Effective Date **12/15/2024**
Coverage Policy Number **IP0070**

Pegfilgrastim

Table of Contents

Related Coverage Resources

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. 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

This policy supports medical necessity review for the following pegfilgrastim products:

- **Fulphila**™ (pegfilgrastim-jmdb subcutaneous injection)
- **Fylnetra**® (pegfilgrastim-pbbk subcutaneous injection)
- **Neulasta**® (pegfilgrastim subcutaneous injection)
- **Nyvepria**™ (pegfilgrastim-apgf subcutaneous injection)
- **Stimufend**® (pegfilgrastim-fpgk subcutaneous injection)
- **Udenyca**™ (pegfilgrastim-cbqv subcutaneous injection)
- **Ziextenzo**™ (pegfilgrastim-bmez subcutaneous injection)

Additional criteria that support the review for medical necessity exceptions of non-covered products are located in the Non-Covered Product Table by the respective plan type and drug list where applicable.

Medical Necessity Criteria

Pegfilgrastim products (Fulphila, Fylnetra, Neulasta, Nyvepria, Stimufend, Udenyca, and Ziextenzo) are considered medically necessary when ONE of the following is met:

1. **Treatment of an individual receiving myelosuppressive chemotherapy.** Individual meets **BOTH** of the following criteria:
   A. Has non-myeloid malignancy and is receiving myelosuppressive chemotherapy associated with an increased risk of febrile neutropenia
   B. Non-Covered Product Criteria is met, refer to below table(s)

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

2. **Treatment of Radiation Syndrome (Hematopoietic Syndrome of Acute Radiation Syndrome [ARS]).** Individual meets **BOTH** of the following criteria:
   A. Has had exposure to myelosuppressive doses of radiation (suspected or confirmed exposure to radiation levels greater than 2 gray (Gy)
   B. Non-Covered Product Criteria is met, refer to below table(s)

      Dosing. Up to 6 mg given by subcutaneous injection given no more frequently than 1 week apart.

3. **Peripheral Blood Progenitor Cell Transplantation in an individual with Cancer.** Individual meets **BOTH** of the following criteria:
   A. Supportive care to reduce the duration of severe neutropenia in individuals post-autologous hematopoietic cell transplant who received high-dose chemotherapy
   B. Non-Covered Product Criteria is met, refer to below table(s)

      Dosing. ONE of the following dosing regimens:[1]
      1. In adults, 6 mg by subcutaneous injection one time
      2. In children, up to 200 mcg/kg by subcutaneous injection

Employer Group Non-Covered Products and Criteria:

Non-Covered Product	Criteria
Fulphila (pegfilgrastim-jmdb subcutaneous injection)	**Standard/Performance/Value/Advantage/Legacy Drug List Plans:** Documentation of **ONE** of the following: 1. Trial of AND cannot continue to use the alternative(s) due to a formulation difference in the inactive ingredient(s) which, according to the prescriber, would result in a significant allergy or serious adverse reaction to **ALL** of the following: a. Neulasta b. Nyvepria c. Udenyca 2. 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)
Fylnetra (pegfilgrastim-pbbk subcutaneous injection)	**Standard/Performance/Value/Advantage/Legacy Drug List Plans:** Documentation of **ONE** of the following: 1. Trial of AND cannot continue to use the alternative(s) due to a formulation difference in the inactive ingredient(s) which, according to the prescriber, would result in a significant allergy or serious adverse reaction to **ALL** of the following:

Non-Covered Product	Criteria
	a. Neulasta b. Nyvepria c. Udenyca 2. 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) **<u>Cigna Total Savings Drug List Plans:</u>** Documentation of **ONE** of the following criteria: 1. Trial of AND cannot continue to use the alternative(s) due to a formulation difference in the inactive ingredient(s) which, according to the prescriber, would result in a significant allergy or serious adverse reaction to **ALL** of the following: a. Fulphila b. Nyvepria c. Udenyca d. Ziextenzo 2. 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)
Neulasta (pegfilgrastim) injection, for subcutaneous use; single-dose prefilled syringe for manual use only **Neulasta** (pegfilgrastim) injection, for subcutaneous use; single-dose prefilled syringe co-packaged with the on-body injector	**<u>Cigna Total Savings Drug List Plans:</u>** Documentation of **ONE** of the following: 1. Trial of AND cannot continue to use the alternative(s) due to a formulation difference in the inactive ingredient(s) which, according to the prescriber, would result in a significant allergy or serious adverse reaction to **ALL** of the following: a. Fulphila b. Nyvepria c. Udenyca d. Ziextenzo 2. 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)
Stimufend (pegfilgrastim-fpgk subcutaneous injection)	**<u>Standard/Performance/Value/Advantage/Legacy Drug List Plans:</u>** Documentation of **ONE** of the following: 1. Trial of AND cannot continue to use the alternative(s) due to a formulation difference in the inactive ingredient(s) which, according to the prescriber, would result in a significant allergy or serious adverse reaction to **ALL** of the following: a. Neulasta b. Nyvepria c. Udenyca 2. Individual requires a single dose of the requested colony stimulating factor to complete the current cycle of chemotherapy and will

