

PRIOR AUTHORIZATION POLICY

POLICY: Colony Stimulating Factors – Pegfilgrastim Products Prior Authorization Policy

- Neulasta[®] (pegfilgrastim subcutaneous injection – Amgen)
- Fulphila[™] (pegfilgrastim-jmdb subcutaneous injection – Mylan)
- Fylnetra[®] (pegfilgrastim-pbbk subcutaneous injection – Amneal)
- 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: 10/09/2024

OVERVIEW

Pegfilgrastim, a granulocyte colony stimulating factor (G-CSF), is indicated for the following uses:¹⁻⁷

- **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])

Fulphila, Fylnetra, Nyvepria, Stimufend, Udenyca, and Ziextenzo are biosimilars to Neulasta.¹⁻⁷ Only Neulasta, Fylnetra, Stimufend, Udenyca, and Ziextenzo labeling carries the indication for treatment of H-ARS.^{1,3,4,7}

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.^{8,9}

- **Hematopoietic Cell Transplantation:** Guidelines (version 2.2024 – August 30, 2024) recommend pegfilgrastim for hematopoietic cell mobilization for autologous donors as a single agent or in combination with other treatments.⁸
- **Hematopoietic Growth Factors:** Guidelines (version 3.2024 – January 30, 2024) recommend pegfilgrastim, along with other colony stimulating factors (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.⁹ 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. Of note, pegfilgrastim, Rolvedon, and Ryzneuta have only been studied for prophylactic use, not for treatment of febrile neutropenia.

The American Society of Clinical Oncology clinical practice guidelines for the use of white blood cell growth factors (2015) recommends CSFs to reduce the risk of febrile neutropenia in patients receiving cancer chemotherapy.⁸ CSFs may be considered in patients receiving radiation therapy alone if prolonged delays secondary to neutropenia are expected. The guidelines state CSFs should be avoided in patients receiving concomitant chemotherapy and radiation therapy, particularly involving the mediastinum.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of pegfilgrastim. 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 criteria:

FDA-Approved Indications

- 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 (creatinine clearance < 50 mL/min); poor performance status; human immunodeficiency virus (HIV) infection patients with 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.
- 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.

Other Uses with Supportive Evidence

- 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.

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.¹¹ Guidelines from the NCCN for MDS (version 3.2024 – July 25, 2024) do not mention use of pegfilgrastim in this patient population.¹²
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; March 2021.
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. The NCCN Hematopoietic Cell Transplantation Clinical Practice Guidelines in Oncology (version 2.2024 – August 30, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on October 3, 2024.
9. The NCCN Hematopoietic Growth Factors Clinical Practice Guidelines in Oncology (version 3.2024 – January 30, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on October 3, 2024.
10. Smith TJ, Bohlke K, Lyman GH, Carson KR, et al. Recommendations for the use of WBC growth factors: American Society of Clinical Oncology Clinical Practice Guideline Update. *J Clin Oncol*. 2015;33(28):3199-3212.
11. 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.
12. The NCCN Myelodysplastic Syndromes Clinical Practice Guidelines in Oncology (version 3.2024 – July 25, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on October 3, 2024.

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 “creatinine 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.	10/09/2024
Update	Overview: New indication for Hematopoietic Subsyndrome of Acute Radiation Syndrome for Fylnetra was added to Overview.	05/15/2025