

**Clinical Policy: Pegfilgrastim (Neulasta), Pegfilgrastim-jmdb (Fulphila), Pegfilgrastim-cbqv (Udenyca), Pegfilgrastim-bmez (Ziextenzo), Pegfilgrastim-apgf (Nyvepria)**

**Reference Number: LA.PHAR.296**

**Effective Date:**

**Last Review Date: 01.21**

**Line of Business: Medicaid**

**[Coding Implications](#)**

**[Revision Log](#)**

**See [Important Reminder](#) at the end of this policy for important regulatory and legal information.**

**Description**

**Pegfilgrastim (Neulasta®) and its biosimilars, pegfilgrastim-jmdb (Fulphila™), pegfilgrastim-cbqv (Udenyca™), pegfilgrastim-bmez (Ziextenzo™), and Pegfilgrastim-apgf (Nyvepria™) are leukocyte growth factors.**

**FDA Approved Indication(s)**

**Neulasta, Nyvepria, Fulphila, Udenyca, and Ziextenzo are 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 (FN).**

**Neulasta is also indicated to increase survival in patients acutely exposed to myelosuppressive doses of radiation (hematopoietic subsyndrome of acute radiation syndrome).**

**Limitation(s) of use: Neulasta, Nyvepria, Fulphila, Udenyca, and Ziextenzo are not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation.**

**Policy/Criteria**

***Prior authorization is required. Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.***

**It is the policy of Louisiana Healthcare Connections that Neulasta, Nyvepria, Fulphila, Udenyca, and Ziextenzo are medically necessary when the following criteria are met:**

**I. Initial Approval Criteria**

**A. Chemotherapy-Induced Neutropenia (must meet all):**

- 1. Diagnosis of non-myeloid malignancy;**
- 2. Prescribed for use following myelosuppressive chemotherapy;**
- 3. One of the following (a or b)**
  - a. Request is for treatment associated with Stage IV or metastatic cancer or associated conditions. Exception if “clinically equivalent therapy, contains identical active ingredient(s), and proven to have same efficacy;**

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- b. All of the following (i, ii and iii)
    - i. For members age  $\geq$  18 years, failure of Zarxio, unless one of the following (1, 2, or 3):
      - 1. Member has intolerance or contraindication to Zarxio;
      - 2. Documentation of member's inability to self-administer Zarxio due to both of the following (a and b):
        - a) Lack of caregiver or support system for assistance with administration;
        - b) Inadequate access to healthcare facility or home care interventions;
      - 3. Member requires  $\geq$  10 doses of Zarxio;  
*\*Prior authorization may be required for Zarxio*
    - ii. Request is for a biosimilar pegfilgrastim product (i.e., Fulphila, Udenyca, Ziextenzo, Nyvepria);
    - iii. For requests other than Ziextenzo: Medical justification supports inability to use Ziextenzo\* (e.g., contraindications to excipients);  
*\*Prior authorization may be required for Ziextenzo*
  - 4. Confirmation that there is at least 12 days between pegfilgrastim dose and the next cycle of chemotherapy;
  - 5. For members receiving palliative chemotherapy, provider attestation that chemotherapy dose reduction has been considered;
  - 6. Dose does not exceed 6 mg (1 syringe) per chemotherapy cycle.
- Approval duration:  
Medicaid – 6 months

### B. Acute Radiation Syndrome (must meet all):

- 1. Prescribed for use following suspected or confirmed acute exposure to myelosuppressive doses of radiation;
- 2. One of the following (a or b)
  - a. Request is for treatment associated with Stage IV or metastatic cancer or associated conditions. Exception if “clinically equivalent therapy, contains identical active ingredient(s), and proven to have same efficacy;
- b. All of the following (i, ii and iii)
  - i. For members age  $\geq$  18 years, failure of Zarxio, unless one of the following (1, 2, or 3):
    - 1. Member has intolerance or contraindication to Zarxio;
    - 2. Documentation of member's inability to self-administer Zarxio due to both of the following (a and b):
      - a) Lack of caregiver or support system for assistance with administration;
      - b) Inadequate access to healthcare facility or home care interventions;
    - 3. Member requires  $\geq$  10 doses of Zarxio;  
*\*Prior authorization may be required for Zarxio*