Non-Covered Product	Criteria
	change to a health plan preferred pegfilgrastim product for the next cycle of chemotherapy (if needed) **<u>Cigna Total Savings Drug List Plans:</u>** Documentation of **ONE** of the following criteria: 1. Trial of AND cannot continue to use the alternative(s) due to a formulation difference in the inactive ingredient(s) which, according to the prescriber, would result in a significant allergy or serious adverse reaction to **ALL** of the following: a. Fulphila b. Nyvepria c. Udenyca d. Ziextenzo 2. 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)
Ziextenzo (pegfilgrastim-bmez subcutaneous injection)	**<u>Standard/Performance/Value/Advantage/Legacy Drug List Plans:</u>** Documentation of **ONE** of the following: 1. Trial of AND cannot continue to use the alternative(s) due to a formulation difference in the inactive ingredient(s) which, according to the prescriber, would result in a significant allergy or serious adverse reaction to **ALL** of the following: a. Neulasta b. Nyvepria c. Udenyca 2. 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)

Individual and Family Plan Non-Covered Products and Criteria:

Non-Covered Product	Criteria
Fulphila (pegfilgrastim-jmdb)	Documentation of **ONE** of the following: 1. Trial of AND cannot continue to use the alternative(s) due to a formulation difference in the inactive ingredient(s) which, according to the prescriber, would result in a significant allergy or serious adverse reaction to **ALL** of the following: a. Neulasta b. Nyvepria c. Udenyca 2. 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)
Fylnetra (pegfilgrastim-pbbk subcutaneous injection)	Documentation of **ONE** of the following: 1. Trial of AND cannot continue to use the alternative(s) due to a formulation difference in the inactive ingredient(s) which, according to the prescriber, would result in a significant allergy or serious adverse reaction to **ALL** of the following: a. Neulasta

Non-Covered Product	Criteria
	b. Nyvepria c. Udenyca 2. 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)
Stimufend (pegfilgrastim-fpgk subcutaneous injection)	Documentation of **ONE** of the following: 1. Trial of AND cannot continue to use the alternative(s) due to a formulation difference in the inactive ingredient(s) which, according to the prescriber, would result in a significant allergy or serious adverse reaction to **ALL** of the following: a. Neulasta b. Nyvepria c. Udenyca 2. 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)
Ziextenzo (pegfilgrastim-bmez subcutaneous injection)	Documentation of **ONE** of the following: 1. Trial of AND cannot continue to use the alternative(s) due to a formulation difference in the inactive ingredient(s) which, according to the prescriber, would result in a significant allergy or serious adverse reaction to **ALL** of the following: a. Neulasta b. Nyvepria c. Udenyca 2. 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)

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

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

Reauthorization Criteria

Continuation of pegfilgrastim products (Fulphila, Fylnetra, Neulasta, Nyvepria, Stimufend, Udenyca, and Ziextenzo) is considered medically necessary for **ALL** covered diagnoses when the above medical necessity criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration: up to 12 months
Reauthorization approval duration: up to 12 months

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

Myelodysplastic Syndrome (MDS). Only limited data report use of pegfilgrastim for patients with MDS.[9] Guidelines from the NCCN for MDS (version 3.2022 – January 13, 2022) do not mention use of pegfilgrastim in this patient population.[10]

Coding Information

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, biosimilar, (Fulphila), 0.5 mg
Q5111	Injection, pegfilgrastim-cbqv, biosimilar, (Udenyca), 0.5 mg
Q5120	Injection, pegfilgrastim-bmez, biosimilar, (Ziextenzo), 0.5 mg
Q5122	Injection, pegfilgrastim-apgf, biosimilar, (Nyvepria), 0.5 mg
Q5127	Injection, pegfilgrastim-fpgk (Stimufend), biosimilar, 0.5 mg (Code effective 04/01/2023)
Q5130	Injection, pegfilgrastim-pbbk (Fylnetra), biosimilar, 0.5 mg (Code effective 04/01/2023)

Background

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, 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.

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]. Piscataway, NJ: Kashiv; May 2022.
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

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