

Clinical Policy: Pegfilgrastim (Neulasta), Pegfilgrastim-jmdb (Fulphila)

Reference Number: CP.PHAR.296

Effective Date: 12.01.16

Last Review Date: 02.19

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 biosimilar, pegfilgrastim-jmdb (Fulphila™), are leukocyte growth factors.

**For Health Insurance Marketplace (HIM), Fulphila is non-formulary and cannot be approved using these criteria; refer to the formulary exception policy, HIM.PA.103.*

FDA Approved Indication(s)

Neulasta and Fulphila 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 and Fulphila 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 health plans affiliated with Centene Corporation® that Neulasta and Fulphila 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. Dose does not exceed 6 mg (1 syringe) per chemotherapy cycle.

Approval duration:

Medicaid – 6 months

HIM – 6 months for Neulasta (*refer to HIM.PA.103 for Fulphila*)

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. Dose does not exceed two 6 mg doses administered one week apart.

Approval duration:

Medicaid – 6 months

HIM – 6 months for Neulasta (*refer to HIM.PA.103 for Fulphila*)

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 both of the following (a and b), unless contraindicated or clinically significant adverse effects are experienced:
 - a. Neupogen[®], Granix[®], or Zarxio[®];
 - b. Leukine[®];

**Prior authorization is (or may be) required for Neupogen, Granix, Zarxio, and Leukine*
3. 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 – 6 months

HIM – 6 months for Neulasta (*refer to HIM.PA.103 for Fulphila*)

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

HIM – 6 months for Neulasta (*refer to HIM.PA.103 for Fulphila*)

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.

Approval duration: Duration of request or 6 months (whichever is less); or

2. 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:

- 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 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

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® (pegfilgrastim) , Zarxio® (pegfilgrastim- sndz), Granix® (tbo- pegfilgrastim)	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

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).

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Pegfilgrastim (Neulasta), pegfilgrastim-jmdb (Fulphila)	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	6 mg/dose

Drug Name	Indication	Dosing Regimen	Maximum Dose
		Weight based dosing for pediatric patients < 45 kg	

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

VII. References

1. Neulasta Prescribing Information. Thousand Oaks, CA: Amgen, Inc.; December 2017. Available at www.neulasta.com. Accessed May 8, 2018.
2. National Comprehensive Cancer Network. Myeloid Growth Factors Version 1.2018. Available at: http://www.nccn.org/professionals/physician_gls/pdf/myeloid_growth.pdf. Accessed June 13, 2018.
3. Pegfilgrastim. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at NCCN.org. Accessed June 25, 2018.
4. DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed May 2, 2018.
5. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: <http://www.clinicalpharmacology-ip.com/>. Accessed May 2, 2018.
6. Fulphila Prescribing Information. Zurich, Switzerland: Mylan GmbH; June 2018. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/761075s0001bl.pdf. Accessed June 13, 2018.

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

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.	11.16	12.16

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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.		
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

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, 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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.

©2016 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene® and Centene Corporation® are registered trademarks exclusively owned by Centene Corporation.