

Coverage of any drug intervention discussed in the plans prior authorization guideline is subject to the limitations and exclusions outlined in the member's benefit certificate or policy and to applicable state and/or federal laws.

Colony Stimulating Factors – Pegfilgrastim: Neulasta[®]; Fulphila[®]; Udenyca[®]; Ziextenzo[™]; Nyvepria[™] (Subcutaneous)

Document Number: MH-0234

Last Review Date: 07/20/2022

Date of Origin: 10/17/2008

Dates Reviewed: 06/2009, 12/2009, 06/2010, 07/2010, 09/2010, 12/2010, 03/2011, 06/2011, 09/2011, 12/2011, 03/2012, 06/2012, 09/2012, 12/2012, 03/2013, 06/2013, 09/2013, 12/2013, 03/2014, 06/2014, 09/2014, 12/2014, 03/2015, 05/2015, 08/2015, 11/2015, 02/2016, 05/2016, 08/2016, 11/2016, 02/2017, 05/2017, 08/2017, 11/2017, 02/2018, 06/2018, 09/2018, 12/2018, 03/2019, 06/2019, 09/2019, 12/2019, 02/2020, 06/2020, 07/2020, 09/2020, 01/2021, 04/2021, 10/2021, 04/2022, 07/2022

Customization Date: 07/20/2022

Effective Date: 01/01/2023

I. Length of Authorization^{1-5,10-14}

- Bone marrow transplantation (BMT) failure or engraftment delay: Coverage will be provided for 1 dose only and may not be renewed.
- Peripheral blood progenitor cell (PBPC) mobilization and transplant: Coverage will be provided for 1 dose only and may not be renewed.
- All other indications: Coverage will be provided for four months and may be renewed unless otherwise specified.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Neulasta 6 mg prefilled syringe: 1 syringe per 14 days
- Neulasta Onpro kit: 1 kit per 14 days
- Fulphila 6 mg prefilled syringe: 1 syringe per 14 days
- Udenyca 6 mg prefilled syringe: 1 syringe per 14 days
- Ziextenzo 6 mg prefilled syringe: 1 syringe per 14 days
- Nyvepria 6 mg prefilled syringe: 1 syringe per 14 days

B. Max Units (per dose and over time) [HCPCS Unit]:

Acute Radiation Exposure

- 12 billable units weekly x 2 doses

BMT failure or engraftment delay/ PBPC mobilization and transplant

- 12 billable units x 1 dose

All other indications:

- 12 billable units per 14 days

III. Initial Approval Criteria ^{1-10,18,19}

Coverage is provided in the following conditions:

Applicable to Commercial and IFB members

- **New Starts Only:** Patient must have tried and failed treatment with one of the preferred products (Fulphila or Ziextenzo), a contraindication exists, or the patient would have a life threatening situation if required to meet step therapy requirements. This requirement does not apply to patients using another pegfilgrastim product for an indication not shared by the preferred product; **AND**

Prophylactic use in patients with solid tumors or non-myeloid malignancy †

- Patient is undergoing myelosuppressive chemotherapy with an expected incidence of febrile neutropenia* of greater than 20% §; **OR**
- Patient is undergoing myelosuppressive chemotherapy with an expected incidence of febrile neutropenia* of 10% to 20% § **AND** one or more of the following co-morbidities:
 - Age >65 years receiving full dose intensity chemotherapy
 - Extensive prior exposure to chemotherapy
 - Previous exposure of pelvis, or other areas of large amounts of bone marrow, to radiation
 - Persistent neutropenia (ANC ≤ 1000/mm³)
 - Bone marrow involvement by tumor
 - Patient has a condition that can potentially increase the risk of serious infection (i.e., HIV/AIDS with low CD4 counts)
 - Recent surgery and/or open wounds
 - Poor performance status
 - Renal dysfunction (creatinine clearance <50 mL/min)
 - Liver dysfunction (elevated bilirubin >2.0 mg/dL)
 - Chronic immunosuppression in the post-transplant setting, including organ transplant

Note: Dose-dense therapy, in general, requires growth factor support to maintain dose intensity and schedule. In the palliative setting, consideration should be given to dose reduction or change in regimen.

