

Drug Policy

Policy:	201827-MRX (04-24)	Initial Effective Date: 10/30/2014
Code(s):	HCPCS J2506, Q5108, Q5111, Q5120, Q5122, Q5127, Q5130, J1449, J3590	Annual Review Date: 04/18/2024
SUBJECT:	Long-Acting Granulocyte Colony Stimulating Factors – Pegfilgrastim, Eflapegrastim, Efbemalenograstim alfa <ul style="list-style-type: none"> - Neulasta® (Pegfilgrastim) - Fulphila™ (pegfilgrastim-jmdb) - Nyvepria™ (pegfilgrastim-apgf) - Udenyca™ (pegfilgrastim-cbqv) - Ziextenzo (pegfilgrastim-bmez) - Fylnetra (pegfilgrastim-pbbk) - Stimufend (pegfilgrastim-fpgk) - Rolvedon (eflapegrastim-xnst) - Ryzneuta (efbemalenograstim alfa) 	Last Revised Date: 04/18/2024

Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.

POLICY STATEMENT

This policy involves the use of pegfilgrastim products. Prior authorization is recommended for medical benefit coverage of pegfilgrastim products. Approval is recommended for those who meet the conditions of coverage in the **Initial Approval and Renewal Criteria, Preferred Drug (when applicable), Dosing/Administration, Length of Authorization, and Site of Care (when applicable)** for the diagnosis provided. The requirement that the patient meet the Criteria and Preferred Drug for coverage of the requested medication applies to the initial authorization only. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy.

I. Length of Authorization ^{1-9,16-21}

- 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.
- Acute exposure to myelosuppressive doses of radiation (Hematopoietic Acute Radiation Syndrome [H-ARS]): Coverage will be provided for 2 doses and may not be renewed.
- All other indications: Coverage will be provided for four months and may be renewed unless otherwise specified.

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II. Dosing Limits

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

- Neulasta 6 mg single-dose prefilled syringe: 1 syringe per 14 days
- Neulasta 6 mg single-dose prefilled syringe Onpro kit: 1 kit per 14 days
- Fulphila 6 mg single-dose prefilled syringe: 1 syringe per 14 days
- Udenyca 6 mg single-dose prefilled syringe: 1 syringe per 14 days
- Udenyca 6 mg single-dose prefilled autoinjector: 1 autoinjector per 14 days
- Udenyca 6 mg single-dose prefilled syringe ONBODY kit: 1 kit per 14 days
- Ziextenzo 6 mg single-dose prefilled syringe: 1 syringe per 14 days
- Nyvepria 6 mg single-dose prefilled syringe: 1 syringe per 14 days
- Fylnetra 6 mg single-dose prefilled syringe: 1 syringe per 14 days
- Stimufend 6 mg single-dose prefilled syringe: 1 syringe per 14 days
- Rolvedon 13.2 mg single-dose prefilled syringe: 1 syringe per 14 days
- Ryzneuta 20 mg single-dose prefilled syringe: 1 syringe per 14 days

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

Drug Name	Indication	Billable Units
Neulasta, Fulphila, Udenyca, Ziextenzo, Nyvepria, Fylnetra, and Stimufend	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
Rolvedon	Acute Radiation Exposure	132 billable units weekly x 2 doses
	All other indications	132 billable units per 14 days
Ryzneuta	Acute Radiation Exposure	20 mg weekly x 2 doses
	All other indications	20 mg per 14 days

III. Initial Approval Criteria ¹⁻⁹

Coverage is provided in the following conditions:

- **If the request is for Nyvepria, Udenyca, Ziextenzo, Fylnetra, Stimufend, Rolvedon, or Ryzneuta, the patient had an inadequate response, or has a contraindication or intolerance to Neulasta or Fulphila; AND**
- Patient is at least 18 years of age (*Rolvedon and Ryzneuta ONLY*); **AND**

Prophylactic use in patients with solid tumors or non-myeloid malignancy † ‡ ^{1-12,22,24-30}

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- Patient is undergoing myelosuppressive chemotherapy with an expected incidence of febrile neutropenia❖ of > 20% §; **OR**
- Patient is undergoing myelosuppressive chemotherapy with an expected incidence of febrile neutropenia❖ of 10% to 20% § **AND** one or more patient-related risk factors ¥; **OR**
- Patient is undergoing myelosuppressive chemotherapy with an expected incidence of febrile neutropenia❖ of <10% § **AND** two or more patient-related risk factors ¥**

