**Pegfilgrastim (Neulasta®), pegfilgrastim-jmdb (Fulphila™), pegfilgrastim-cbqv (Udenyca™), or pegfilgrastim-bmez (Ziextenzo™) are considered medically necessary when ANY of the following criteria are met:**

- Non-myeloid malignancy and receiving myelosuppressive chemotherapy associated with an increased risk of febrile neutropenia
- Hematopoietic subsyndrome of acute radiation syndrome (ARS) with exposure to myelosuppressive doses of radiation (suspected or confirmed exposure to radiation levels greater than 2 gray (Gy))
- Supportive care to reduce the duration of severe neutropenia in individuals post-autologous hematopoietic cell transplant who received high-dose chemotherapy

**Initial and reauthorization is up to 12 months unless otherwise stated.**

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.
Pegfilgrastim (Neulasta), pegfilgrastim-jmdb (Fulphila), pegfilgrastim-cbqv (Udenyca), or pegfilgrastim-bmez (Ziextenzo) are considered experimental, investigational or unproven for ANY other use.

Note: Receipt of sample product does not satisfy any criteria requirements for coverage.

**FDA Approved Indications**

**FDA Approved Indication**
Fulphila (pegfilgrastim-jmdb), Udenyca (pegfilgrastim-cbqv), and Ziextenzo (pegfilgrastim-bmez) are approved as biosimilars to Neulasta (pegfilgrastim).

**Patients with Cancer Receiving Myelosuppressive Chemotherapy**
Neulasta, Fulphila, Udenyca, and Ziextenzo are 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.

Neulasta, Fulphila, Udenyca, and Ziextenzo are not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation.

**Patients with Hematopoietic Subsyndrome of Acute Radiation Syndrome**
Neulasta is indicated to increase survival in patients acutely exposed to myelosuppressive doses of radiation.

**Recommended Dosing**

**FDA Recommended Dosing**

**Patients with Cancer Receiving Myelosuppressive Chemotherapy**
The recommended dosage of Neulasta, Fulphila, Udenyca or Ziextenzo is a single subcutaneous injection of 6 mg administered once per chemotherapy cycle. For dosing in pediatric patients weighing less than 45 kg, refer to Table 1. Do not administer pegfilgrastim between 14 days before and 24 hours after administration of cytotoxic chemotherapy.

**Patients with Hematopoietic Subsyndrome of Acute Radiation Syndrome**
The recommended dose of Neulasta is two doses, 6 mg each, administered subcutaneously one week apart. For dosing in pediatric patients weighing less than 45 kg, refer to Table 1. Administer the first dose as soon as possible after suspected or confirmed exposure to radiation levels greater than 2 gray (Gy). Administer the second dose one week after the first dose.

Obtain a baseline complete blood count (CBC). Do not delay administration of Neulasta if a CBC is not readily available. Estimate a patient’s absorbed radiation dose (i.e., level of radiation exposure) based on information from public health authorities, biodosimetry if available, or clinical findings such as time to onset of vomiting or lymphocyte depletion kinetics.

**Administration**
Neulasta, Fulphila, Udenyca, or Ziextenzo is administered subcutaneously via a single prefilled syringe for manual use or for use with the On-body Injector for Neulasta which is co-packaged with a single prefilled syringe. Use of the On-body Injector for Neulasta is not recommended for patients with Hematopoietic Subsyndrome of Acute Radiation Syndrome. Use of the On-body Injector for Neulasta has not been studied in pediatric patients.

*Pediatric Patients weighing less than 45 kg*
The Neulasta, Fulphila, Udenyca, or Ziextenzo prefilled syringe is not designed to allow for direct administration of doses less than 0.6 mL (6 mg). The syringe does not bear graduation marks which are necessary to accurately measure doses of pegfilgrastim less than 0.6 mL (6 mg) for direct administration to patients. Thus, the direct administration to patients requiring dosing of less than 0.6 mL (6 mg) is not recommended due to the potential for dosing errors. Refer to Table 1.
Table 1. Dosing of pegfilgrastim for pediatric patients weighing less than 45 kg

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Pegfilgrastim Dose</th>
<th>Volume to Administer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 10 kg*</td>
<td>See below*</td>
<td>See below*</td>
</tr>
<tr>
<td>10 – 20 kg</td>
<td>1.5 mg</td>
<td>0.15 mL</td>
</tr>
<tr>
<td>21 – 30 kg</td>
<td>2.5 mg</td>
<td>0.25 mL</td>
</tr>
<tr>
<td>31 – 44 kg</td>
<td>4 mg</td>
<td>0.4 mL</td>
</tr>
</tbody>
</table>

* For pediatric patients weighing less than 10 kg, administer 0.1 mg/kg (0.01 mL/kg) of pegfilgrastim.

**Drug Availability**

Neulasta is supplied as follows:
- Injection: 6 mg/0.6 mL solution in a single-dose prefilled syringe for manual use only.
- Injection: 6 mg/0.6 mL solution in a single-dose prefilled syringe co-packaged with the On-body Injector for Neulasta (Neulasta Onpro kit).

Fulphila is supplied as an injection of 6 mg/0.6 mL of pegfilgrastim in a single-dose prefilled syringe for manual use only.

Udenyca is supplied as an injection of 6 mg/0.6 mL of pegfilgrastim in a single-dose prefilled syringe for manual use only.

Ziextenzo is supplied as an injection of 6 mg/0.6 mL of pegfilgrastim is a single-dose prefilled syringe for manual use only.

