Utilization Review Policy 213

POLICY: Biosimilars – Fylnetra, Nyvepria, Stimufend and Ziextenzo

- Fylnetra™ (pegfilgrastim-pbbk injection for subcutaneous use – Amneal)
- Nyvepria™ (pegfilgrastim-apgf subcutaneous injection – Pfizer)
- Stimufend® (pegfilgrastim-fpgk subcutaneous injection – Fresenius Kabi)
- Ziextenzo™ (pegfilgrastim-bmez injection for subcutaneous use – Sandoz)

EFFECTIVE DATE: 1/1/2021

LAST REVISION DATE: 10/22/25; selected revision 12/3/2025

COVERAGE CRITERIA FOR: All Aspirus Medicare Plans

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 FDA-approved 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 3.2025 – September 24, 2025) recommend pegfilgrastim for hematopoietic cell mobilization for autologous donors in combination with other treatments.[8]
- **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.[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. 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.

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. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. 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 Fylnetra, Nyvepria, Stimufend, Ziextenzo is recommended for requests meeting both the preferred product step therapy requirements and indication requirements.

Preferred Product(s): Fulphila, Neulasta, Udenyca
Non-Preferred Products(s): Fylnetra, Nyvepria, Stimufend, Ziextenzo

Step Therapy Requirements:

Authorization for a non-preferred biologic product or biosimilar will be granted if the patient has had *any one of the listed issues below (A, B, C, or D) with all preferred product(s)*. *Chart notes documenting* the issue must be provided at time of request:

A. Allergic reaction to a specific inactive ingredient in all preferred biologic products or biosimilars OR

B. Adverse reaction to a specific inactive ingredient in all preferred biologic products or biosimilars OR

C. Therapeutic success while taking a non-preferred biologic product or biosimilar and therapeutic failure during an adequate trial of all preferred biologic products or biosimilars which allowed sufficient time for a positive treatment outcome documented by medical chart notes OR

D. The patient has a diagnosis not included in the FDA-approved indications of all preferred products, but is included in the FDA-approved indications of the non-preferred product

Please note:

- Factors such as patient or prescriber preference or healthcare facility's or pharmacy's inability or unwillingness to order or stock the preferred product(s) will not be considered

- Common side effects to all products and infusion-related reactions are not considered documented allergic reactions to a preferred product as they would be expected with the innovator and biosimilar products
- Continuation of therapy overrides are not available to bypass required trial(s) of preferred biosimilar or biologic reference product
- Generally, an adequate trial of a drug is considered to be three months or longer in order to allow time for efficacy to be established

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.

   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.[11] Guidelines from the NCCN for MDS (version 1.2026 – October 9, 2025) do not mention use of pegfilgrastim in this patient population.[10]

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. 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.
9. 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.
10. 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.
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.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	08/18/2021
Annual Revision	No criteria changes.	08/31/2022
Selected Revision	Fylnetra, a biosimilar to Neulasta, was added to the policy.	10/05/2022
Selected Revision	Stimufend, a biosimilar to Neulasta, was added to the policy.	01/04/2023
Aspirus Revision	Combined Medicare Policy with Health Exchange and Medicaid Policy due to retirement of Local Coverage Article A52408 (L33394). Update Biosimilar Step Therapy Requirement section to include lookback period for both Medicare (365 days) and Medicaid and Commercial patients (180 days).	7/28/2023
Aspirus Revision	Ziextenzo move from a preferred product to a non-preferred product and will not require review prior to approval and Nyvepria moved from a non-preferred product to a preferred product and with no longer require review prior to use.	9/8/2023
Annual Revision	No criteria changes.	09/20/2023
Aspirus P&T Review	Policy reviewed and approved by Aspirus P&T committee. Annual review process	09/16/2024
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
Aspirus Update	Updated step therapy criteria to require clinical need for non-preferred product over the preferred products including chart note documentation to support the need for a non-preferred product.	05/07/2025
Aspirus P&T Review	Policy reviewed and approved by Aspirus P&T committee. Annual review process	09/15/2025
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
Aspirus Update	Updated preferred products to remove Nyvepria and include Fulphila effective 1/1/26.	12/3/2025