Patient who experience a neutropenic complication from a prior cycle of the same chemotherapy † ‡

Note: Dose-dense therapy, in general, requires growth factor support to maintain dose intensity and schedule. In the palliative setting, consideration should be given to dose reduction or change in regimen.

Patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Acute Radiation Syndrome [H-ARS]) † Φ

Bone marrow transplantation (BMT) failure or engraftment delay ‡

Peripheral blood progenitor cell (PBPC) mobilization and transplant ‡

Wilms Tumor (Nephroblastoma) ⁷ ‡

- Patient has favorable histology disease; **AND**
- Used in combination with a cyclophosphamide-based chemotherapy regimen (i.e., Regimen M or I only)

† FDA-labeled indication(s); ‡ Compendia recommended indication(s); Φ Orphan Drug

***Febrile neutropenia is defined as:**

- Temperature: a single temperature ≥ 38.3 °C orally or ≥ 38.0 °C over 1 hour; **AND**
- Neutropenia: < 500 neutrophils/mcL or $< 1,000$ neutrophils/mcL and a predicted decline to ≤ 500 neutrophils/mcL over the next 48 hours

§ Expected incidence of febrile neutropenia percentages for myelosuppressive chemotherapy regimens can be found in the NCCN Hematopoietic Growth Factors Clinical Practice Guideline at NCCN.org⁸

IV. Renewal Criteria ^{1-10,18,19}

Note: Coverage for use in BMT failure or engraftment delay and PBPC mobilization and transplant may NOT be renewed.

Coverage for all other indications can be renewed based upon the following criteria:

- Patient continues to meet indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: splenic rupture, acute respiratory distress syndrome (ARDS), serious allergic reactions/anaphylaxis, sickle cell crisis, glomerulonephritis, leukocytosis, thrombocytopenia, capillary leak syndrome, potential for tumor growth stimulation of malignant cells, aortitis, myelodysplastic syndrome and acute myeloid leukemia, etc.

V. Dosage/Administration ^{1-10,13-19}

Indication	Dose
Prophylactic use in patients with non-myeloid malignancy Patient who experienced a neutropenic complication from a prior cycle of the same chemotherapy	<ul style="list-style-type: none"> 6 mg subcutaneously once per chemotherapy cycle and dosed no more frequently than every 14 days For pediatric patients weighing <45 kg: <ul style="list-style-type: none"> <10 kg = 0.1 mg/kg 10-20 kg = 1.5 mg 21-30 kg = 2.5 mg 31-44 kg = 4 mg
Acute Radiation Exposure (Hematopoietic Acute Radiation Syndrome)	<ul style="list-style-type: none"> 6 mg subcutaneously weekly x 2 doses For pediatric patients weighing <45 kg: <ul style="list-style-type: none"> <10 kg = 0.1 mg/kg 10-20 kg = 1.5 mg 21-30 kg = 2.5 mg 31-44 kg = 4 mg
BMT failure or engraftment delay PBPC mobilization and transplant	6 mg subcutaneously for 1 dose only

*Do not administer within 14 days before and 24 hours after administration of cytotoxic chemotherapy.

*Onpro On-body Injector may be applied on the same day as chemotherapy as long as the Neulasta is administered no less than 24 hours after administration of chemotherapy. Not recommended for use in patients with acute radiation exposure or in pediatric patients.

