INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer’s particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer’s benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer’s benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Coverage Policy

Cigna covers pegfilgrastim (Neulasta®) as 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

Cigna does not cover the use of pegfilgrastim (Neulasta) for any other indication because it is considered experimental, investigational or unproven.

When coverage is available and medically necessary, the dosage, frequency, site of care, and duration of therapy should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to pegfilgrastim (Neulasta).

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

FDA Approved Indications
Patients with Cancer Receiving Myelosuppressive Chemotherapy
Neulasta 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.

Neulasta is 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.

**FDA Recommended Dosing**

**Patients with Cancer Receiving Myelosuppressive Chemotherapy**
The recommended dosage of Neulasta 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 Neulasta 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 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 Onbody Injector for Neulasta has not been studied in pediatric patients.

**Pediatric Patients weighing less than 45 kg**
The Neulasta 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 Neulasta 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>
<thead>
<tr>
<th>Body Weight</th>
<th>Neulasta 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 Neulasta.

**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).

**General Background**

**Pharmacology**
Pegfilgrastim (Neulasta), 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 allogeneics 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 (NCCN, 2018).

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>
</thead>
<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>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>J2505</td>
<td>Injection, pegfilgrastim, 6 mg</td>
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</tbody>
</table>


References


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