UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Colony Stimulating Factors – Pegfilgrastim Products Utilization Management Medical Policy

- Armlupeg® (pegfilgrastim-unne subcutaneous injection – Lupin)
- Fulphila® (pegfilgrastim-jmdb subcutaneous injection – Mylan)
- Fylnetra® (pegfilgrastim-pbbk subcutaneous injection – Amneal)
- Neulasta® (pegfilgrastim subcutaneous injection – Amgen)
- Nyvepria™ (pegfilgrastim-apgf subcutaneous injection – Pfizer)
- Stimufend® (pegfilgrastim-fpgk subcutaneous injection – Fresenius Kabi)
- Udenyca® (pegfilgrastim-cbqv subcutaneous injection – Coherus)
- Ziextenzo™ (pegfilgrastim-bmez subcutaneous injection – Sandoz)

REVIEW DATE: 10/22/2025; selected revision 09/02/2026

OVERVIEW

Pegfilgrastim, a granulocyte colony stimulating factor (G-CSF), is indicated for the following uses: [1-8]

- **Decrease the incidence of infection, as manifested by febrile neutropenia**, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia
- **Increase survival in patients acutely exposed to myelosuppressive doses of radiation** (Hematopoietic Syndrome of Acute Radiation Syndrome [H-ARS])

Armlupeg, Fulphila, Fylnetra, Nyvepria, Stimufend, Udenyca, and Ziextenzo are FDA-approved biosimilars to Neulasta.[1-8] Only Armlupeg, Fylnetra, Neulasta, Stimufend, Udenyca, and Ziextenzo labeling carries the indication for treatment of H-ARS.

Guidelines

The National Comprehensive Cancer Network (NCCN) addresses the use of pegfilgrastim products in several guidelines. Of note, throughout the recommendations, it is acknowledged that an FDA-approved biosimilar is an appropriate substitute for pegfilgrastim.[9,10]

- **Hematopoietic Cell Transplantation:** Guidelines (version 3.2025 – September 24, 2025) recommend pegfilgrastim for hematopoietic cell mobilization for autologous donors in combination with other treatments.[9]
- **Hematopoietic Growth Factors:** Guidelines (version 1.2025 – October 11, 2024) recommend pegfilgrastim, along with other CSFs, for prophylactic use if the patient is receiving anti-cancer medications that are associated with a high (> 20%) incidence of severe neutropenia with fever.[10] Consider CSF therapy for patients with an intermediate (10% to 20%) probability of developing febrile neutropenia based on risk factors. The NCCN guidelines also recommend therapy with CSFs in other scenarios in those given myelosuppressive chemotherapy. Pegfilgrastim is also recommended as an appropriate option for the treatment of patients with radiation-induced myelosuppression following a radiologic/nuclear incident (Hematopoietic Syndrome of Acute Radiation Syndrome [H-ARS]). Of note, pegfilgrastim products, Rolvedon, and Ryzneuta have only been studied for prophylactic use, not for treatment of febrile neutropenia.

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POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of pegfilgrastim products. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with pegfilgrastim as well as the monitoring required for adverse events and long-term efficacy, approval requires pegfilgrastim to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of pegfilgrastim products is recommended in those who meet one of the following:

FDA-Approved Indications

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1. **Cancer in a Patient Receiving Myelosuppressive Chemotherapy**. Approve for 6 months if the patient meets BOTH of the following (A and B):
   - **A)** Patient meets ONE of the following (i, ii, or iii):
     - **i.** Patient is receiving myelosuppressive anti-cancer medications that are associated with a high risk of febrile neutropenia (the risk is at least 20% based on the chemotherapy regimen); OR
     - **ii.** Patient meets BOTH of the following (a and b):
       - **a)** Patient is receiving myelosuppressive anti-cancer medications that are associated with a risk of febrile neutropenia, but the risk is less than 20% based on the chemotherapy regimen; AND
       - **b)** Patient has at least one risk factor for febrile neutropenia according to the prescriber; OR
         Note: Examples of risk factors include age > 65 year receiving full chemotherapy dose intensity; prior chemotherapy or radiation therapy; persistent neutropenia; bone marrow involvement by tumor; recent surgery and/or open wounds; liver dysfunction (bilirubin > 2.0 mg/dL); renal dysfunction (creatine clearance < 50 mL/min); poor performance status; patient with human immunodeficiency virus (HIV) infection and low CD4 counts.
     - **iii.** Patient meets BOTH of the following (a and b):
       - **a)** Patient has had a neutropenic complication from a prior chemotherapy cycle and did not receive prophylaxis with a colony stimulating factor; AND
         Note: Examples of colony stimulating factors include filgrastim products, pegfilgrastim products, Ryzneuta (efbemalenograstim alfa-vuxw subcutaneous injection), Rolvedon (eflapegrastim-xnst subcutaneous injection).
       - **b)** A reduced dose or frequency of chemotherapy may compromise treatment outcome; AND
   - **B)** The medication is prescribed by or in consultation with an oncologist or hematologist.

