

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

Reference Number: CA.CP.PHAR.296

Effective Date: 12.01.16

Last Review Date: 11.19

Line of Business: Commercial, HIM 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[™]), and Pegfilgrastim-bmez (Ziextenzo[™]) are leukocyte growth factors.

FDA Approved Indication(s)

Neulasta, 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, Fulphila, Udenyca, and Ziextenzo are not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation.

Policy/Criteria

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 California Health & Wellness[®] and Health Net[®] that Neulasta, 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. For members age \geq 18 years old, failure of Zarxio, unless one of the following (a, b, or c):
 - a. Member has intolerance or contraindication to Zarxio;
 - b. Documentation of member's inability to self-administer Zarxio due to both of the following (i and ii):
 - i. Lack of caregiver or support system for assistance with administration;
 - ii. Inadequate access to healthcare facility or home care interventions;

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- c. Member requires ≥ 10 doses of Zarxio;
4. If request is for Neulasta, failure of a biosimilar product (i.e. Fulphila, Udenyca, or Ziextenzo);
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/HIM – 6 months

Commercial – 6 months or to the member’s renewal date, whichever is longer

B. Acute Radiation Syndrome (must meet all):

1. Prescribed for use following suspected or confirmed acute exposure to myelosuppressive doses of radiation;
2. For members age ≥ 18 years old, failure of Zarxio, unless one of the following (a, b, or c):
 - a. Member has intolerance or contraindication to Zarxio;
 - b. Documentation of member’s inability to self-administer Zarxio due to both of the following (i and ii):
 - i. Lack of caregiver or support system for assistance with administration;
 - ii. Inadequate access to healthcare facility or home care interventions;
 - c. Member requires ≥ 10 doses of Zarxio;
3. If request is for Neulasta, failure of a biosimilar product (i.e. Fulphila, Udenyca, or Ziextenzo);
4. Dose does not exceed two 6 mg doses administered one week apart.

Approval duration:

Medicaid/HIM – 6 months

Commercial – 6 months or to the member’s renewal date, whichever is longer

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[®], unless contraindicated or clinically significant adverse effects are experienced;*
3. For members age ≥ 18 years old, failure of Zarxio, unless one of the following (a, b, or c):
 - a. Member has intolerance or contraindication to Zarxio;
 - b. Documentation of member’s inability to self-administer Zarxio due to both of the following (i and ii):

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- i. Lack of caregiver or support system for assistance with administration;
- ii. Inadequate access to healthcare facility or home care interventions;
- c. Member requires ≥ 10 doses of Zarxio;*
**Prior authorization may be required for Zarxio, and Leukine*
- 4. If request is for Neulasta, failure of a biosimilar product (i.e. Fulphila, Udenyca, or Ziextenzo);
- 5. Request meets one of the following (a or b):
 - a. Dose does not exceed 6 mg/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:

Medicaid/HIM – 6 months

Commercial – 6 months or to the member’s renewal date, whichever is longer

D. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. 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 administered once per chemotherapy cycle;
 - b. Acute radiation syndrome: two 6 mg doses administered one week apart;
 - c. Bone marrow transplantation: 6 mg/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:

Medicaid – 6 months

Commercial – 6 months or to the member’s renewal date, whichever is longer

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

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- Approval duration: Duration of request or 6 months (whichever is less);** or
- Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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

- 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 policies – CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.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 not be a formulary agent for all relevant lines of business and may require prior authorization.

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

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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

- 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

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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.

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Pegfilgrastim (Neulasta), pegfilgrastim-jmdb (Fulphila), pegfilgrastim-cbqv (Udenyca), pegfilgrastim-bmez (Ziextenzo)	Myelosuppressive chemotherapy	6 mg administered SC once per chemotherapy cycle. Do not administer between 14 days before and 24 hours after administration of cytotoxic chemotherapy. Weight based dosing for pediatric patients < 45 kg	6 mg/dose
Pegfilgrastim (Neulasta)	Members acutely exposed to myelosuppressive doses of radiation	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 Weight based dosing for pediatric patients < 45 kg	6 mg/dose

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VI. Product Availability

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

VII. References

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4. DRUGDEX[®] System [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed May 15, 2019.
5. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: <http://www.clinicalpharmacology-ip.com/>. Accessed November 21, 2019.
6. Fulphila Prescribing Information. Zurich, Switzerland: Mylan GmbH; March 2019. Available at: www.fulphila.com. Accessed November 21, 2019.
7. Udenyca Prescribing Information. Redwood City, CA: Coherus BioSciences, Inc.; April 2019. Available at: www.udenyca.com. Accessed November 21, 2019.
8. Zarxio Prescribing Information. Princeton, NJ: Sandoz, Inc. Available at: www.zarxio.com. Accessed November 21, 2019.
9. Ziextenzo Prescribing Information. Princeton, NJ: Sandoz, Inc. Available at www.ziextenzo.com. Accessed November 21, 2019.
10. Smith TJ, Khatcheressian J, Lyman GH, et al. 2006 Update of Recommendations for the Use of White Blood Cell Growth Factors: An Evidence-Based Clinical Practice Guideline. JCO 2006 July. 24(19): 3187-3205.

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11. Smith TJ, Bohlke K, Lyman GH, et al. Recommendations for the Use of WBC Growth Factors: American Society of Clinical Oncology Clinical Practice Guideline Update. 2015 October. JCO 33(28): 3199-3212.

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.

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

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Neulasta is split from CP.PHAR.26.Colony Stimulating Factors 2015, and converted to a new template. Max dose and contraindications added per PI. Labeled use: Acute radiation syndrome added per PI. Removed “Neulasta will not be given from 14 days before to 24 hours after chemotherapy.” Off-label use: Posttransplant support added per NCCN.	11.16	12.16
Updated template and references. Removed off-label use.	08.16.17	11.17
3Q 2018 annual review: policies combined for Medicaid and Commercial lines of business; added HIM line of business; added off-label indications for mobilization of peripheral-blood progenitor cells and supportive care post autologous hematopoietic cell transplantation with redirection to FDA approved treatments Leukine and Neupogen, Granix, or Zarxio; references reviewed and updated.	05.08.18	08.18
Newly FDA-approved biosimilar added: Fulphila; references reviewed and updated.	07.31.18	02.19
Newly FDA-approved biosimilar added: Udenyca.	03.21.19	
3Q 2019 annual review: added Nivestym to list of filgrastim products required for bone marrow transplant indication, updated HCPCS coding table to include biosimilar products; references reviewed and updated.	05.15.19	08.19

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
For chemotherapy-induced neutropenia and acute radiation syndrome, added redirection to Zarxio per SDC; For bone marrow transplant narrowed previous redirection to Neupogen, Zarxio, Granix, or Nivestym to Zarxio only. For Zarxio redirection added the following scenarios where redirection is not required: a. Member has intolerance or contraindication to Zarxio; b. Documentation of member's inability to self-administer Zarxio due to both of the following (i and ii): i. Lack of caregiver or support system for assistance with administration; ii. Inadequate access to healthcare facility or home care interventions; c. Member requires ≥ 10 doses of Zarxio. For chemotherapy-induced neutropenia added requirement for members receiving palliative chemotherapy, provider's attestation that chemotherapy dose reduction has been considered. Appendix D updated to include ASCO recommendations related to consideration of chemotherapy dose reduction.	09.03.19	11.19
Policy renamed as CA.CP.PHAR.296 with direction to biosimilars (Fulphila, Udenyca, or Ziextenzo). Added pegfilgrastim-bmez (Ziextenzo) to policy. References reviewed and updated.	11.21.19	1.20

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy,

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contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan 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.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy.

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