**Use in this setting is based on clinical judgment.

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 ‡^{11,12}

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]) † ‡ Ⓢ^{1,3,4,7,11,12,31,32}

Bone marrow transplantation (BMT) failure or engraftment delay ‡¹⁶⁻²⁰ (Neulasta, Fulphila, Udenyca, Ziextenzo, Nyvepria, Fylnetra, and Stimufend ONLY)

Peripheral blood progenitor cell (PBPC) mobilization and transplant ‡¹¹ (Neulasta, Fulphila, Udenyca, Ziextenzo, Nyvepria, Fylnetra, and Stimufend ONLY)

Wilms Tumor (Nephroblastoma) ‡¹¹ (Neulasta, Fulphila, Udenyca, Ziextenzo, Nyvepria, Fylnetra, and Stimufend ONLY)

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

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Ⓢ Orphan Drug

¥ Patient risk factors for febrile neutropenia¹²

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- Age >65 years receiving full dose intensity chemotherapy
- Prior exposure to chemotherapy or radiation therapy
- Persistent neutropenia (ANC \leq 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

❖ **Febrile neutropenia is defined as:** ¹²

- **Temperature:** a single temperature \geq 38.3 °C orally or \geq 38.0 °C over 1 hour; **AND**
- **Neutropenia:** <500 neutrophils/mcL or <1,000 neutrophils/mcL and a predicted decline to \leq 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.org ¹²

IV. **Renewal Criteria** ^{1-9,16-21}

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

- **If the request is for Nyvepria, Udenyca, Ziextenzo, Fynetra, Stimufend, Rolvedon, or Ryzneuta, the patient had an inadequate response, or has a contraindication or intolerance to Neulasta or Fulphila; AND**
- 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 in patients with breast and lung cancer, etc.; **AND**

Bone marrow transplantation (BMT) failure or engraftment delay (*Neulasta, Fulphila, Udenyca, Ziextenzo, Nyvepria, Fynetra, and Stimufend ONLY*)

- Coverage may not be renewed

Peripheral blood progenitor cell (PBPC) mobilization and transplant (*Neulasta, Fulphila, Udenyca, Ziextenzo, Nyvepria, Fynetra, and Stimufend ONLY*)

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- Coverage may not be renewed

Acute exposure to myelosuppressive doses of radiation (Hematopoietic Acute Radiation Syndrome [H-ARS])

- Coverage may not be renewed

V. Dosage/Administration ^{1-9,16-21}

Neulasta, Fulphila, Udenyca, Ziextenzo, Nyvepria, Fylnetra, and Stimufend

Indication	Dose
Prophylactic use in patients with non-myeloid malignancy Patient who experienced a neutropenic complication from a prior cycle of the same chemotherapy Wilms Tumor (Nephroblastoma)	<ul style="list-style-type: none"> • Administer 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"> • Administer 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	Administer 6 mg subcutaneously for 1 dose only
<u>NOTE:</u> <ul style="list-style-type: none"> • Do not administer within 14 days before and 24 hours after administration of cytotoxic chemotherapy. • Use of the pre-filled syringe products may be self-administered or administered by a caregiver or healthcare professional. • A healthcare provider must fill the on-body injector with Neulasta or Udenyca using the prefilled syringe and then apply the on-body injector to the patient’s skin (abdomen or back of arm). 	

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- On-body Injectors may be applied on the same day as chemotherapy as long as the Neulasta or Udenyca 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.

Rolvedon

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"> • Administer 13.2 mg subcutaneously once per chemotherapy cycle approximately 24 hours after cytotoxic chemotherapy
Acute Radiation Exposure (Hematopoietic Acute Radiation Syndrome)	<ul style="list-style-type: none"> • Administer 13.2 mg subcutaneously weekly x 2 doses
<u>NOTE:</u> <ul style="list-style-type: none"> • Do not administer within 14 days before and 24 hours after administration of cytotoxic chemotherapy. • Rolvedon may be self-administered or administered by a caregiver or healthcare professional. 	

Ryzneuta

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"> • Administer 20 mg subcutaneously once per chemotherapy cycle at least 24 hours after cytotoxic chemotherapy.
Acute Radiation Exposure (Hematopoietic Acute Radiation Syndrome)	<ul style="list-style-type: none"> • Administer 20 mg subcutaneously weekly x 2 doses
<u>NOTE:</u> <ul style="list-style-type: none"> • Do not administer within 14 days before and <24 hours after administration of cytotoxic chemotherapy. 	

