Long-acting Granulocyte Colony Stimulating Factor
EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO052

Description
Granulocyte-colony stimulating factors (G-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
pegfilgrastim (Neulasta)	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	6 mg/0.6 mL prefilled syringe	Two prefilled syringes per 28-day supply
pegfilgrastim (Neulasta Onpro)		6 mg/0.6 mL prefilled syringe with on-body injector kit	Two kits per 28-day supply
pegfilgrastim-jmdb (Fulphila)		6 mg/0.6 mL prefilled syringe	Two prefilled syringes per 28-day supply
pegfilgrastim-cbqv (Udenyca)			
pegfilgrastim-bmez (Ziextenzo)			
pegfilgrastim-apgf (Nyvepria)			
pegfilgrastim-pbbk (Fylnetra)			
pegfilgrastim-fpgk (Stimufend)			

Initial Evaluation

I. **Pegfilgrastim-bmez (Ziextenzo) and pegfilgrastim-jmdb (Fulphila)** may be considered medically necessary when the following criteria below are met:

A. A diagnosis of the following:
   1. **Peripheral Blood Progenitor Cell (PBPC) mobilization and transplant; OR**
   2. **A neutropenic complication from a prior cycle of the same chemotherapy; OR**
   3. **Bone Marrow Transplantation (BMT) failure or Engraftment Delay; OR**
   4. **Member acutely exposed to myelosuppressive doses of radiation (Hematopoietic Subsyndrome of Acute Radiation Syndrome); OR**
   5. **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:
         a. Age 65 years or older AND receiving full dose intensity chemotherapy; **OR**
         b. History of recurrent febrile neutropenia from chemotherapy; **OR**
         c. Extensive prior exposure to chemotherapy; **OR**
         d. Previous exposure of pelvis, or other areas of large amounts of bone marrow, to radiation; **OR**
         e. Pre-existing neutropenia (ANC ≤ 1000/mm3) or bone marrow involvement with tumor; **OR**
         f. Member has a condition that can potentially increase the risk of serious infection (e.g. HIV/AIDS) ; **OR**
         g. Infection/open wounds; **OR**
         h. Recent surgery; **OR**
         i. Poor performance status; **OR**
         j. Poor renal function (creatinine clearance <50mL/min) ; **OR**
         k. Liver dysfunction (elevated bilirubin >2.0mg/dL) ; **OR**
         l. Chronic immunosuppression in the post-transplant setting including organ transplant.

II. **Pegfilgrastim (Neulasta, Neulasta Onpro), pegfilgrastim-cbqv (Udenyca), pegfilgrastim-apgf (Nyvepria), pegfilgrastim-pbbk (Fylnetra), and pegfilgrastim-fpgk (Stimufend)** may be considered medically necessary when the following criteria below are met:
   A. Criteria I(A) above is met; **AND**
   B. Treatment with pegfilgrastim-jmdb (Fulphila) AND pegfilgrastim-bmez (Ziextenzo) have been ineffective, contraindicated, or not tolerated.

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 pegfilgrastim as once per chemotherapy cycle, but no sooner than 14 days before and 24 hours after chemotherapy administration. Generally, chemotherapy is administered every 2-3 weeks, whereby frequency of pegfilgrastim is not expected to be more often than every two weeks. There are insufficient data to support use of weekly pegfilgrastim. For other indications, such as transplant, therapy is continued until adequate neutrophil recovery is achieved. Accordingly, quantity exceptions may be considered when frequent administration of pegfilgrastim is deemed medically necessary.

III. Duration of approval is based on usual duration of chemotherapy or radiation therapy cycles. 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. 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 biosimilars pegfilgrastim-bmez (Ziextenzo) and pegfilgrastim-jmdb (Fulphila) is

required prior to approval of non-preferred pegfilgrastim products.

References

1. Neulasta [Prescribing Information]. Amgen Inc. Thousand Oaks, CA. February 2021.
2. Fulphila [Prescribing Information]. Mylan GmbH. Zurich, Switzerland. June 2018.
3. Udenyca [Prescribing Information]. Coherus Biosciences, Inc. Redwood City, CA. April 2019.
4. Ziextenzo [Prescribing Information]. Sandoz Inc. Princeton, NJ. November 2019.
5. Nyvepria [Prescribing Information]. Hospira, Inc., a Pfizer Company. Lake Forest, IL. October 2021.
6. Fylnetra [Prescribing Information]. Kashiv BioSciences, LLC. Piscataway, NJ. May 2022.
7. Stimufend [Prescribing Information]. Fresenius Kabi USA, LLC. Lake Zurich, IL. September 2022.
8. 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.
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 1/23/2018 with effective date 02/1/2018. Accessed March 2018.
10. 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.
11. 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.
12. 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.
13. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology for Hematopoietic Growth Factors, Version 1.2022. Updated December 22, 2021.
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
Short-acting Granulocyte-colony stimulating factor (CSF) and Granulocyte macrophage-CSF (GM-CSF)	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 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

Policy Implementation/Update:

Action and Summary of Changes	Date
Added new product pegfilgrastim-fpgk (Stimufend) after trial of pegfilgrastim-jmdb (Fulphila) AND pegfilgrastim-bmez (Ziextenzo)	09/2022
Updated policy supporting evidence and references. Added related policies table. Added new product Fylnetra (pegfilgrastim-pbbk) after trial of pegfilgrastim-jmdb (Fulphila) AND pegfilgrastim-bmez (Ziextenzo)	08/2022
Updated policy name from "pegfilgrastim (Neulasta®; Neulasta Onpro®; Fulphila®; Udenyca®; Ziextenzo®, Nyvepria™)" to "Long-acting Granulocyte colony stimulating factor"	04/2022
Updated pegfilgrastim-jmdb (Fulphila) as preferred product; removed pegfilgrastim-cbqv (Udenyca) from preferred products. (Effective 7/1/2021)	05/2021
Updated preferred products to add Ziextenzo (effective 1/1/2021) and move Neulasta/Neulasta Onpro to non-preferred (effective 1/1/2021). Added Nyvepria, biosimilar to Neulasta.	11/2020
Updated policy to allow for 28 days supply	02/2020
Added Ziextenzo, biosimilar to Neulasta; update quantity limits to allow for 30 days supply	12/2019
Added Udenyca, biosimilar to Neulasta	01/2019
Neulasta, Neulasta Onpro preferred GCSF	12/2018
Added Fulphila, biosimilar to Neulasta	07/2018
Policy created	02/2018