Short-acting Granulocyte-colony stimulating factor (CSF) and Granulocyte macrophage-CSF

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO031

Description

Granulocyte-colony stimulating factors (G-CSF) and granulocyte macrophage-CSF (GM-CSF) act on the hematopoietic cells by binding to specific cell surface receptors thereby stimulating the production, maturation, and activation of neutrophils.

Length of Authorization

- Initial: Four months
- Renewal: Four months

Quantity Limits

Product Name	Indication	Dosage Form	Quantity Limit
Neupogen (filgrastim)	• Bone marrow transplant • Peripheral progenitor cell (PBPC) mobilization and transplant • Prophylactic use in patients with non-myeloid malignancy • Treatment of chemotherapy-induced febrile neutropenia • Neutropenic complications from prior chemotherapy cycle • Acute myeloid leukemia (AML) patient following induction or consolidation chemotherapy • Bone marrow transplantation failure or engraftment delay • Severe chronic neutropenia • Myelodysplastic syndrome • Exposure to myelosuppressive doses of radiation	300 mcg/mL vial	15 prefilled syringes or vials per 30-day supply
		300 mcg/0.5mL syringe	
		480 mcg/1.6mL vial	
		480 mcg/0.8mL syringe	
Zarxio (filgrastim-sndz)*		300 mcg/0.5mL syringe	
		480 mcg/0.8mL syringe	
Nivestym (filgrastim-aafi)		300 mcg/mL vial	
		300 mcg/0.5mL syringe	
		480 mcg/1.6mL vial	
		480 mcg/0.8mL syringe	
Granix (tbo-filgrastim)		300 mcg/mL vial	
		300 mcg/0.5mL syringe	
		480 mcg/1.6mL vial	
		480 mcg/0.8mL syringe	
Releuko (filgrastim-ayow)		300 mcg/mL vial	
		300 mcg/0.5mL syringe	
		480 mcg/1.6mL vial	
		480 mcg/0.8mL syringe	
Leukine (sargramostim)		250 mcg/mL vial	

Initial Evaluation

I. Products may be considered medically necessary when the following criteria below are met:

Zarxio is the preferred short-acting G-CSF

- **Patients must have failed, or have a contraindication, or intolerance to Zarxio prior to consideration of any other short-acting G-CSF**
  - There is no prior authorization* required for Zarxio unless requesting above the quantity limit noted above.

A. A diagnosis of:
    1. **Peripheral Blood Progenitor Cell (PBPC) mobilization and transplant; OR**
    2. **Patient who experienced a neutropenic complication from a prior cycle of the same chemotherapy; OR**
    3. **Bone Marrow Transplant (BMT); OR**
    4. **Bone Marrow Transplantation (BMT) failure or Engraftment Delay; OR**
    5. **Patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Subsyndrome of Acute Radiation Syndrome); OR**
    6. **Acute Myeloid Leukemia (AML) patient following induction or consolidation chemotherapy; OR**
    7. **Prophylactic use in patients with non-myeloid malignancy; AND**
        i. Member is undergoing myelosuppressive chemotherapy with an expected incidence of febrile neutropenia of 20% or greater; **OR**
        ii. Member is undergoing myelosuppressive chemotherapy with an expected incidence of febrile neutropenia of 10% or greater **AND** has one or more of the following co-morbidities:
            a. Age 65 years or older AND receiving full dose intensity chemotherapy
            b. History of recurrent febrile neutropenia from chemotherapy
            c. Extensive prior exposure to chemotherapy
            d. Previous exposure of pelvis, or other areas of large amounts of bone marrow, to radiation
            e. Pre-existing neutropenia (ANC ≤ 1000/mm3) or bone marrow involvement with tumor
            f. Member has a condition that can potentially increase the risk of serious infection (i.e. HIV/AIDS)
            g. Infection/open wounds
            h. Recent surgery
            i. Poor performance status
            j. Poor renal function (creatinine clearance <50)
            k. Liver dysfunction (elevated bilirubin >2.0)
            l. Chronic immunosuppression in the post-transplant setting including organ transplant; **OR**
    8. **Myelodysplastic Syndrome**; **AND**
        i. Endogenous serum erythropoietin level of ≤500 mUnits/mL; **AND**
        ii. Member has lower risk disease (i.e., defined as IPSS-R [Very Low, Low, Intermediate], IPSS [Low/Intermediate-1], WPSS [Very Low, Low, Intermediate]); **AND**
        iii. Used for treatment of symptomatic anemia in patients without del(5q); **AND**
        iv. Member is receiving concurrent therapy with Erythropoiesis Stimulating Agents (ESA); **AND**
            a. Member has ring sideroblasts < 15% and will use in combination with lenalidomide following no response (despite adequate iron stores) or loss or response to an ESA alone; **OR**

