that are recognized as medically accepted indications as defined in any one of the following standard reference compendia: American Hospital Formulary Service Drug information (AHFS-DI), Thomson Micromedex DrugDex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs, or Peer-reviewed published medical literature indicating that sufficient evidence exists to support use. Neighborhood does not provide coverage for drugs when used for investigational purposes.

Applicable Codes:
Below is a list of billing codes applicable for covered treatment options. The below tables are provided for reference purposes and may not be all-inclusive. Requests received with codes from tables below do not guarantee coverage. Requests must meet all criteria provided in the procedure section.

The following HCPCS/CPT codes are:

HCPCS/CPT Code	Description
Q5101	Injection, filgrastim-sndz, biosimilar, (Zarxio)
J1442	Injection, filgrastim (g-csf), excludes biosimilar, 1microgram
J1447	Injection, tbo-filgrastim, 1 microgram
Q5110	Injection, filgrastim-aafi, biosimilar, (nivestym), 1 microgram.

References:

1. Zarxio [package insert]. Princeton, NJ; Sandoz Inc; December 2017. Accessed July 2018.
2. Granix [package insert]. North Wales, PA; Teva Pharmaceuticals USA, Inc.; June 2017. Accessed March 2018
3. Neupogen [package insert]. Thousand Oaks, CA; Amgen Inc; June 2016. Accessed March 2018
4. Nivestym [package insert]. Lake Forest, IL; Hospira Inc; July 2018. Accessed July 2018.
5. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) filgrastim-sndz. National Comprehensive Cancer Network, 2018. 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 July 2018.

6. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Myeloid Growth Factors. Version 1.2018. National Comprehensive Cancer Network, 2018. 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 July 2018.
7. Kelaidi C Beyne-Rauzy O, Braun T, et al. High Response rate and improved exercise capacity and quality of life with a new regimen of darbepoetin alfa with or without filgrastim in lower-risk myelodysplastic syndromes: a phase II study by the GFM. Ann Hematol 2013; 92:621-631.
8. First Coast Service Options, Inc. Local Coverage Determination (LCD): G-CSF (Neupogen®, Granix™, Zarxio™) (L34002). Centers for Medicare & Medicaid Services, Inc. Updated on 4/25/2018 with effective date 4/1/2018. Accessed July 2018.
9. National Government Services, Inc. Local Coverage Article: Filgrastim, Pegfilgrastim, Tbo-filgrastim, Filgrastim-sndz (e.g., Neupogen®, Neulasta™, Granix™, Zarxio™) - Related to LCD L33394 (A52408). Centers for Medicare & Medicaid Services, Inc. Updated on 7/06/2018 with effective date 7/15/2018. Accessed July 2018.
10. Wisconsin Physicians Service Insurance Corporation. Local Coverage Determination (LCD): Human Granulocyte/Macrophage Colony Stimulating Factors (L34699). Centers for Medicare & Medicaid Services, Inc. Updated on 4/20/2018 with effective date 05/1/2018. Accessed July 2018.
11. Palmetto GBA. Local Coverage Determination (LCD): White Cell Colony Stimulating Factors (L37176). Centers for Medicare & Medicaid Services, Inc. Updated on 5/4/2018 with effective date 4/1/2018. Accessed July 2018.