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.

Overview
This policy supports medical necessity review for pegfilgrastim products under medical and pharmacy benefit plans where available for Employer Group, and Individual and Family Plans.

This policy also supports preferred product requirements where applicable by specific benefit plan.

Pegfilgrastim products include:
- **Fulphila™** (pegfilgrastim-jmdb)
- **Neulasta®** (pegfilgrastim)
- **Nyvepria™** (pegfilgrastim-apgf)
- **Udenyca™** (pegfilgrastim-cbqv)
- **Ziextenko™** (pegfilgrastim-bmez)
Coverage Policy

Pegfilgrastim is considered medically necessary when the following criteria are met:

1. Individual has **ONE** of the following diagnoses:
   a. Non-myeloid malignancy and receiving myelosuppressive chemotherapy associated with an increased risk of febrile neutropenia
   b. 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)
   c. Supportive care to reduce the duration of severe neutropenia in individuals post-autologous hematopoietic cell transplant who received high-dose chemotherapy

2. For those plans that have preferred product requirements, **ONE** of the following:
   a. Documented intolerance (for example, hypersensitivity) to **ALL** preferred covered alternatives by drug list in the table below:
   b. The individual requires continuation of treatment with requested colony stimulating factor to complete the current cycle of chemotherapy.
      - Authorization is 1 time only to complete the current cycle of chemotherapy.

Employer Group Non-Covered Products and Preferred Covered Alternatives by Drug List:

<table>
<thead>
<tr>
<th>Non-Covered Product</th>
<th>Standard / Performance Value / Advantage Legacy</th>
<th>Cigna Total Savings</th>
</tr>
</thead>
</table>
| **Fulphila** (pegfilgrastim-jmdb) | Covered when criteria (1) AND (2) above are met, AND ALL of the following:  
• Neulasta  
• Nyvepria  
• Ziextenzo | Covered when criteria (1) above is met. |
| **Neulasta** (pegfilgrastim) injection, for subcutaneous use; single-dose prefilled syringe for manual use only | Covered when criteria (1) above is met. | Covered when criteria (1) AND (2) above are met, AND ALL of the following:  
• Fulphila  
• Nyvepria  
• Udenyca  
• Ziextenzo |
| **Neulasta** (pegfilgrastim) injection, for subcutaneous use; single-dose prefilled syringe co-packaged with the on-body injector | Covered when criteria (1) above is met. | Covered when criteria (1) above is met. |
| **Nyvepria** (pegfilgrastim-apgf) | Covered when criteria (1) above is met. | Covered when criteria (1) above is met. |
| **Udenyca** (pegfilgrastim-cbqv) | Covered when criteria (1) AND (2) above are met, AND ALL of the following:  
• Neulasta  
• Nyvepria  
• Ziextenzo | Covered when criteria (1) above is met. |
| **Ziextenzo** (pegfilgrastim-bmez) | Covered when criteria (1) above is met. | Covered when criteria (1) above is met. |

For Individual and Family Plan Covered Alternatives:

<table>
<thead>
<tr>
<th>Product</th>
<th>Preferred Products Requirement</th>
</tr>
</thead>
</table>
| **Fulphila** (pegfilgrastim-jmdb) | Covered when criteria (1) AND (2) above are met, AND ALL of the following:  
• Neulasta |
<table>
<thead>
<tr>
<th>Product</th>
<th>Preferred Products Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neulasta (pegfilgrastim) injection, for subcutaneous use; single-dose prefilled syringe for manual use only</td>
<td>Covered when criteria (1) above is met.</td>
</tr>
<tr>
<td>Neulasta (pegfilgrastim) injection, for subcutaneous use; single-dose prefilled syringe co-packaged with the on-body injector</td>
<td>Covered when criteria (1) above is met.</td>
</tr>
<tr>
<td>Nyvepria (pegfilgrastim-apgf)</td>
<td>Covered when criteria (1) above is met.</td>
</tr>
<tr>
<td>Udenyca (pegfilgrastim-cbqv)</td>
<td>Covered when criteria (1) above is met.</td>
</tr>
<tr>
<td>Zieaxtenzo (pegfilgrastim-bmez)</td>
<td>Covered when criteria (1) AND (2) above are met, AND ALL of the following:</td>
</tr>
<tr>
<td></td>
<td>• Neulasta</td>
</tr>
<tr>
<td></td>
<td>• Nyvepria</td>
</tr>
<tr>
<td></td>
<td>• Udenyca</td>
</tr>
</tbody>
</table>

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.

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

**Documentation:** When documentation is required, the prescriber must provide written documentation supporting the trials of these other agents. Documentation may include, but is not limited to, chart notes, prescription claims records, and/or prescription receipts.

**Reauthorization Criteria**

Pegfilgrastim products are considered medically necessary for continued use when initial criteria are met AND documentation of beneficial response.

**Authorization Duration**

Initial approval duration is 12 months unless otherwise stated.

Reauthorization approval duration:

- Approve for 12 months

**Conditions Not Covered**

Pegfilgrastim products are considered experimental, investigational or unproven for ANY other use including the following (this list may not be all inclusive):

1. **Myelodysplastic Syndrome (MDS).** Only limited data report use of pegfilgrastim for individuals with MDS.\(^1\) Guidelines from the NCCN for MDS (version 2.2019 – October 18, 2018) do not mention use of pegfilgrastim in this population.\(^2\)

Any other exception is considered not medically necessary.

**Background**

**OVERVIEW**

Neulasta, a leukocyte growth factor, is sometimes also referred to as a granulocyte colony stimulating factor (G-CSF).\(^1\) Fulphila, Udenyca, and Zieaxtenzo are biosimilars to Neulasta.\(^1\,^3\) Pegfilgrastim products are indicated
to decrease the incidence of infection, as manifested by febrile neutropenia, in individuals with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia. Neulasta is additionally indicated to increase survival in individuals acutely exposed to myelosuppressive doses of radiation (Hematopoietic Subsyndrome of Acute Radiation Syndrome). For individuals with cancer receiving myelosuppressive chemotherapy, do not administer pegfilgrastim in the period between 14 days before and 24 hours after administration of cytotoxic chemotherapy. The dose is given subcutaneously once per chemotherapy cycle. For individuals acutely exposed to myelosuppressive doses of radiation, administer the first dose as soon as possible after suspected or confirmed exposure to myelosuppressive doses of radiation; give the second dose 1 week after the first dose.

Guidelines
The National Comprehensive Cancer Network (NCCN) guidelines for hematopoietic growth factors (version 2.2019 – March 27, 2019) recommend pegfilgrastim, along with other granulocyte colony-stimulating factors (CSFs), for prophylactic use if the individual is receiving anti-cancer medications that are associated with a high (> 20%) incidence of severe neutropenia with fever (category 1). Consider CSF therapy for individuals with an intermediate (10% to 20%) probability of developing febrile neutropenia based on risk factors. The NCCN guidelines also recommend therapy with a CSFs in other scenarios in those given myelosuppressive chemotherapy. The American Society of Clinical Oncology (ASCO) also has clinical practice guidelines for the use of white blood cell growth factors (2015) that also recommends CSFs to reduce the risk of febrile neutropenia in individuals receiving cancer chemotherapy. The NCCN guidelines for hematopoietic growth factors (version 2.2019 – March 27, 2019) recommend pegfilgrastim products as supportive care after post-autologous hematopoietic cell transplantation. Data are also available.

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>
</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>Q5120</td>
<td>Injection, pegfilgrastim-bmez, biosimilar, (Ziextenzo) 0.5 mg</td>
</tr>
</tbody>
</table>


References