b. Member has ring sideroblasts ≥ 15%; **OR**

9. **Treatment of chemotherapy-induced febrile neutropenia; AND**
    i. Member has been on prophylactic therapy with filgrastim; **OR**
    ii. Member has not received prophylactic therapy with a granulocyte colony stimulating factor; **AND**
        a. Member has one or more of the following risk factors for developing infection-related complications:
            i. Sepsis Syndrome
            ii. Age >65
            iii. Absolute neutrophil count [ANC] <100/mcL
            iv. Duration of neutropenia expected to be greater than 10 days
            v. Pneumonia or other clinically documented infections
            vi. Invasive fungal infection
            vii. Hospitalization at the time of fever
            viii. Prior episode of febrile neutropenia; **OR**
10. **Severe chronic neutropenia; AND**
    i. Member has an absolute neutrophil count (ANC) < 500/mm3; **AND**
    ii. Member has a diagnosis of one of the following:
        a. Congenital neutropenia
        b. Cyclic neutropenia
        c. Idiopathic neutropenia; **OR**
11. **Management of CAR-T related Toxicity; AND**
    i. Member has been receiving therapy with CAR T-cell therapy (e.g. tisangenleclecleucel (Kymriah), Axicabtagene Ciloleucel (Yescarta), etc.); **AND**
    ii. Member is experiencing neutropenia related to their therapy.

Renewal Evaluation

I. Same as initial prior authorization policy criteria.

Supporting Evidence

I. Indications listed under section I are supported by FDA-labeled indication(s) or are recommended per Compendia.

II. Quantity limits are based on usual FDA dosing of once daily until complete blood count (CBC) or absolute neutrophil count (ANC) has returned to an appropriate range. Generally, chemotherapy is administered every 2-3 weeks, whereby frequency of filgrastim is not expected to be needed for greater than two weeks. For other indications, such as transplant, myelodysplastic syndrome, or chronic neutropenia, therapy is continued until adequate neutrophil recovery is achieved. Accordingly, quantity exceptions may be considered when frequent administration of filgrastim is deemed medically necessary.

III. Duration of approval is based on usual duration of chemotherapy or radiation therapy cycle. There is no guideline consensus on optimal duration of G-CSF or GM-CSF treatment or prophylaxis, therefore continued use is driven by clinical scenario and lab monitoring.

IV. Risk of developing febrile neutropenia is related to intensity and toxicity of chemotherapy regimen, as well as patient-specific factors. Expected incidence of febrile neutropenia percentages for myelosuppressive chemotherapy regimens can be found in the NCCN Hematopoietic Growth Factors Clinical Practice Guideline at NCCN.org. NCCN and ASCO guidelines recommend use of a G-CSF for prophylaxis when risk is 20% or greater. When risk is between 10-20%, prophylactic G-CSF is recommended when patients have one or more of the risk factors listed above. Routine prophylaxis with G-CSF for febrile neutropenia when risk is less than 10% is not recommended.

V. In myelodysplastic syndromes (MDS), G-CSF may be used in combination with an erythropoiesis-stimulating agent (ESA) when patients have symptomatic anemia, as G-CSF can boost erythroid response. Likelihood of erythroid response is influenced by serum erythropoietin, MDS prognostic category, presence of ring sideroblasts, and other factors, therefore criteria outlined above follow NCCN guidelines to target the patient population expected to achieve a response.

VI. All FDA-approved biosimilars undergo a rigorous testing process to compare safety, purity, and potency between the proposed biosimilar and the parent or originator product, otherwise known as the reference product, to ensure there are no clinically meaningful differences. Only minor differences between products are allowed, such as in clinically inactive components. Biosimilars may be approved for all, or a subset, of the indications for the reference product. It is not uncommon for biosimilars to have fewer labeled indications if the reference product has remaining patent or exclusivity rights. It can be expected that biosimilar products will have the same clinical efficacy and safety profile as the reference product due to thorough FDA testing. With a goal to increase access to high-quality, cost-effective care, biosimilars may fill an unmet need as a more affordable alternative to brand biologic therapies. Notably, NCCN Guidelines similarly recommend that FDA-approved biosimilars be used as substitutes for originator filgrastim and pegfilgrastim. In addition, ASCO recommends that pegfilgrastim, filgrastim and biosimilars be considered therapeutically equivalent, with product selection being based on convenience, cost and clinical situation (i.e., chemotherapy frequency). As such, trial of preferred short-acting G-CSF biosimilar Zarxio (filgrastim-sndz) is required prior to approval of non-preferred filgrastim products.