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- ii. Request is for a biosimilar pegfilgrastim product (i.e., Fulphila, Udenyca, Ziextenzo, Nyvepria);
  - iii. For requests other than Ziextenzo: Medical justification supports inability to use Ziextenzo\* (e.g., contraindications to excipients);  
*\*Prior authorization may be required for Ziextenzo*
3. Dose does not exceed two 6 mg doses administered one week apart.  
Approval duration:  
Medicaid – 6 months

### C. Bone Marrow Transplantation (off-label) (must meet all):

1. Prescribed for one of the following (a or b):
  - a. Supportive care post autologous hematopoietic cell transplantation;
  - b. Mobilization of peripheral-blood progenitor cells prior to autologous transplantation;
2. Failure of Leukine<sup>®</sup>, unless contraindicated or clinically significant adverse effects are experienced;  
*\*Prior authorization may be required for Leukine*
3. One of the following (a or b)
  - a. Request is for treatment associated with Stage IV or metastatic cancer or associated conditions. Exception if “clinically equivalent therapy, contains identical active ingredient(s), and proven to have same efficacy;
  - b. All of the following (i, ii and iii)
    - i. For members age ≥ 18 years, failure of Zarxio, unless one of the following (1, 2, or 3):
      1. Member has intolerance or contraindication to Zarxio;
      2. Documentation of member’s inability to self-administer Zarxio due to both of the following (a and b):
        - a) Lack of caregiver or support system for assistance with administration;
        - b) Inadequate access to healthcare facility or home care interventions;
      3. Member requires ≥ 10 doses of Zarxio;  
*\*Prior authorization may be required for Zarxio*
    - ii. Request is for a biosimilar pegfilgrastim product (i.e., Fulphila, Udenyca, Ziextenzo, Nyvepria);
    - iii. For requests other than Ziextenzo: Medical justification supports inability to use Ziextenzo\* (e.g., contraindications to excipients);  
*\*Prior authorization may be required for Ziextenzo*
4. Request meets one of the following (a or b):
  - a. Dose does not exceed 6 mg (1 syringe) per dose;
  - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval duration:  
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### D. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): LA.PMN.53 for Medicaid.

## II. Continued Therapy

### A. All Indications in Section I (must meet all):

1. Currently receiving medication via Louisiana Healthcare Connections benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. One of the following (a or b)
  - a. Request is for treatment associated with Stage IV or metastatic cancer or associated conditions. Exception if “clinically equivalent therapy, contains identical active ingredient(s), and proven to have same efficacy;
  - b. All of the following (i, ii and iii)
    - i. For members age  $\geq$  18 years, failure of Zarxio, unless one of the following (1, 2, or 3):
      1. Member has intolerance or contraindication to Zarxio;
      2. Documentation of member’s inability to self-administer Zarxio due to both of the following (a and b):
        - a) Lack of caregiver or support system for assistance with administration;
        - b) Inadequate access to healthcare facility or home care interventions;
      3. Member requires  $\geq$  10 doses of Zarxio;  
*\*Prior authorization may be required for Zarxio*
    - ii. Request is for a biosimilar pegfilgrastim product (i.e., Fulphila, Udenyca, Ziextenzo, Nyvepria);
    - iii. For requests other than Ziextenzo: Medical justification supports inability to use Ziextenzo\* (e.g., contraindications to excipients);  
*\*Prior authorization may be required for Ziextenzo*
4. If request is for a dose increase, new dose does not exceed one of the following (a, b, or c):
  - a. Chemotherapy-induced neutropenia: 6 mg (1 syringe) administered once per chemotherapy cycle;
  - b. Acute radiation syndrome: two 6 mg doses administered one week apart;
  - c. Bone marrow transplantation: 6 mg (1 syringe) per dose, or dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval duration:

