



## 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:** 10/22/2025

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### **INSTRUCTIONS FOR USE**

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

## **CIGNA NATIONAL FORMULARY COVERAGE:**

### **OVERVIEW**

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

- **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, Flyneta, Nyvepria, Stimufend, Udenyca, and Ziextenzo are FDA-approved biosimilars to Neulasta.<sup>1-7</sup> Only Neulasta, Flyneta, Stimufend, Udenyca, and Ziextenzo labeling carries the indication for treatment of H-ARS.<sup>1,3,4,7</sup>

## 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.<sup>8,9</sup>

- **Hematopoietic Cell Transplantation:** Guidelines (version 3.2025 – September 24, 2025) recommend pegfilgrastim for hematopoietic cell mobilization for autologous donors in combination with other treatments.<sup>8</sup>
- **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.<sup>9</sup> 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 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.

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**is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):**

## **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; 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 alfavuxw subcutaneous injection), Rolvedon (eflapograstim-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 COVERED**

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**is(are) considered not medically necessary for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):**

**1. Myelodysplastic Syndrome (MDS).** Only limited data report use of pegfilgrastim for patients with MDS.<sup>11</sup> Guidelines from the NCCN for MDS (version 1.2026 – October 9, 2025) do not mention use of pegfilgrastim in this patient population.<sup>10</sup>

### **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<sup>®</sup> subcutaneous injection [prescribing information]. Redwood City, CA: Coherus BioSciences; August 2024.
4. Ziextenzo<sup>™</sup> subcutaneous injection [prescribing information]. Princeton, NJ: Sandoz; March 2021.
5. Nyvepria<sup>™</sup> subcutaneous injection [prescribing information]. New York, NY: Pfizer; June 2023.
6. Fylnetra<sup>®</sup> subcutaneous injection [prescribing information]. Bridgewater, NJ: Amneal; April 2025.
7. Stimufend<sup>®</sup> 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.	09/20/2023
Annual Revision	<p><b>Cancer in a Patient Receiving Myelosuppressive Chemotherapy:</b>            The Note providing examples of risk factors for febrile neutropenia was updated from "≥ 65 years" to "&gt; 65 years of age receiving full chemotherapy dose intensity", liver dysfunction was defined as "bilirubin &gt; 2.0 mg/dL", renal dysfunction was defined as "creatinine clearance &lt; 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.</p> <p><b>Peripheral Blood Progenitor Cell (PBPC) Collection and Therapy:</b>            The diagnosis was updated from "Peripheral Blood Progenitor Cell Transplantation in Patients with Cancer" to as listed.</p>	10/09/2024
Update	<b>Overview:</b> New indication for Hematopoietic Subsyndrome of Acute Radiation Syndrome for Fylnetra was added to Overview.	05/15/2025
Annual Revision	<b>Cancer in a Patient Receiving Myelosuppressive Chemotherapy:</b> 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

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