MEDICAL MUTUAL®

Drug Policy

Policy:	**201827-MRX (02-20)**	**Initial Effective Date: 10/30/2014**
Code(s):	**HCPCS J2505, Q5108, Q5111, J3590, C9399, C9058**	**Annual Review Date: 08/15/2019**
SUBJECT:	**Colony Stimulating Factors - Pegfilgrastim** - **Neulasta® (Pegfilgrastim)** - **Fulphila™ (pegfilgrastim-jmdb)** - **Udenyca™ (pegfilgrastim-cbqv)** - **Ziextenzo (pegfilgrastim-bmez)**	**Last Revised Date: 02/20/2020**

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

DESCRIPTION

Neulasta is a leukocyte growth factor, sometimes referred to as a granulocyte colony stimulating factor (G-CSF).[1] Pegfilgrastim is 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 clinically significant incidence of febrile neutropenia.[1] For this indication, pegfilgrastim is to be administered as a single subcutaneous (SC) injection (6 mg) once per chemotherapy cycle. The Neulasta prescribing information also gives dosing recommendations in pediatric patients weighing < 45 kg. Pegfilgrastim should not be administered in the period between 14 days before and 24 hours after administration of cytotoxic chemotherapy. Pegfilgrastim is also indicated to increase survival in patients acutely exposed to myelosuppressive doses of radiation (patients with hematopoietic subsyndrome of acute radiation syndrome). For this indication, the recommended dose of pegfilgrastim is two doses, 6 mg each, given SC once week apart. Refer to the pegfilgrastim prescribing information for pediatric patients < 45 kg. Administer the first dose as soon as possible after suspected or confirmed exposure to radiation levels greater than 2 gray. Give the second dose 1 week after the first dose. Fulphila and Udenyca are biosimilars to Neulasta.[23] The dosing for Fulphila and Udenyca are similar to that common indication for Neulasta.

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.

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Drug Policy

I. Length of Authorization[1,3,4,9,10,11,12,13]

- 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 month 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
- 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

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

	Neulasta (J2505)	Fulphila (Q5108)	Udenyca (Q5111)	Ziextenzo (J3590/C9399/C9058)
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
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
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

III. Initial Approval Criteria [1-9,17,18]

Coverage is provided in the following conditions:

Universal Criteria

Prophylactic use in patients with non-myeloid malignancy †

- Patient is undergoing myelosuppressive chemotherapy with an expected incidence of febrile neutropenia***** of 20% or greater **§**; **OR**
- Patient is undergoing myelosuppressive chemotherapy with an expected incidence of febrile neutropenia***** of 10% or greater **§ AND** one or more of the following co-morbidities:

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- Age >65 receiving full dose intensity
- History of recurrent febrile neutropenia from 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)
- Liver dysfunction (elevated bilirubin >2.0)
- 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 §‡

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 Subsyndrome of Acute Radiation Syndrome) †

Bone marrow transplantation (BMT) failure or engraftment delay ‡

Peripheral blood progenitor cell (PBPC) mobilization and transplant ‡

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

*****Febrile neutropenia is defined as:

- 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

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

IV. Renewal Criteria [1-9,17,18]

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 universal and other 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, capillary leak syndrome, potential for tumor growth stimulation of malignant cells, aortitis, etc.

V. Dosage/Administration[1-9,12-18]

Indication	Dose
Prophylactic use in patients with non-myeloid malignancy Patient who experienced a neutropenic complication from a prior cycle of the same chemotherapy	• 6 mg subcutaneously once per chemotherapy cycle and dosed no more frequently than every 14 days • 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 Subsyndrome of 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

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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:

- J2505 – Injection, pegfilgrastim, 6 mg; 1 billable unit = 6 mg
- 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
- J3590 – Unclassified biologic *(applicable to Ziextenzo ONLY)*
- C9399 – Unclassified drugs or biologicals *(applicable to Ziextenzo ONLY)*
- C9058 – Injection, pegfilgrastim-bmez, biosimilar, (Ziextenzo), 0.5 mg; 1 billable unit = 0.5mg *(effective 04/01/2020)*

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

VII. References

1. Neulasta [package insert]. Thousand Oaks, CA; Amgen Inc; January 2020. Accessed January 2020.
2. Fulphila [package insert]. Zurich, Switzerland; Mylan GmbH; May 2019. Accessed January 2020.
3. Udenyca [package insert]. Redwood City, California; Coherus Biosciences; September 2019. Accessed January 2020.
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6. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) pegfilgrastim. National Comprehensive Cancer Network, 2020. 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

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Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed January 2020.

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14. 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.
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23. Palmetto GBA. Local Coverage Article: Billing and Coding: White Cell Colony Stimulating Factors (A56748). Centers for Medicare & Medicaid Services, Inc. Updated on 12/10/2019 with effective date 01/01/2020. Accessed January 2020.

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.

FOR MEDICAL BENEFIT COVERAGE REQUESTS:

***MMO Site of Care Medical Necessity Criteria:**

Medications in this policy will be administered in a place of service that is a non-hospital facility based location (i.e., home infusion provider, provider's office, free-standing ambulatory infusion center) unless *at least one* of the following are met†:

1. Age less than 18* years; or
2. Clinically unstable based upon documented medical history (e.g., patient is hemodynamically unstable); or
3. History of a severe adverse event from previous administration of the prescribed medication; or
4. Requested medication is being administered as follows:
   - part of a chemotherapy regimen (e.g., anti-neoplastic agent, colony stimulating factor, erythropoiesis-stimulating agent, anti-emetic) for treatment of cancer; or
   - administered with dialysis; or
5. Physical or cognitive impairment and caregiver is not available to assist with safe administration of prescribed medication in the home; or
6. Experiencing adverse events that are not managed by premedication or resources available at a non-hospital facility based location.

No initial doses are allowed in a hospital based outpatient facility without other above criteria being met.
* Effective 01/01/2019, age criterion applies to 18 years of older. Age at original effective date (03/01/2016) was 21 years or older.
†This criterion does not apply to Medicare or Medicare Advantage members.

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