References

1. Neupogen [Prescribing Information]. Amgen Inc. Thousand Oaks, CA. February 2021.
2. Zarxio [Prescribing Information]. Sandoz Inc. Princeton, NJ. August 2019.
3. Nivestym [Prescribing Information]. Hospira Inc., a Pfizer Company. Lake Forest, IL. July 2018.
4. Granix [Prescribing Information]. UAB Teva Baltics. Vilnius, Lithuania. November 2019.
5. Leukine [Prescribing Information]. Sanofi-aventis U.S. LLC. Bridgewater, NJ. March 2018.
6. Releuko [Prescribing Information]. Kashiv BioSciences, LLC. Piscataway, NJ. February 2022.
7. Smith TJ, Bohlke K, Lyman GH, et al. Recommendations for the use of wbc growth factors: American Society of Clinical Oncology clinical practice guideline update. JCO. 2015;33(28):3199-3212.
8. Wisconsin Physicians Service Insurance Corporation. Local Coverage Determination (LCD): Human Granulocyte/Macrophage Colony Stimulating Factors (L34699). Centers for Medicare & Medicaid Services, Inc. Updated on 1/23/2018 with effective date 02/1/2018. Accessed March 2018.

9. First Coast Service Options, Inc. Local Coverage Determination (LCD): G-CSF (Neupogen®, Granix™, Zarxio™) (L34002). Centers for Medicare & Medicaid Services, Inc. Updated on 6/10/2016 with effective date 7/5/2016. Accessed March 2018.
10. National Government Services, Inc. Local Coverage Article: Filgrastim, Pegfilgrastim, Tbofilgrastim, Filgrastim-sndz (e.g., Neupogen®, Neulasta™, Granix™, Zarxio™) - Related to LCD L33394 (A52408). Centers for Medicare & Medicaid Services, Inc. Updated on 9/23/2016 with effective date 10/1/2016. Accessed March 2018.
11. Palmetto GBA. Local Coverage Determination: White Cell Colony Stimulating Factors (L37176). Centers for Medicare & Medicaid Services, Inc. Updated on 12/7/2017 with effective date 2/26/2018. Accessed March 2018.
12. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology for Hematopoietic Growth Factors, Version 1.2022. Updated December 22, 2021.
13. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Myelodysplastic Syndromes, Version 3.2022. Updated January 13, 2022.
14. U.S. Food and Drug Administration. Biosimilars – Healthcare provider materials. Updated July 28, 2021. https://www.fda.gov/drugs/biosimilars/health-care-provider-materials?utm_campaign=cder-factsheets&utm_content=&utm_medium=social&utm_source=linkedin
15. Biologics and Biosimilars Collective Intelligence Consortium. Biosimilar facts. https://www.bbcic.org/resources/biosimilars-facts.

Related Policies

Policies listed below may be related to the current policy. Related policies are identified based on similar indications, similar mechanisms of action, and/or if a drug in this policy is also referenced in the related policy.

Policy Name	Disease state
Long-acting Granulocyte Colony Stimulating Factor (G-CSF)	Prophylactic use in patients with non-myeloid malignancy
	Neutropenic complications from prior chemotherapy cycle
	Exposure to myelosuppressive doses of radiation
	Bone marrow transplantation failure or engraftment delay
	Peripheral progenitor cell (PBPC) mobilization and transplant

Policy Implementation/Update:

Action and Summary of Changes	Date
Updated policy supporting evidence and references. Added related policies table.	08/2022
Added Releuko (filgrastim-ayow) to policy in the non-preferred position	04/2022
Updated quantity level limit to allow 15 doses per 30-day supply	12/2019
Policy title change, designate Zarxio as a preferred product, add “No PA Required” to Initial Evaluation Section 1 boxed information	10/2019
Previous Reviews	12/2018
Added Nivestym, biosimilar to Neupogen	10/2018
Previous Reviews	02/2018; 07/2018
Criteria update. Zarxio is the preferred short-acting G-CSF	2/2017