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### B. Other diagnoses/indications (must meet 1 or 2):

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1. **Currently receiving medication via Louisiana Healthcare Connections benefit and documentation supports positive response to therapy.**  
**Approval duration: Duration of request or 6 months (whichever is less); or**
2. **Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): LA.PMN.53 for Medicaid.**

### III. **Diagnoses/Indications for which coverage is NOT authorized:**

- A. **Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy –LA.PMN.53 for Medicaid, or evidence of coverage documents.**

### IV. **Appendices/General Information**

#### **Appendix A: Abbreviation/Acronym Key**

**ANC: absolute neutrophil count**

**ASCO: American Society of Clinical  
Oncology**

**CSFs: colony-stimulating factors**

**FDA: Food and Drug Administration**

**FN: febrile neutropenia**

**NCCN: National Comprehensive  
Cancer Network**

#### **Appendix B: Therapeutic Alternatives**

**This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may require prior authorization.**

<b><u>Drug Name</u></b>	<b><u>Dosing Regimen</u></b>	<b><u>Dose Limit/ Maximum Dose</u></b>
<b><u>Neupogen® (filgrastim), Zarxio® (filgrastim- sndz), Granix® (tbo-filgrastim), Nivestym® (filgrastim-aafi)</u></b>	<b><u>Supportive care post autologous hematopoietic cell transplantation 10 mcg/kg IV or SC infusion QD</u></b>	<b><u>10 mcg/kg/day</u></b>
	<b><u>Mobilization of peripheral-blood progenitor cells prior to autologous transplantation 10 mcg/kg SC bolus or continuous infusion QD</u></b>	<b><u>10 mcg/kg/day</u></b>
<b><u>Leukine® (sargramostim)</u></b>	<b><u>Supportive care post autologous hematopoietic cell transplantation 250 mcg/m<sup>2</sup>/day IV</u></b>	<b><u>500 mcg/m<sup>2</sup>/day</u></b>
	<b><u>Mobilization of peripheral-blood progenitor cells prior to autologous transplantation 250 mcg/m<sup>2</sup>/day IV or SC QD</u></b>	<b><u>250 mcg/m<sup>2</sup>/day</u></b>

**Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.**

#### **Appendix C: Contraindications/Boxed Warnings**

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- **Contraindication(s): history of serious allergic reactions to human granulocyte colony-stimulating factors such as pegfilgrastim or filgrastim products**
- **Boxed warning(s): none reported**

### *Appendix D: General Information*

- **Neutropenia is defined as an absolute neutrophil count (ANC) of < 500 neutrophils/mcL or an ANC of < 1,000 neutrophils/mcL and a predicted decline to ≤ 500 neutrophils/mcL over the next 48 hours. Neutropenia can progress to FN, defined as a single temperature of ≥ 38.8 C orally or ≥ 38.0 C over 1 hour.**
- **The development of FN is a common dose-limiting toxicity of many chemotherapy regimens. This risk is directly related to the intensity of the chemotherapy regimen. Chemotherapy regimens that have an incidence of FN greater than 20% in clinical trials in chemotherapy naïve patients are considered by the National Comprehensive Cancer Network (NCCN) panel at high risk. Prophylaxis with myeloid growth factors is recommended at this level of risk (category 1 recommendation). NCCN Compendium recommend prophylaxis be considered in intermediate-risk (10-20% overall risk of FN) patients (category 2A recommendation). In addition to chemotherapy regimens, other risk factors such as: treatment-related, patient related, cancer-related, and co-morbidities have also been associated with an increased risk of FN. Therefore, the type of chemotherapy regimen is only one component of the risk assessment.**
- **Harvesting of peripheral blood stem cells prior to autologous stem-cell transplantation has a recommendation of Class IIa in DRUGDEX.**
- **The NCCN Compendium recommends Neulasta for supportive care post autologous hematopoietic cell transplant (category 2A).**
- **According to the ASCO, 2006 Clinical Practice Guideline for the Use of White Blood Cell Growth Factors, dose reduction or delay remains an appropriate strategy for the palliative treatment of cancer, as there is no evidence that dose maintenance or escalation improves clinically important outcomes in this setting. The 2015 updates to this guideline found no new data supporting the use of colony-stimulating factors (CSFs) to maintain dose-intensity in the treatment of metastatic disease, and the review found no demonstrable benefit in the use of myeloid growth factors to in patients with metastatic lung, small-cell lung, colorectal, hormone-refractory prostate, or breast cancer. To date, there have been no improvements in disease-free or OS reported for any common cancer with the use of CSFs to maintain dose-intensity, instead of dose reduction. The ASCO Panel recognizes that there may be individual patients who will not tolerate effective doses of chemotherapy without CSFs. Medical Oncologists making the decision to use prophylactic MGFs, or not, may need to consider not only the optimal chemotherapy regimen, but also the individual member risk factors and the intention of treatment; that is, curative, prolongation of life, or symptom control and palliation.**