VI. Billing Code/Availability Information

HCPCS Code:

- J2506 – Injection, pegfilgrastim, 0.5 mg; 1 billable unit = 0.5 mg (*Neulasta only*)
- Q5108 – Injection, pegfilgrastim-jmdb, biosimilar, (Fulphila), 0.5 mg; 1 billable unit = 0.5 mg
- Q5111 – Injection, pegfilgrastim-cbqv, biosimilar, (Udenyca), 0.5 mg; 1 billable unit = 0.5 mg
- Q5120 – Injection, pegfilgrastim-bmez, biosimilar, (Ziextenzo), 0.5 mg; 1 billable unit = 0.5 mg
- Q5122 – Injection, pegfilgrastim-apgf, biosimilar, (Nyvepria), 0.5 mg; 1 billable unit = 0.5 mg

NDC:

- Neulasta 6 mg prefilled syringe: 55513-0190-xx
- Neulasta 6 mg prefilled syringe Onpro Kit: 55513-0192-xx
- Fulphila 6 mg prefilled single-dose syringe: 67457-0833-xx
- Udenyca 6 mg prefilled single-dose syringe: 70114-0101-xx
- Ziextenzo 6 mg single-dose prefilled syringe: 61314-0866-xx
- Nyvepria 6 mg single-dose prefilled syringe: 00069-0324-xx

PEGFILGRASTIM
(NEULASTA®; FULPHILA™; UDENYCA®; ZIEXTENZO™; NYVEPRIA™)
Prior Auth Criteria

Proprietary Information. Restricted Access – Do not disseminate or copy without approval.
 ©2022, Magellan Rx Management

VII. References

1. Neulasta [package insert]. Thousand Oaks, CA; Amgen Inc; February 2021. Accessed March 2022.
2. Fulphila [package insert]. Morgantown, WV; Mylan Pharmaceuticals; October 2021. Accessed March 2022.
3. Udenyca [package insert]. Redwood City, California; Coherus Biosciences; June 2021. Accessed March 2022.
4. Ziextenzo [package insert]. Princeton, NJ; Sandoz, Inc; March 2021. Accessed March 2022.
5. Nyvepria [package insert]. Lake Forest, IL; Pfizer Oncology; October 2021. Accessed March 2022.
6. Vogel CL, Wojtukiewicz MZ, Carroll RR, et al. First and subsequent cycle use of pegfilgrastim prevents febrile neutropenia in patients with breast cancer: a multicenter, double-blind, placebo-controlled phase III study. *J Clin Oncol.* 2005 Feb 20;23(6):1178-84.
7. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) pegfilgrastim. National Comprehensive Cancer Network, 2022. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed March 2022.
8. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Hematopoietic Growth Factors. Version 1.2022. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed March 2022.
9. Holmes FA, O'Shaughnessy JA, Vukelja S, et al. Blinded, randomized, multicenter study to evaluate single administration pegfilgrastim once per cycle versus daily filgrastim as an adjunct to chemotherapy in patients with high-risk stage II or stage III/IV breast cancer. *J Clin Oncol.* 2002;20:727–31.
10. Green MD, Koelbl H, Baselga J, et al.; International Pegfilgrastim 749 Study Group. A randomized double-blind multicenter phase III study of fixed-dose single-administration pegfilgrastim versus daily filgrastim in patients receiving myelosuppressive chemotherapy. *Ann Oncol.* 2003;14(1):29-35.
11. Burris HA, Belani CP, Kaufman PA, et al. Pegfilgrastim on the same day versus next day of chemotherapy in patients with breast cancer, non-small-cell lung cancer, ovarian cancer, and non-Hodgkin's lymphoma: Results of four multicenter, double-blind, randomized phase II studies. *J Oncol Pract.* 2010;6(3):133-140.

