CLINICAL GUIDELINES FOR MEDICAL NECESSITY

MEDICAL POLICY

Pegfilgrastim and Biosimilars (Fulphila®, Fylnetra®, Neulasta®, Neulasta-OnPro®, Nyvepria®, Stimufend®, Udenyca®, Ziextenzo®)

EFFECTIVE DATE: 8/28/2025

Version: 2.0

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For Medicare members/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Please refer to the CMS website at http://www.cms.gov for additional information.

For Medicaid members/enrollees, circumstances when state Medicaid coverage provisions conflict with the coverage provisions within 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.

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Pegfilgrastim (Neulasta®, Neulasta-OnPro®); Pegfilgrastim-apgf (Nyvepria®); Pegfilgrastim-bmez (Ziextenzo®); Pegfilgrastim-cbqv (Udenyca®); Pegfilgrastim-fpgk (Stimufend®); Pegfilgrastim-jmdb (Fulphila®); Pegfilgrastim-pbbk (Fylnetra®)

Discussion

Pegfilgrastim is a colony-stimulating factor that acts on hematopoietic cells by binding to specific cell surface receptors, thereby stimulating proliferation, differentiation, commitment, and the activation of end cells.

Common adverse reactions include bone pain and pain in extremities. Clinically significant adverse reactions include splenic rupture and splenomegaly, acute respiratory distress syndrome, allergic reactions/hypersensitivity (including anaphylaxis), allergies to acrylics, sickle cell crisis, glomerulonephritis, leukocytosis, thrombocytopenia, capillary leak syndrome, potential for tumor growth stimulatory effects on malignant cells, myelodysplastic syndrome, acute myeloid leukemia, and aortitis.

Pegfilgrastim, pegfilgrastim-apgf, pegfilgrastim-bmez, pegfilgrastim-cbqv, pegfilgrastim-fpgk, pegfilgrastim-jmdb, and pegfilgrastim-pbbk are approved by the Food and Drug Administration (FDA) for patients with cancer receiving myelosuppressive chemotherapy.[1,2,3,4,5,6,7]

Pegfilgrastim and biosimilars are endorsed by the National Comprehensive Cancer Network's (NCCN) for following cancers: Hodgkin lymphoma, pediatric aggressive mature b-cell lymphomas, hematopoietic cell transplantation, pediatric Hodgkin lymphoma, and Wilms tumor and the management of neutropenia.[8,9,10,11,12]

Definitions

- **Biosimilar Drug** - An FDA-approved biological drug that is like another biological drug (called the reference drug), which is made from living organisms, but may be made in a different way from the reference drug and of slightly different substances. A biosimilar drug must be shown to be as safe, same dose, work as well, works in the same way, and for the same condition as the reference drug.[13]
- **Food And Drug Administration (FDA)** - The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.[14]
- **National Comprehensive Cancer Network (NCCN)** - An alliance of more than 30 leading cancer centers devoted to patient care, research, and education. The NCCN guidelines are utilized for Radiation Therapy and Medical Oncology standards. NCCN consensus clinical standards are periodically updated and NantHealth, Inc. reviews these and updates its policies within a timely manner.[15]

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Policy

Coverage will be considered for FDA approved indications and for NCCN category 1, 2A, or 2B recommendations when all criteria are met:

Hematopoietic Growth Factors - Management of Neutropenia

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **FDA** required criteria coverage:

3. Decrease the incidence of febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.[1,2,3,4,5,6,7]

For **NCCN** required criteria coverage:

4. Prophylaxis of chemotherapy-induced febrile neutropenia or other dose-limiting neutropenic events for one of the following:
   a) High-risk (>20% overall risk of febrile neutropenia) patients with solid tumors and non-myeloid malignancies receiving treatment in the curative/adjuvant or palliative settings
   b) Intermediate-risk (10% to 20% overall risk of febrile neutropenia) patients with solid tumors and non-myeloid malignancies receiving treatment in the curative/adjuvant or palliative settings who have one or more patient risk factors
   c) Low-risk (<10% overall risk of febrile neutropenia) patients with solid tumors and non-myeloid malignancies receiving treatment in the curative/adjuvant or palliative settings who have 2 or more patient-related risk factors. Use of granulocyte colony-stimulating factors in this setting is based on clinical judgment.[8]

Hematopoietic Cell Transplantation

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For NCCN required criteria coverage:

3. Hematopoietic cell mobilization for autologous donors in combination with plerixafor.8

Hodgkin Lymphoma - Classic Hodgkin Lymphoma

1. 18 to 60 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. In combination with one of the following regimens:
   a) Brentuximab vedotin in combination with AVD (doxorubicin, vinblastine, dacarbazine)
   b) BrECADD (brentuximab vedotin, etoposide, cyclophosphamide, doxorubicin, dacarbazine, dexamethasone).[9]

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Pediatric Aggressive Mature B-Cell Lymphomas

1. Less than 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

Primary Mediastinal Large B-Cell Lymphoma

For **NCCN** required criteria coverage:

3. Administered with DA-EPOCH-R (dose adjusted-etoposide, prednisolone, vincristine, cyclophosphamide, and doxorubicin) with rituximab regimen; OR

