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

Reference Number: ERX.SPA.59
Effective Date: 09.01.17
Last Review Date: 11.18

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.

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 significant incidence of febrile neutropenia (FN).

Neulasta is also indicated to increase survival in patients acutely exposed to myelosuppressive doses of radiation (hematopoietic syndrome 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 Envolve Pharmacy Solutions™ 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: 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. Dose does not exceed two 6 mg doses administered one week apart.

Approval duration: 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 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: 6 months

D. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions 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: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 – ERX.PA.01 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 ≥ 38.8ºC orally or ≥ 38.0ºC 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 febrile neutropenia 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). The NCCN Compendiums 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 Weight based dosing for pediatric patients < 45 kg	6 mg/dose

VI. Product Availability

Drug Name	Availability
Pegfilgrastim (Neulasta)	• 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)	• 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/2018/761075s000lbl.pdf. Accessed June 13, 2018.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy split from ERX.SPMN.07 Colony Stimulating Factors and converted to new template. Added Hematopoietic Syndrome of Acute Radiation Syndrome as a labeled indication. Renewal criteria added. Removed "Neulasta will not be given from 14 days before to 24 hours after chemotherapy."	07.17	08.17
3Q 2018 annual review: 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	11.18

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.