12. Russel N, Mesters R, Schubert J, et al. A phase 2 pilot study of pegfilgrastim and filgrastim for mobilizing peripheral blood progenitor cells in patients with non-Hodgkin's lymphoma receiving chemotherapy. *Haematologica* March 2008;93:405-412;doi:10.3324/haematol.11287
13. Isidori A, Tani M, Bonifazi F, et al. Phase II study of a single pegfilgrastim injection as an adjunct to chemotherapy to mobilize stem cells into the peripheral blood of pretreated lymphoma patients. *Haematologica* January 2005;90:225-231
14. Jagasia MH, Greer JP, Morgan DS, et al. Pegfilgrastim after high-dose chemotherapy and autologous peripheral blood stem cell transplant: phase II study. *Bone Marrow Transplant.* 2005 Jun;35(12):1165-9.
15. Bruns I, Steidl U, Kronenwett R, et al. A single dose of 6 or 12 mg of pegfilgrastim for peripheral blood progenitor cell mobilization results in similar yields of CD34+ progenitors in patients with multiple myeloma. *Transfusion.* 2006 Feb;46(2):180-5.
16. Staber PB, Holub R, Linkesch W, et al. Fixed-dose single administration of Pegfilgrastim vs daily Filgrastim in patients with haematological malignancies undergoing autologous peripheral blood stem cell transplantation. *Bone Marrow Transplant.* 2005 May;35(9):889-93.
17. Vanstraelen G, Frere P, Ngirabacu MC, et al. Pegfilgrastim compared with Filgrastim after autologous hematopoietic peripheral blood stem cell transplantation. *Exp Hematol.* 2006 Mar;34(3):382-8.
18. Spunt S, Irving H, Frost J, et al. Phase II, Randomized, Open-Label Study of Pegfilgrastim-Supported VDC/IE Chemotherapy in Pediatric Sarcoma Patients. *J Clin Oncol.* 2010 Mar 10; 28(8): 1329–1336.
19. Hankey KG, Farese AM, Blaauw EC, et al. Pegfilgrastim Improves Survival of Lethally Irradiated Nonhuman Primates. *Radiat Res.* 2015 Jun;183(6):643-55. Epub 2015 Jun 2.
20. Waller CF, Ranganna GM, Pennella EJ, et al. Randomized phase 3 efficacy and safety trial of proposed pegfilgrastim biosimilar MYL-1401H in the prophylactic treatment of chemotherapy-induced neutropenia. *Ann Hematol.* 2019 May;98(5):1217-1224. doi: 10.1007/s00277-019-03639-5. Epub 2019 Mar 1.
21. Hoy SM. Pegfilgrastim-jmdb/MYL-1401H: A Pegfilgrastim Biosimilar. *BioDrugs.* 2019 Feb;33(1):117-120. doi: 10.1007/s40259-019-00334-9.
22. Blackwell K, Donskih R, Jones CM, et al. A Comparison of Proposed Biosimilar LA-EP2006 and Reference Pegfilgrastim for the Prevention of Neutropenia in Patients With Early-Stage Breast Cancer Receiving Myelosuppressive Adjuvant or Neoadjuvant Chemotherapy: Pegfilgrastim Randomized Oncology (Supportive Care) Trial to Evaluate Comparative Treatment (PROTECT-2), a Phase III, Randomized, Double-Blind Trial. *Oncologist.* 2016 Jul; 21(7): 789–794. Published online 2016 Apr 18. doi: 10.1634/theoncologist.2016-0011
23. Nakov R, Gattu S, Wang J, et al. Abstract P3-14-10: Proposed biosimilar pegfilgrastim LA-EP2006 shows similarity in pharmacokinetics and pharmacodynamics to reference pegfilgrastim in healthy subjects. *Abstracts: 2017 San Antonio Breast Cancer Symposium;*

December 5-9, 2017; San Antonio, Texas. DOI: 10.1158/1538-7445.SABCS17-P3-14-10
Published February 2018

