Policy Title:	Short Acting Granulocyte Colony Stimulating Factors: Nivestym (filgrastim-aafi), Neupogen (filgrastim), Granix (tbo-filgrastim), Releuko (filgrastim-ayow), (Zarxio (filgrastim-sndz) **NON-ONCOLOGY POLICY**		
		Department:	PHA
Effective Date:	01/01/2020		
Review Date:	04/19/2019, 09/18/2019, 12/13/2019, 1/29/2020, 8/3/2020, 7/22/2021, 6/16/2022, 10/6/2022, 2/9/2023, 12/07/2023, 01/04/2024		

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

Scope: Medicaid, Commercial, 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. **For oncology indications, please refer to Myeloid Growth Factors Policy.**

Procedure:

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

Summary of Evidence:

Short-acting G-CSFs stimulate the production and function of neutrophils, thereby reducing the duration and severity of chemotherapy-induced neutropenia and its associated complications. Clinical studies have shown that short-acting G-CSFs reduce the incidence of febrile neutropenia, the need for hospitalization due to neutropenic complications, and the use of intravenous antibiotics in patients receiving myelosuppressive chemotherapy. Common adverse reactions are bone pain, injection site reactions, and mild-to-moderate musculoskeletal symptoms.

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
  - 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; OR
  - Bone Marrow Transplantation (BMT) failure or Engraftment Delay; 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), Releuko (filgrastim-ayow), or Granix (tbo-filgrastim) can remain on treatment OR MMP members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements

Coverage Duration: 4 months

Per §§ 42 CFR 422.101, this clinical medical policy only applies to INTEGRITY in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD).

Policy Rationale:
Nivestym, Neupogen, Granix, Releuko, and Zarxio were reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Nivestym, Neupogen, Granix, Releuko, and Zarxio according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using these drugs for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For INTEGRITY (Medicare-Medicaid Plan) members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.

Dosage/Administration:

Indication	**Dose**	**Maximum dose (1 billable unit = 1 mcg)**
BMT/PBPC	• 10mcg/kg daily for up to 14 days	• 1200 billable units per day
Severe Chronic Neutropenia	• 5 mcg/kg daily for up to 14 days for idiopathic or cyclic neutropenia • 6mcg/kg twice daily for severe congenital neutropenia	• 1380 billable units per day
All other indications	• 5mcg/kg daily for up to 14 days	• 600 billable units per day

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 Q5125	Injection, filgrastim-aafi, biosimilar, (nivestym), 1 microgram Injection, filgrastim-ayow, biosimilar, (releuko), 1 microgram

References:

1. Zarxio [package insert]. Princeton, NJ; Sandoz Inc; September 2022. Accessed November 2023.
2. Granix [package insert]. North Wales, PA; Teva Pharmaceuticals USA, Inc.; April 2020. Accessed November 2023.
3. Neupogen [package insert]. Thousand Oaks, CA; Amgen Inc; April 2023. Accessed November 2023.
4. Nivestym [package insert]. Lake Forest, IL; Hospira Inc; August 2023. Accessed November 2023.
5. Releuko [package insert]. Bridgewater, NJ; Amneal Pharmaceuticals; August 2023. Accessed 2023.
6. 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.
7. 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.
8. 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.
9. 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.
10. 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.