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- Ryzneuta is administered subcutaneously via a single-dose prefilled syringe by a healthcare professional.

VI. Billing Code/Availability Information

HCPCS Code(s):

- J2506 – Injection, pegfilgrastim, excludes biosimilar, 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
- Q5127 – Injection, pegfilgrastim-fpgk, biosimilar, (Stimufend), 0.5 mg; 1 billable unit = 0.5 mg
- Q5130 – Injection, pegfilgrastim-pbbk, biosimilar, (Fylnetra), 0.5 mg; 1 billable unit = 0.5 mg
- J1449 – Injection, eflapegrastim-xnst, 0.1 mg; 1 billable unit = 0.1 mg (*Rolvedon only*)
- J3590 – Unclassified biologics (*Ryzneuta only*)

NDC(s):

- Neulasta 6 mg single-dose prefilled syringe: 55513-0190-xx
- Neulasta 6 mg single-dose prefilled syringe Onpro Kit: 55513-0192-xx
- Fulphila 6 mg single-dose prefilled syringe: 83257-0005-xx
- Udenyca 6 mg single-dose prefilled syringe: 70114-0101-xx
- Udenyca 6 mg single-dose prefilled autoinjector: 70114-0120-xx
- Udenyca 6 mg single-dose prefilled syringe ONBODY kit: 70114-0130-xx
- Ziextenzo 6 mg single-dose prefilled syringe: 61314-0866-xx
- Nyvepria 6 mg single-dose prefilled syringe: 00069-0324-xx
- Fylnetra 6 mg single-dose prefilled syringe: 70121-1627-xx
- Stimufend 6 mg single-dose prefilled syringe: 65219-0371-xx
- Rolvedon 13.2 mg single-dose prefilled syringe: 76961-0101-xx
- Ryzneuta 20 mg/mL prefilled syringe: 73491-0627-xx

VII. References

1. Neulasta [package insert]. Thousand Oaks, CA; Amgen Inc.; February 2021. Accessed March 2024.
2. Fulphila [package insert]. Cambridge, MA; Biocon Biologics Inc.; June 2023. Accessed March 2024.
3. Udenyca [package insert]. Redwood City, CA; Coherus Biosciences, Inc.; December 2023. Accessed March 2024.
4. Ziextenzo [package insert]. Princeton, NJ; Sandoz, Inc.; February 2024. Accessed March 2024.
5. Nyvepria [package insert]. Lake Forest, IL; Hospira, Inc.; March 2023. Accessed March 2024.

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6. Fylnetra [package insert]. Piscataway, NJ; Kashiv BioSciences, LLC; May 2022. Accessed March 2024.
7. Stimufend [package insert]. Lake Zurich, IL; Fresenius Kabi USA, LLC; September 2023. Accessed March 2024.
8. Rolvedon [package insert]. Irvine, CA; Spectrum Pharmaceuticals, Inc; June 2023. Accessed March 2024.
9. Ryzneuta [package insert]. Singapore; Evive Biotechnology, LTD; November 2023. Accessed March 2024.
10. 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.
11. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) pegfilgrastim. National Comprehensive Cancer Network, 2024. 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 2024.
12. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Hematopoietic Growth Factors. Version 3.2024. National Comprehensive Cancer Network, 2023. 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 2024.
13. 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.
14. 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.
15. 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.
16. 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 200893:405-412;doi:10.3324/haematol.11287.
17. 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 200590:225-231.

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18. 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.
19. 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.
20. 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.
21. 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.
22. 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.
23. 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.
24. 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.
25. Hoy SM. Pegfilgrastim-jmdb/MYL-1401H: A Pegfilgrastim Biosimilar. *BioDrugs*. 2019 Feb;33(1):117-120. doi: 10.1007/s40259-019-00334-9.
26. 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
27. 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
28. 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.