24. Glaspy JA, O'Connor PG, Tang H, et al. Randomized, single-blind, crossover study to assess the pharmacokinetic and pharmacodynamic bioequivalence of CHS-1701 to pegfilgrastim in healthy subjects *Journal of Clinical Oncology* 35, no. 15_suppl. DOI: 10.1200/JCO.2017.35.15_suppl.e21693. Published online May 30, 2017.
25. National Government Services, Inc. Local Coverage Article: Billing and Coding: Filgrastim, Pegfilgrastim, Tbo-filgrastim and biosimilars (A52408). Centers for Medicare & Medicaid Services, Inc. Updated on 12/22/2021 with effective date 01/01/2022. Accessed March 2022.
26. Palmetto GBA. Local Coverage Article: Billing and Coding: Neulasta® (pegfilgrastim) Onpro® Kit (On-body Injector) (A54682). Centers for Medicare & Medicaid Services, Inc. Updated on 01/03/2022 with effective date 01/01/2022. Accessed March 2022.
27. First Coast Service Options, Inc. Local Coverage Article: Billing and Coding: Pegfilgrastim (A57725). Centers for Medicare & Medicaid Services, Inc. Updated on 01/14/2022 with effective date 01/01/2022. Accessed March 2022.
28. Palmetto GBA. Local Coverage Article: Billing and Coding: White Cell Colony Stimulating Factors (A56748). Centers for Medicare & Medicaid Services, Inc. Updated on 01/03/2022 with effective date 01/01/2022. Accessed March 2022.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
D61.81	Pancytopenia
C64.1	Malignant neoplasm of right kidney, except renal pelvis
C64.2	Malignant neoplasm of left kidney, except renal pelvis
C64.9	Malignant neoplasm of unspecified kidney, except renal pelvis
D70.1	Agranulocytosis secondary to cancer chemotherapy
D70.9	Neutropenia, unspecified
T45.1X5A	Adverse effect of antineoplastic and immunosuppressive drugs initial encounter
T45.1X5D	Adverse effect of antineoplastic and immunosuppressive drugs subsequent encounter
T45.1X5S	Adverse effect of antineoplastic and immunosuppressive drugs sequela
T66.XXXA	Radiation sickness, unspecified, initial encounter
T66.XXXD	Radiation sickness, unspecified, subsequent encounter
T66.XXXS	Radiation sickness, unspecified, sequela
W88.1	Exposure to radioactive isotopes
W88.8	Exposure to other ionizing radiation
Z41.8	Encounter for other procedures for purposes other than remedying health state
Z48.290	Encounter for aftercare following bone marrow transplant
Z51.11	Encounter for antineoplastic chemotherapy
Z51.12	Encounter for antineoplastic immunotherapy

PEGFILGRASTIM
(NEULASTA®; FULPHILA™; UDENYCA®; ZIEXTENZO™; NYVEPRIA™)
Prior Auth Criteria

Proprietary Information. Restricted Access – Do not disseminate or copy without approval.
©2022, Magellan Rx Management

ICD-10	ICD-10 Description
Z51.89	Encounter for other specified aftercare
Z52.011	Autologous donor, stem cells
Z76.89	Persons encountering health services in other specified circumstances
Z94.81	Bone marrow transplant status
Z94.84	Stem cells transplant status

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: <http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA):

Jurisdiction(s): 6, K	NCD/LCD/LCA Document (s): A52408 https://www.cms.gov/medicare-coverage-database/search/document-id-search-results.aspx?DocID=A52408&bc=gAAAAAAAAAAAA&
Jurisdiction(s): N	NCD/LCD/LCA Document (s): A57725 https://www.cms.gov/medicare-coverage-database/search/article-date-search.aspx?DocID=A57725&bc=gAAAAAAAAAAAA
Jurisdiction(s): J, M	NCD/LCD/LCA Document (s): A56748 https://www.cms.gov/medicare-coverage-database/search/article-date-search.aspx?DocID=A56748&bc=gAAAAAAAAAAAA
Jurisdiction(s): J, M	NCD/LCD/LCA Document (s): A54682 https://www.cms.gov/medicare-coverage-database/search/article-date-search.aspx?DocID=A54682&bc=gAAAAAAAAAAAA

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.

PEGFILGRASTIM
(NEULASTA®; FULPHILA™; UDENYCA®; ZIEXTENZO™; NYVEPRIA™)
Prior Auth Criteria

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