Post-Transplant Lymphoproliferative Disorders

For **NCCN** required criteria coverage:

4. Administered with CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) regimen.[10]

Pediatric Hodgkin Lymphoma - Classic Hodgkin Lymphoma

1. Less than 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Administered with one of the following:
   a) Bv-AVD (brentuximab vedotin, doxorubicin, vinblastine, dacarbazine) regimen
   b) Nivolumab-AVD (doxorubicin, vinblastine, dacarbazine) regimen.[11]

Wilms Tumor (Nephroblastoma)

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Administered with Regimen M and Regimen I for courses of one of the following:
   a) Cyclophosphamide and etoposide
   b) Cyclophosphamide, doxorubicin, and vincristine.[12]

Authorization Period and Renewal Criteria

1. Initial Authorization Period: 12 months
2. Renewal Criteria: No evidence of disease progression or unacceptable toxicity
3. Renewal Authorization Period: 12 months

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Coding (CPT®, ICD 10 and HCPCS)

Procedure codes appearing in medical policy documents are only included as a general reference. This list may not be all-inclusive and is subject to updates. In addition, the codes listed are not a guarantee of payment. CPT codes are available through the AMA.

Code	Description
C81	Hodgkin lymphoma
C85.2	Mediastinal (thymic) large B-cell lymphoma
D47.Z1	Post-transplant lymphoproliferative disorder (PTLD)
D70.1	Agranulocytosis secondary to cancer chemotherapy
J2506	Injection, pegfilgrastim, excludes biosimilar
Q5108	Injection, pegfilgrastim-jmdb (fulphila), biosimilar
Q5111	Injection, pegfilgrastim-cbqv (udenyca), biosimilar
Q5120	Injection, pegfilgrastim-bmez (ziextenzo), biosimilar
Q5122	Injection, pegfilgrastim-apgf (nyvepria), biosimilar
Q5127	Injection, pegfilgrastim-fpgk (stimufend), biosimilar
Q5130	Injection, pegfilgrastim-pbbk (fylnetra), biosimilar

Revision and Review History

No.	Description	Date(s)
1	Original Effective Date:	1/1/2024
2	Policy Annual Review Dates:	7/7/2023, 8/15/2024, 8/21/2025
3	Department Owner:	Medical Affairs
4	NH Advisory Committee Approval Dates:	8/7/2023, 8/15/2024, 8/28/2025

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5	Revision Changes:	8/21/2025 Updated discussion section, added adverse reactions, and added 1 NCCN indication each for hematopoietic cell transplantation, classic Hodgkin lymphoma, Wilms tumor, and 3 for pediatric aggressive mature B-cell lymphomas; added 1 NCCN and 1 FDA for the management of neutropenia; v.2.0

Reference

[1] Neulasta, Neulasta-OnPro (Pegfilgrastim) [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/125031s203lbl.pdf. Accessed August 21, 2025.

[2] Nyvepria (Pegfilgrastim-apgf) [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761111s004lbl.pdf. Accessed August 21, 2025.

[3] Ziextenzo (Pegfilgrastim-bmez) [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761045Orig1s014lbl.pdf. Accessed August 21, 2025.

[4] Udenyca (Pegfilgrastim-cbqv) [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761039Orig1s015lbl.pdf. Accessed August 21, 2025.

[5] Stimufend (Pegfilgrastim-fpgk) [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/761173Orig1s000correctedlbl.pdf. Accessed August 21, 2025.

[6] Fulphila (Pegfilgrastim-jmdb) [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761075s012lbl.pdf. Accessed August 21, 2025.

[7] Fylnetra (Pegfilgrastim-pbbk) [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761084s007lbl.pdf. Accessed August 21, 2025.

[8] National Comprehensive Cancer Network. NCCN Guidelines: Hematopoietic Growth Factors. https://www.nccn.org/professionals/physician_gls/pdf/growthfactors.pdf. Accessed August 21, 2025.

[9] National Comprehensive Cancer Network. NCCN Guidelines: Hodgkin Lymphoma (Age ≥18 years). https://www.nccn.org/professionals/physician_gls/pdf/hodgkins.pdf. Accessed August 21, 2025.

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[10] National Comprehensive Cancer Network. NCCN Guidelines: Pediatric Aggressive Mature B-Cell Lymphomas. https://www.nccn.org/professionals/physician_gls/pdf/ped_b-cell.pdf. Accessed August 21, 2025.

[11] National Comprehensive Cancer Network. NCCN Guidelines: Pediatric Hodgkin Lymphoma. https://www.nccn.org/professionals/physician_gls/pdf/ped_hodgkin.pdf. Accessed August 21, 2025.

[12] National Comprehensive Cancer Network. NCCN Guidelines: Wilms Tumor (Nephroblastoma). https://www.nccn.org/professionals/physician_gls/pdf/wilms_tumor.pdf. Accessed August 21, 2025.

[13] National Cancer Institute. Biosimilar Drug. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/biosimilar-drug. Accessed August 21, 2025.

[14] U.S. Food & Drug Administration. https://www.fda.gov/about-fda/what-we-do. Accessed August 21, 2025.

[15] National Comprehensive Cancer Network. https://www.nccn.org/home. Accessed August 21, 2025.

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