Drug Policy

29. Lickliter J, Kanceva R, Vincent E, et al. Pharmacokinetics and Pharmacodynamics of a Proposed Pegfilgrastim Biosimilar MSB11455 Versus the Reference Pegfilgrastim Neulasta in Healthy Subjects: A Randomized, Double-blind Trial. *Clin Ther*. 2020 Aug;42(8):1508-1518.e1. doi: 10.1016/j.clinthera.2020.05.020. Epub 2020 Jul 11.
30. Wynne C, Schwabe C, Vincent E, et al. Immunogenicity and safety of a proposed pegfilgrastim biosimilar MSB11455 versus the reference pegfilgrastim Neulasta® in healthy subjects: A randomized, double-blind trial. *PRP*, Volume8, Issue2, April 2020, e00578. <https://doi.org/10.1002/prp2.578>.
31. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) eflapegrastim. National Comprehensive Cancer Network, 2024. 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 2024.
32. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) efbemalenograstim. National Comprehensive Cancer Network, 2024. 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 2024.
33. Schwartzberg LS, Bhat G, Bharadwaj JS, et al. Eflapegrastim, a novel and potent long-acting GCSF for reducing chemotherapy-induced neutropenia: Integrated results from two phase III trials in breast cancer patients. DOI: 10.1200/JCO.2019.37.15_suppl.539 *Journal of Clinical Oncology* 37, no. 15_suppl (May 20, 2019) 539-539.
34. Schwartzberg LS, Bhat G, Peguero J, et al. Eflapegrastim, a Long-Acting Granulocyte-Colony Stimulating Factor for the Management of Chemotherapy-Induced Neutropenia: Results of a Phase III Trial, *The Oncologist*, Volume 25, Issue 8, August 2020, Pages e1233–e1241, <https://doi.org/10.1634/theoncologist.2020-0105>
35. Cobb PW, Moon YW, Mezei K, et al. A comparison of eflapegrastim to pegfilgrastim in the management of chemotherapy-induced neutropenia in patients with early-stage breast cancer undergoing cytotoxic chemotherapy (RECOVER): A Phase 3 study. *Cancer Medicine*. Volume9, Issue17. September 2020. Pages 6234-6243. <https://doi.org/10.1002/cam4.3227>.
36. Glaspy J, Bondarenko I, Burdaeva O, et al. Efbemalenograstim alfa, an Fc fusion protein, long-acting granulocyte-colony stimulating factor for reducing the risk of febrile neutropenia following chemotherapy: results of a phase III trial. *Support Care Cancer*. 2023 Dec 16;32(1):34. doi: 10.1007/s00520-023-08176-6. PMID: 38103088; PMCID: PMC10725375.
37. 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. *J Clin Oncol*. 2015 Oct 1;33(28):3199-212. doi: 10.1200/JCO.2015.62.3488.

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38. Palmetto GBA. Local Coverage Article: Billing and Coding: Neulasta® (pegfilgrastim) Onpro® Kit/UDENYCA® ONBODY™ (On-body Injector) (A54682). Centers for Medicare & Medicaid Services, Inc. Updated on 01/25/2024 with effective date 01/01/2024. Accessed March 2024.
39. Palmetto GBA. Local Coverage Article: Billing and Coding: White Cell Colony Stimulating Factors (A56748). Centers for Medicare & Medicaid Services, Inc. Updated on 08/10/2023 with effective date 10/01/2023. Accessed March 2024.

Appendix 1 – Covered Diagnosis Codes

Neulasta, Fulphila, Udenyca, Ziextenzo, Nyvepria, Fylnetra, & Stimufend

ICD-10	ICD-10 Description
D61.810	Antineoplastic chemotherapy induced 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
Z51.89	Encounter for other specified aftercare
Z52.011	Autologous donor, stem cells
Z52.091	Other blood donor, stem cells
Z76.89	Persons encountering health services in other specified circumstances
Z94.81	Bone marrow transplant status

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ICD-10	ICD-10 Description
Z94.84	Stem cells transplant status

Rolvedon & Rvzneuta

ICD-10	ICD-10 Description
D61.810	Antineoplastic chemotherapy induced pancytopenia
D61.811	Other drug-induced pancytopenia
D61.818	Other pancytopenia
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
Z51.11	Encounter for antineoplastic chemotherapy
Z51.12	Encounter for antineoplastic immunotherapy
Z51.89	Encounter for other specified aftercare
Z76.89	Persons encountering health services in other specified circumstances

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

The preceding information is intended for non-Medicare coverage determinations. 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 Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: <https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

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Medicare Part B Covered Diagnosis Codes		
Jurisdiction	NCD/LCA/LCD Document (c)	Contractor
J, M	A56748	Palmetto GBA
J, M	A54682	Palmetto GBA

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,	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.
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
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drugs provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

Prior approval is required for HCPCS Codes J2506, Q5108, Q5111, Q5120, Q5122, Q5127, Q5130, J1449, J3590

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