**General Background**

**Pharmacology**

Pegfilgrastim, a covalent conjugate of filgrastim (a human granulocyte colony-stimulating factor [G-CSF]) and monomethoxypolyethylene glycol (PEG), is a biosynthetic hematopoietic agent that principally affects the proliferation and differentiation of neutrophils within the bone marrow. Filgrastim used in the manufacture of pegfilgrastim is produced using recombinant DNA technology and cultures of *Escherichia coli* that have been genetically modified to incorporate the human G-CSF gene and is identical to that contained in commercially available filgrastim (recombinant DNA origin) (Neupogen). Studies on cellular proliferation, receptor binding, and neutrophil function demonstrate that filgrastim and pegfilgrastim have the same mechanism of action.

**Guidelines**

- **American Society of Clinical Oncology (ASCO)**
  When the risk of febrile neutropenia (FN) is at least 20% or higher (based on myelotoxicity of specific agents used and patient and disease characteristics) and no equally efficacious and safe chemotherapy protocol exists that does not require CSF support, the use of prophylactic CSFs is appropriate. This primary prophylaxis should be initiated with the first cycle of chemotherapy and continue throughout the protocol. If a patient experiences a treatment cycle delay or a dose reduction, which jeopardizes clinical outcomes, due to a neutropenic episode, secondary prophylaxis is warranted. Alternatively, a dose reduction or therapy delay may be in order. The guidelines suggest that dose-dense protocols that require CSF support should be administered as part of a clinical trial or if there is strong evidence of efficacy. In the case of exposure to lethal doses of total-body radiotherapy, not at a level high enough to cause death, the recommendation is timely administration of CSFs. The committee did not address CSF use in adults with acute myeloid leukemia or myelodysplastic syndromes. The organization states that pegfilgrastim, filgrastim, tbo-filgrastim and filgrastim-sndz, and future biosimilars, are options for the prevention of treatment related FN, and the decision of which agent to use should be guided by convenience, cost and the clinical facts. ASCO provides a strong recommendation for use of CSFs after autologous stem cell transplant and a weak recommendation for use of CSFs after allogeneic stem cell transplant to reduce the duration of severe neutropenia. (Smith 2015)

- **European Society for Medical Oncology (ESMO)**
  When the chemotherapy protocol presents a 10%-20% risk of febrile neutropenia, a patient’s overall risk should be reviewed, including the individual’s age and existing comorbidities. In individuals who have decreased bone
marrow reserve resulting from radiation therapy or in HIV infected patients who are neutropenic, G-CSF is a treatment option. ESMO is a proponent of primary prophylaxis because the chance of febrile neutropenia is very likely during the initial course of treatment. The organization recommends secondary prophylaxis in circumstances, such as therapy with a curative intent, where dose reduction or therapy delays would not be appropriate. (Klastersky, 2016)

- **National Comprehensive Cancer Network (NCCN)**
  The NCCN provides recommendations for the use of myeloid growth factors. The guidelines advocate continuing the same G-CSF throughout treatment. Pegfilgrastim, filgrastim, filgrastim-sndz, and tbo-filgrastim are all recommended for prophylactic use for febrile neutropenia in individuals with solid tumors and non-myeloid malignancies at a high or intermediate risk. For individuals presenting with febrile neutropenia who were not on prophylactic G-CSF and have risk factors for an infection-associated complication, NCCN recommends myeloid growth factors with a notation that tbo-filgrastim and pegfilgrastim have only been evaluated for prophylactic use. For individuals presenting with febrile neutropenia who received prophylactic pegfilgrastim, no additional G-CSF is recommended, although there is a consideration for those with prolonged neutropenia. Where NCCN refers to use with a G-CSF in their guidelines, the recommendations include for the following approved products: pegfilgrastim, pegfilgrastim-jmdb and pegfilgrastim-cbqv. (NCCN, 2019)

In addition, NCCN recommends the use of pegfilgrastim for supportive care post autologous hematopoietic cell transplant (HCT). Several randomized trials have demonstrated efficacy of G-CSF in reducing time to neutrophil recovery (Kawano,1998; Klumpp, 1995; Lee, 1998; Linch, 1997; Spitzer, 1994). A randomized trial in patients who received high-dose chemotherapy and underwent autologous HCT concluded that pegfilgrastim is non-inferior to filgrastim. (Castagna, 2010)

### Coding/Billing Information

**Note:**

1. This list of codes may not be all-inclusive.
2. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

**Covered when medically necessary:**

<table>
<thead>
<tr>
<th>CPT® Codes</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>96372</td>
<td>Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); subcutaneous or intramuscular</td>
</tr>
<tr>
<td>96377</td>
<td>Application of on-body injector (includes cannula insertion) for timed subcutaneous injection</td>
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</table>

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>J2505</td>
<td>Injection, pegfilgrastim, 6 mg</td>
</tr>
<tr>
<td>Q5108</td>
<td>Injection, pegfilgrastim-jmdb, biosimilar, (Fulphila), 0.5 mg</td>
</tr>
<tr>
<td>Q5111</td>
<td>Injection, pegfilgrastim-cbqv, biosimilar, (Udenyca), 0.5 mg</td>
</tr>
<tr>
<td>C9399†</td>
<td>Unclassified drugs or biologics</td>
</tr>
<tr>
<td>J3590†</td>
<td>Unclassified biologics</td>
</tr>
</tbody>
</table>

†Note: When used to report Injection, pegfilgrastim-bmez, biosimilar, (Ziextenzo), 6mg/0.6ml


### References


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