



Drug Coverage Policy

Effective Date 3/1/2026

Coverage Policy Number IP0070

Policy Title Pegfilgrastim Products

Colony Stimulating Factors – Pegfilgrastim Products

- 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)

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.

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.¹⁰ 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.

Coverage Policy

POLICY STATEMENT

Prior Authorization is required for the benefit coverage of pegfilgrastim products. Approval is required 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.

Documentation: Documentation is required where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory tests, claims records, and/or other information. All documentation must include patient-specific identifying information.

Pegfilgrastim products are considered medically necessary when ONE of the following is met:

1. Cancer in a Patient Receiving Myelosuppressive Chemotherapy. Approve for 6 months if the patient meets ALL of the following (A, B, and C):

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 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.

C) Preferred product criteria is met for the product(s) as listed in the below table(s)

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

2. Radiation Syndrome (Hematopoietic Syndrome of Acute Radiation Syndrome [H-ARS]). Approve for 1 month if the patient meets **BOTH** of the following criteria:

A. Medication is prescribed by or in consultation with a physician with expertise in treating acute radiation syndrome.

B. Preferred product criteria is met for the product(s) as listed in the below table(s)

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

3. Peripheral Blood Progenitor Cell (PBPC) Collection and Therapy. Approve one dose if the patient meets **BOTH** of the following criteria:

- A. Medication is prescribed by or in consultation with an oncologist, a hematologist, or a physician who specializes in transplantation.
- B. Preferred product criteria is met for the product(s) as listed in the below table(s)

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

Employer Plans:

Product	Criteria
<p>Fulphila (pegfilgrastim-jmdb subcutaneous injection)</p>	<p><u>Standard/Performance/Value/Advantage/Legacy Drug List Plans:</u></p> <p>Patient meets BOTH of the following:</p> <ol style="list-style-type: none"> 1. Patient has tried ALL of the following [documentation required]: <ul style="list-style-type: none"> a. Neulasta b. Nyvepria c. Udenyca 2. Patient cannot continue to use each of the formulary alternative(s) due to a formulation difference in the inactive ingredient(s) [e.g., differences in stabilizing agent, buffering agent, and/or surfactant] which, according to the prescriber, would result in a significant allergy or serious adverse reaction.
<p>Fylnetra (pegfilgrastim-pbbk subcutaneous injection)</p>	<p><u>Standard/Performance/Value/Advantage/Legacy Drug List Plans:</u></p> <p>Patient meets BOTH of the following:</p> <ol style="list-style-type: none"> 1. The patient has tried ALL of the following [documentation required]: <ul style="list-style-type: none"> a. Neulasta b. Nyvepria c. Udenyca <p>Patient cannot continue to use each of the formulary alternative(s) due to a formulation difference in the inactive ingredient(s) [e.g., differences in stabilizing agent, buffering agent, and/or surfactant] which, according to the prescriber, would result in a significant allergy or serious adverse reaction.</p> <p><u>Total Savings Drug List Plans:</u></p> <p>Patient meets BOTH of the following:</p> <ol style="list-style-type: none"> 1. The patient has tried ALL of the following [documentation required]: <ul style="list-style-type: none"> a. Fulphila b. Nyvepria c. Udenyca d. Ziextenzo