   Dosing. Approve up to 6 mg given by subcutaneous injection no more frequently than once every 2 weeks.

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2. **Radiation Syndrome (Hematopoietic Syndrome of Acute Radiation Syndrome [H-ARS]).** Approve for 1 month if the agent is prescribed by or in consultation with a physician who has expertise in treating acute radiation syndrome.

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Dosing. Approve two doses of up to 6 mg by subcutaneous injection given no more frequently than 1 week apart.

Other Uses with Supportive Evidence

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3. **Peripheral Blood Progenitor Cell (PBPC) Collection and Therapy.** Approve one dose if prescribed by or in consultation with an oncologist, a hematologist, or a physician who specializes in transplantation.

Dosing. Approve up to 6 mg given by subcutaneous injection one time.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of pegfilgrastim products is not recommended in the following situations:

1. **Myelodysplastic Syndrome (MDS).** Only limited data report use of pegfilgrastim for patients with MDS.[12] Guidelines from the NCCN for MDS (version 1.2026 – October 9, 2025) do not mention use of pegfilgrastim in this patient population.[11]

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Neulasta® subcutaneous injection [prescribing information]. Thousand Oaks, CA: Amgen; April 2025.
2. Fulphila® subcutaneous injection [prescribing information]. Rockford, IL: Mylan; October 2021.
3. Udenyca® subcutaneous injection [prescribing information]. Redwood City, CA: Coherus BioSciences; August 2024.
4. Ziextenzo™ subcutaneous injection [prescribing information]. Princeton, NJ: Sandoz; March 2021.
5. Nyvepria™ subcutaneous injection [prescribing information]. New York, NY: Pfizer; June 2023.
6. Fylnetra® subcutaneous injection [prescribing information]. Bridgewater, NJ: Amneal; April 2025.
7. Stimufend® subcutaneous injection [prescribing information]. Lake Zurich, IL: Fresenius Kabi; September 2022.
8. Armlupeg® subcutaneous injection [prescribing information]. Maharashtra, India: Lupin; July 2026.
9. The NCCN Hematopoietic Cell Transplantation Clinical Practice Guidelines in Oncology (version 3.2025 – September 24, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on October 7, 2025.
10. The NCCN Hematopoietic Growth Factors Clinical Practice Guidelines in Oncology (version 1.2025 – October 11, 2024). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on October 7, 2025.
11. The NCCN Myelodysplastic Syndromes Clinical Practice Guidelines in Oncology (version 1.2026 – October 9, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on October 16, 2025.
12. Jakob A, Hirsch FW, Engelhardt M. Successful treatment of a patient with myelodysplastic syndrome (RAEB) with darbepoetin alfa in combination with pegfilgrastim. *Ann Hematol*. 2005;84(10):694-695.

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HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	09/20/2023
Annual Revision	**Cancer in a Patient Receiving Myelosuppressive Chemotherapy**: The Note providing examples of risk factors for febrile neutropenia was updated from "≥ 65 years" to "> 65 years of age receiving full chemotherapy dose intensity", liver dysfunction was defined as "bilirubin > 2.0 mg/dL", renal dysfunction was defined as "creatine clearance < 50 mL/min", and human immunodeficiency infection patients was clarified to add "with low CD4 counts." The requirement for a patient to have had a neutropenic complication from "prior chemotherapy" was updated to add "cycle." The Note providing examples of colony stimulating factors was updated to add Ryzneuta and Rolvedon and remove Leukine. **Peripheral Blood Progenitor Cell (PBPC) Collection and Therapy**: The diagnosis was updated from "Peripheral Blood Progenitor Cell Transplantation in Patients with Cancer" to as listed. The dosing limitation was updated from "In adults 6 mg by subcutaneous injection one time; OR In children up to 200 mcg/kg by subcutaneous injection" to "Approve up to 6 mg by subcutaneous injection one time".	10/09/2024
Update	**Overview:** New indication for Hematopoietic Subsyndrome of Acute Radiation Syndrome for Fylnetra was added to Overview.	05/15/2025
Annual Revision	**Cancer in a Patient Receiving Myelosuppressive Chemotherapy**: The Note was updated from "human immunodeficiency virus (HIV) infection patients with low CD4 counts" to "a patient with HIV infection and low CD4 counts."	10/22/2025
Selected Revision	Armlupeg was added to the policy with the same criteria as the other pegfilgrastim (Neulasta, biosimilars) products.	09/02/2026

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