POLICY: Biosimilars – Fulphila, Fylnetra, Stimufend and Ziextenzo

- Fulphila™ (pegfilgrastim-jmdb injection for subcutaneous use – Mylan)
- Fylnetra™ (pegfilgrastim-pbbk injection for subcutaneous use – Amneal)
- Stimufend® (pegfilgrastim-fpgk subcutaneous injection – Fresenius Kabi)
- Ziextenzo™ (pegfilgrastim-bmez injection for subcutaneous use – Sandoz)

EFFECTIVE DATE: 1/1/2021
LAST REVISION DATE: 09/16/2024

COVERAGE CRITERIA FOR: All UCare Plans

OVERVIEW

Pegfilgrastim, a leukocyte growth factor, is indicated to **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.[1-5,11,12] Fulphila, Fylnetra, Nyvepria, Stimufend, Udenyca, and Ziextenzo are biosimilars to Neulasta. Neulasta is additionally indicated to increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Subsyndrome of Acute Radiation Syndrome).[1]

Guidelines

The National Comprehensive Cancer Network (NCCN) addresses the use of pegfilgrastim products in several guidelines.

- **Hematopoietic Cell Transplantation:** Guidelines (version 1.2022 – April 1, 2022) recommend pegfilgrastim for hematopoietic cell mobilization for allogeneic or autologous donors as a single agent or in combination with other treatments.[6]
- **Hematopoietic Growth Factors:** Guidelines (version 1.2022 – December 22, 2021) 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.[7] 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.

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 medical benefit coverage of Fulphila, Fylnetra, Stimufend, and Ziextenzo. 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.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Fulphila, Stimufend, Fylnetra and Ziextenzo is recommended for requests meeting both the preferred product step therapy requirements and indication requirements.

Preferred Product Step Therapy Requirements (New Starts Only)

Criteria. *The patient must meet the following criteria (A or B):*

A) For patients new to Fulphila, Ziextenzo, Fylnetra, and Stimufend therapy only, must have a trial of Udenyca, Nyvepria, or Neulasta (prefilled syringe or Onpro formulation) prior to approval of Fulphila, Ziextenzo, Fylnetra, and Stimufend. New starts to therapy defined as no use of Fulphila, Ziextenzo, Fylnetra, and Stimufend within the past 180 days for Medicaid and Commercial patients. New starts to therapy defined as no use of Fulphila, Ziextenzo, Fylnetra, and Stimufend within the past 365 days for Medicare patients.

B) Patient has a contraindication or other clinical reason why Udenyca, Nyvepria, or Neulasta cannot be tried before Fulphila, Ziextenzo, Fylnetra, and Stimufend.

Note: Preferred biosimilar step only required for indications FDA-Approved for both Fulphila, Ziextenzo, Fylnetra, and Stimufend and the preferred biosimilar(s).

FDA-APPROVED INDICATIONS

1. **Cancer in a Patient Receiving Myelosuppressive Chemotherapy**. Approve for 6 months if the patient meets the following criteria (A and B):
   - **A)** Patient meets ONE of the following conditions (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 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 the patient has at least one risk factor for febrile neutropenia according to the prescriber; OR

       Note: Examples of risk factors include age ≥ 65 years; prior chemotherapy or radiation therapy; persistent neutropenia; bone marrow involvement by tumor; recent surgery and/or open wounds; liver and/or renal dysfunction; poor performance status; or human immunodeficiency virus (HIV) infection.

iii. The patient has had a neutropenic complication from prior chemotherapy and did not receive prophylaxis with a colony stimulating factor and a reduced dose or frequency of chemotherapy may compromise treatment outcome; AND
Note: Examples of colony-stimulating factors include filgrastim products, pegfilgrastim products, and sargramostim products (e.g., Leukine).

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). Approve for 1 month if the agent is prescribed by or in consultation with a physician with 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 Transplantation in Patients with Cancer. Approve one dose if prescribed by or in consultation with an oncologist, a hematologist, or a physician who specializes in transplantation.

Dosing. Approve one dose as follows (A or B):
A) In adults 6 mg by subcutaneous injection one time; OR
B) In children up to 200 mcg/kg by subcutaneous injection.

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.[8] Guidelines from the NCCN for MDS (version 2.2020 – February 28, 2020) do not mention use of pegfilgrastim in this patient population.[9]

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; June 2021.

4. Ziextenzo™ subcutaneous injection [prescribing information]. Princeton, NJ: Sandoz; March 2021.
5. Nyvepria™ subcutaneous injection [prescribing information]. New York, NY: Pfizer; June 2022.
6. The NCCN Hematopoietic Cell Transplantation Clinical Practice Guidelines in Oncology (version 1.2022 – April 1, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 16, 2022.
7. The NCCN Hematopoietic Growth Factors Clinical Practice Guidelines in Oncology (version 1.2022 – December 22, 2021). © 2021 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 16, 2022.
8. 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.
9. 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.
10. The NCCN Myelodysplastic Syndromes Clinical Practice Guidelines in Oncology (version 3.2022 – January 13, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed: August 16, 2022.
11. Fylnetra® subcutaneous injection [prescribing information]. Piscataway, NJ: Kashiv; May 2022.
12. Stimufend® subcutaneous injection [prescribing information]. Lake Zurich, IL: Fresenius Kabi; May 2022.

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
UCare 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
UCare Revision	Ziextenzo move from a preferred product to a non-preferred product and will not require review prior to approval and	9/8/2023

	Nyvepria moved from a non-preferred product to a preferred product and with no longer require review prior to use.	
Annual Revision	No criteria changes.	09/20/2023
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	09/16/2024