Product	Criteria
	<p>2. Patient cannot continue to use each of the formulary alternative(s) due to a formulation difference in the inactive ingredient(s) [e.g., differences in stabilizing agent, buffering agent, and/or surfactant] which, according to the prescriber, would result in a significant allergy or serious adverse reaction.</p>
<p>Neulasta (pegfilgrastim) injection, for subcutaneous use; single-dose prefilled syringe for manual use only</p> <p>Neulasta (pegfilgrastim) injection, for subcutaneous use; single-dose prefilled syringe co-packaged with the on-body injector</p>	<p><u>Total Savings Drug List Plans:</u></p> <p>Patient meets BOTH of the following:</p> <ol style="list-style-type: none"> 1. The patient has tried ALL of the following [documentation required]: <ul style="list-style-type: none"> a. Fulphila b. Nyvepria c. Udenyca d. Ziextenzo 2. Patient cannot continue to use each of the formulary alternative(s) due to a formulation difference in the inactive ingredient(s) [e.g., differences in stabilizing agent, buffering agent, and/or surfactant] which, according to the prescriber, would result in a significant allergy or serious adverse reaction.
<p>Stimufend (pegfilgrastim-fpgk subcutaneous injection)</p>	<p><u>Standard/Performance/Value/Advantage/Legacy Drug List Plans:</u></p> <p>Patient meets BOTH of the following:</p> <ol style="list-style-type: none"> 1. The patient has tried ALL of the following [documentation required]: <ul style="list-style-type: none"> a. Neulasta b. Nyvepria c. Udenyca 2. Patient cannot continue to use each of the formulary alternative(s) due to a formulation difference in the inactive ingredient(s) [e.g., differences in stabilizing agent, buffering agent, and/or surfactant] which, according to the prescriber, would result in a significant allergy or serious adverse reaction. <p><u>Total Savings Drug List Plans:</u></p> <p>Patient meets BOTH of the following:</p> <ol style="list-style-type: none"> 1. The patient has tried ALL of the following [documentation required]: <ul style="list-style-type: none"> a. Fulphila b. Nyvepria c. Udenyca d. Ziextenzo

Product	Criteria
	2. Patient cannot continue to use each of the formulary alternative(s) due to a formulation difference in the inactive ingredient(s) [e.g., differences in stabilizing agent, buffering agent, and/or surfactant] which, according to the prescriber, would result in a significant allergy or serious adverse reaction.
Ziextenzo (pegfilgrastim-bmez subcutaneous injection)	<u>Standard/Performance/Value/Advantage/Legacy Drug List Plans:</u> Patient meets BOTH of the following: 1. The patient has tried ALL of the following [documentation required] : a. Neulasta b. Nyvepria c. Udenyca 2. Patient cannot continue to use each of the formulary alternative(s) due to a formulation difference in the inactive ingredient(s) [e.g., differences in stabilizing agent, buffering agent, and/or surfactant] which, according to the prescriber, would result in a significant allergy or serious adverse reaction.

Individual and Family Plans:

Product	Criteria
Fulphila (pegfilgrastim-jmdb)	Patient meets BOTH of the following: 1. Patient has tried ALL of the following [documentation required] : a. Neulasta b. Nyvepria c. Udenyca 2. Patient cannot continue to use each of the formulary alternative(s) due to a formulation difference in the inactive ingredient(s) [e.g., differences in stabilizing agent, buffering agent, and/or surfactant] which, according to the prescriber, would result in a significant allergy or serious adverse reaction.
Fylnetra (pegfilgrastim-pbbk subcutaneous injection)	Patient meets BOTH of the following: 1. Patient has tried ALL of the following [documentation required] : a. Neulasta b. Nyvepria c. Udenyca 2. Patient cannot continue to use each of the formulary alternative(s) due to a formulation difference in the inactive ingredient(s) [e.g., differences in stabilizing agent, buffering agent, and/or surfactant] which, according to the prescriber, would result in a significant allergy or serious adverse reaction.
Stimufend (pegfilgrastim-fpgk)	Patient meets BOTH of the following: 1. Patient has tried ALL of the following [documentation required] :

Product	Criteria
subcutaneous injection)	<ul style="list-style-type: none"> a. Neulasta b. Nyvepria c. Udenyca 2. Patient cannot continue to use each of the formulary alternative(s) due to a formulation difference in the inactive ingredient(s) [e.g., differences in stabilizing agent, buffering agent, and/or surfactant] which, according to the prescriber, would result in a significant allergy or serious adverse reaction.
Ziextenzo (pegfilgrastim-bmez subcutaneous injection)	Patient meets BOTH of the following: <ul style="list-style-type: none"> 1. Patient has tried ALL of the following [documentation required]: <ul style="list-style-type: none"> a. Neulasta b. Nyvepria c. Udenyca 2. Patient cannot continue to use each of the formulary alternative(s) due to a formulation difference in the inactive ingredient(s) [e.g., differences in stabilizing agent, buffering agent, and/or surfactant] which, according to the prescriber, would result in a significant allergy or serious adverse reaction.

Conditions Not Covered

Pegfilgrastim products for any other use is considered not medically necessary, 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.¹¹ Guidelines from the NCCN for MDS (version 3.2024 – July 25, 2024) do not mention use of pegfilgrastim in this patient population.¹²

Receipt of sample product does not satisfy any criteria requirements for coverage.