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### V. Dosage and Administration

<u>Drug Name</u>	<u>Indication</u>	<u>Dosing Regimen</u>	<u>Maximum Dose</u>
<u>Pegfilgrastim (Neulasta), pegfilgrastim-jmdb (Fulphila), pegfilgrastim-cbqv (Udenyca), pegfilgrastim-bmez (Ziextenzo), pegfilgrastin-apgf (Nyvepria)</u>	<u>Myelosuppressive chemotherapy</u>	<u>6 mg administered SC once per chemotherapy cycle. Do not administer between 14 days before and 24 hours after administration of cytotoxic chemotherapy.</u>  <u>Weight based dosing for pediatric patients &lt; 45 kg</u>	<u>6 mg/dose</u>
<u>Pegfilgrastim (Neulasta)</u>	<u>Members acutely exposed to myelosuppressive doses of radiation</u>	<u>Two doses, 6 mg each, administered SC one week apart. Administer the first dose as soon as possible after suspected or confirmed exposure to myelosuppressive doses of radiation, and a second dose one week after</u>  <u>Weight based dosing for pediatric patients &lt; 45 kg</u>	<u>6 mg/dose</u>

### VI. Product Availability

<u>Drug Name</u>	<u>Availability</u>
<u>Pegfilgrastim (Neulasta)</u>	<ul style="list-style-type: none"> <li><u>Injection: 6 mg/0.6 mL solution in a single-dose prefilled syringe for manual use only</u></li> <li><u>Injection: 6 mg/0.6 mL solution in a single-dose prefilled syringe co-packaged with the on-body injector</u></li> </ul>
<u>Pegfilgrastin-apgf (Nyvepria)</u>	<ul style="list-style-type: none"> <li><u>Injection: 6 mg/0.6 mL solution in a single-dose prefilled syringe for manual use only</u></li> </ul>
<u>Pegfilgrastim-jmdb (Fulphila)</u>	<ul style="list-style-type: none"> <li><u>Injection: 6 mg/0.6 mL solution in a single-dose prefilled syringe for manual use only</u></li> </ul>
<u>Pegfilgrastim-cbqv (Udenyca)</u>	<ul style="list-style-type: none"> <li><u>Injection: 6 mg/0.6 mL solution in a single-dose prefilled syringe for manual use only</u></li> </ul>

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<u>Pegfilgrastim-bmez</u> (Ziextenzo)	<ul style="list-style-type: none"> <li>• <u>Injection: 6 mg/0.6 mL solution in a single-dose prefilled syringe for manual use only</u></li> </ul>
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### VII. References

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### Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

<u>HCPCS Codes</u>	<u>Description</u>
J2505	<u>Injection, pegfilgrastim, 6 mg</u>
Q5111	<u>Injection, pegfilgrastim-cbqv, biosimilar, (Udenyca), 0.5 mg</u>
Q5108	<u>Injection, pegfilgrastim-jmdb, biosimilar, (Fulphila), 0.5 mg</u>



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**discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. LHCC retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.**

**This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.**

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