Pegfilgrastim Products (Neulasta®; Fulphila™; Udenyca®; Ziextenzo™; Nyvepria™)

NDC CODE(S) 55513-0190-XX NEULASTA 6MG/0.6ML Solution (AMGEN)
55513-0192-XX NEULASTA ONPRO 6MG/0.6ML Solution (AMGEN
67457-0833-XX FULPHILA 6MG/0.6ML Solution Prefilled Syringe (MYLAN INSTITUTIONAL)
70114-0101-XX UDENYCA 6MG/0.6ML Solution Prefilled Syringe (COHERUS BIOSCIENCES)
61314-0866-xx ZIEXTENZO 6MG/0.6ML Solution Prefilled Syringe (SANDOZ)
00069-0324-XX NYVEPRIA 6MG/0.6ML Solution Prefilled Syringe (PFIZER U.S.)

DESCRIPTION

Pegfilgrastim is a covalent conjugate of recombinant methionyl human G-CSF and monomethoxypolyethylene glycol. Recombinant methionyl human G-CSF is obtained from the bacterial fermentation of a strain of *E coli* transformed with a genetically engineered plasmid containing the human G-CSF gene. Pegfilgrastim products are colony-stimulating factors that act on hematopoietic cells and act as growth factors, stimulating neutrophils and their precursors in the bone marrow and affecting neutrophil progenitor proliferation, differentiation, commitment, and end-cell functional activation.

Biosimilar products are biological products that are highly similar to an existing FDA-approved innovator product and have no clinically meaningful differences from the innovator product. The differences in the biosimilars must be proven to be in the clinically inactive components of the biosimilars, e.g., stabilizers or buffers.

Currently, the FDA has approved four products biosimilar to pegfilgrastim: Pegfilgrastim-apgf (Nyvepria™) Pegfilgrastim-cbqv (Udenyca™), Pegfilgrastim-jmdb (Fulphila™) and Pegfilgrastim-bmez (Ziextenzo™)

POLICY

- Pegfilgrastim products for the prevention of neutropenia are considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**

- Pegfilgrastim products for the treatment/prevention of other conditions/diseases are considered ***investigational.***

MEDICAL APPROPRIATENESS

INITIAL APPROVAL CRITERIA

Prophylactic use in patients with 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/mm^3)
  - 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 experienced a neutropenic complication from a prior cycle of the same chemotherapy

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

Bone marrow transplantation (BMT) failure or engraftment delay

Peripheral blood progenitor cell (PBPC) mobilization and transplant

Wilms Tumor (Nephroblastoma)

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

***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.org

RENEWAL CRITERIA

Note: Use in BMT failure or engraftment delay and PBPC mobilization and transplant may **NOT** be renewed.

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 the Initial Approval Criteria; **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.

DOSAGE/ADMINISTRATION

INDICATION	DOSE
Prophylactic use in patients with non-myeloid malignancy	• 6 mg subcutaneously once per chemotherapy cycle and dosed no more frequently than every 14 days

Patient who experienced a neutropenic complication from a prior cycle of the same chemotherapy	• For pediatric patients weighing <45 kg: ○ <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)	• 6 mg subcutaneously weekly x 2 doses • For pediatric patients weighing <45 kg: ○ <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.

LENGTH OF AUTHORIZATION

- 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.

DOSING LIMITS

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

	Neulasta	Fulphila	Udenyca	Ziextenzo	Nyvepria
Acute Radiation Exposure	1 billable unit weekly x 2 doses	12 billable units weekly x 2 doses	12 billable units weekly x 2 doses	12 billable units weekly x 2 doses	12 billable units weekly x 2 doses
BMT failure or Engraftment delay/ PBPC mobilization and transplant	1 billable unit x 1 dose	12 billable units x 1 dose	12 billable units x 1 dose	12 billable units x 1 dose	12 billable units x 1 dose
All other indications	1 billable unit per 14 days	12 billable units per 14 days	12 billable units per 14 days	12 billable units per 14 days	12 billable units per 14 days

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

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EFFECTIVE DATE 8/31/2021

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