Coding Information

- Note:**
- 1) This list of codes may not be all-inclusive.
 - 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

CPT®* Codes	Description
96372	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); subcutaneous or intramuscular
96377	Application of on-body injector (includes cannula insertion) for timed subcutaneous injection

HCPCS Codes	Description
J2506	Injection, pegfilgrastim, excludes biosimilar, 0.5 mg
Q5108	Injection, pegfilgrastim-jmdb (fulphila), biosimilar, 0.5 mg
Q5111	Injection, pegfilgrastim-cbqv (udenyca), biosimilar, 0.5 mg
Q5120	Injection, pegfilgrastim-bmez (ziextenzo), biosimilar, 0.5 mg
Q5122	Injection, pegfilgrastim-apgf (nyvepria), biosimilar, 0.5 mg
Q5127	Injection, pegfilgrastim-fpgk (stimufend), biosimilar, 0.5 mg
Q5130	Injection, pegfilgrastim-pbbk (fynetra), biosimilar, 0.5 mg

***Current Procedural Terminology (CPT®) ©2024 American Medical Association: Chicago, IL.**

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. Fynetra® 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.

Revision Details

Type of Revision	Summary of Changes	Date
Selected Revision	No criteria changes	12/15/2024
Selected Revision	Updated policy template.	12/1/2025
Annual Revision	Policy Title.	1/15/2026

	<p>Updated from "Pegfilgrastim" to "Colony Stimulating Factors – Pegfilgrastim Products"</p> <p>Updated policy template.</p> <p>Cancer in a Patient Receiving Myelosuppressive Chemotherapy. Removed "Has non-myeloid malignancy and is receiving myelosuppressive chemotherapy associated with an increased risk of febrile neutropenia; Non-Covered Product Criteria is met, refer to below table(s)" Added "Approve for 6 months if the patient meets ALL of the following (A, B, and C):Patient meets ONE of the following (i, ii, <u>or</u> iii): 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 Patient meets BOTH of the following (a <u>and</u> b):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 Patient has at least one risk factor for febrile neutropenia according to the prescriber; OR <u>Note</u>: 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.Patient meets BOTH of the following (a <u>and</u> b): Patient has had a neutropenic complication from a prior chemotherapy cycle and did not receive prophylaxis with a colony stimulating factor; AND <u>Note</u>: Examples of colony stimulating factors include filgrastim products, pegfilgrastim products, Ryzneuta (efbemalenograstim alfa-vuxw subcutaneous injection), Rolvedon (eflapegrastim-xnst subcutaneous injection).A reduced dose or frequency of chemotherapy may compromise treatment outcome; AND The medication is prescribed by or in consultation with an oncologist or hematologist.Preferred product criteria is met for the product(s) as listed in the below table(s)</p> <p>Radiation Syndrome (Hematopoietic Syndrome of Acute Radiation Syndrome [H-ARS]). Removed "Has had exposure to myelosuppressive doses of radiation (suspected or confirmed</p>	
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	<p>exposure to radiation levels greater than 2 gray (Gy)” Added “Medication is prescribed by or in consultation with a physician with expertise in treating acute radiation syndrome.” Updated dosing</p> <p>Peripheral Blood Progenitor Cell (PBPC) Collection and Therapy. Removed “Supportive care to reduce the duration of severe neutropenia in individuals post-autologous hematopoietic cell transplant who received high-dose chemotherapy” Added “Medication is prescribed by or in consultation with an oncologist, a hematologist, or a physician who specializes in transplantation” Updated dosing.</p> <p>Preferred Product Table. Removed “Individual requires a single dose of the requested colony stimulating factor to complete the current cycle of chemotherapy and will change to a health plan preferred pegfilgrastim product for the next cycle of chemotherapy (if needed)”</p> <p>Coding Information:</p> <ul style="list-style-type: none"> • Editorial changes made to the HCPCS coding description for Q5108, Q5111, Q5120, Q5122 	
Selected Revision	Updated from “Peripheral Blood Progenitor Cell Transplantation in an individual with Cancer” to “Peripheral Blood Progenitor Cell (PBPC) Collection and Therapy”	3/1/2026

The policy effective date is in force until updated or retired.

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