Moda Health Plan, Inc. Medical Necessity Criteria

Colony Stimulating Factors – Pegfilgrastim:
Neulasta®; Fulphila™; Udenyca®; Ziextenzo™; Nyvepria™
(Subcutaneous)

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Last Review Date: 04/06/2021
Date of Origin: 10/17/2008
12/2011, 03/2012, 06/2012, 09/2012, 12/2012, 03/2013, 06/2013, 09/2013, 12/2013, 03/2014, 06/2014,
09/2014, 12/2014, 03/2015, 05/2015, 08/2015, 11/2015, 02/2016, 05/2016, 08/2016, 11/2016, 02/2017,
02/2020, 06/2020, 07/2020, 09/2020, 01/2021, 04/2021

I. 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.

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
- Nyvepria 6 mg prefilled syringe: 1 syringe per 14 days

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

<table>
<thead>
<tr>
<th></th>
<th>Neulasta (J2505)</th>
<th>Fulphila (Q5108)</th>
<th>Udenyca (Q5111)</th>
<th>Ziextenzo (Q5120)</th>
<th>Nyvepria (Q5122)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Radiation Exposure</td>
<td>1 billable unit weekly x 2 doses</td>
<td>12 billable units weekly x 2 doses</td>
<td>12 billable units weekly x 2 doses</td>
<td>12 billable units weekly x 2 doses</td>
<td>12 billable units weekly x 2 doses</td>
</tr>
<tr>
<td>BMT failure or engraftment delay/ PBPC mobilization and transplant</td>
<td>1 billable unit x 1 dose</td>
<td>12 billable units x 1 dose</td>
<td>12 billable units x 1 dose</td>
<td>12 billable units x 1 dose</td>
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</table>
III. Initial Approval Criteria \(^{1-10,18,19}\)

Coverage is provided in the following conditions:

<table>
<thead>
<tr>
<th>All other indications</th>
<th>1 billable unit per 14 days</th>
<th>12 billable units per 14 days</th>
<th>12 billable units per 14 days</th>
<th>12 billable units per 14 days</th>
<th>12 billable units per 14 days</th>
</tr>
</thead>
</table>

Site of care specialty infusion program requirements are met (refer to Moda Site of Care Policy).

Ziextenzo and Fulphila are the preferred long-acting granulocyte colony-stimulating factor products.

- Patients must have failed, or have a contraindication, or intolerance to Ziextenzo AND Fulphila prior to consideration of any other long-acting G-CSF product.

**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 ‡**
**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 Acute Radiation Syndrome [H-ARS]) † Φ**

**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)

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

<table>
<thead>
<tr>
<th><em>Febrile neutropenia is defined as:</em></th>
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<tbody>
<tr>
<td>- <strong>Temperature:</strong> a single temperature ≥38.3 °C orally or ≥38.0 °C over 1 hour; <strong>AND</strong></td>
</tr>
<tr>
<td>- <strong>Neutropenia:</strong> &lt;500 neutrophils/mcL or &lt;1,000 neutrophils/mcL and a predicted decline to ≤500 neutrophils/mcL over the next 48 hours</td>
</tr>
</tbody>
</table>

§ 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

**IV. Renewal Criteria 1-10,18,19**

**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 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, thrombocytopenia, capillary leak syndrome, potential for tumor growth stimulation of malignant cells, aortitis, myelodysplastic syndrome and acute myeloid leukemia, etc.

**V. Dosage/Administration 1-10,13-19**
| Prophylactic use in patients with non-myeloid malignancy | • 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 |
|-----------------------------------------------|-----------------------------------------------|
| 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 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.

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
• Q5120 – Injection, pegfilgrastim-bmez, biosimilar, (Ziextenzo), 0.5 mg; 1 billable unit = 0.5 mg
• Q5122 – Injection, pegfilgrastim-apgf, biosimilar, (Nyvepria), 0.5 mg; 1 billable unit = 0.5 mg

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
• Nyvepria 6 mg single-dose prefilled syringe: 00069-0324-xx
VII. References

7. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) pegfilgrastim. National Comprehensive Cancer Network, 2021. 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 Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed March 2021.


### Appendix 1 – Covered Diagnosis Codes

<table>
<thead>
<tr>
<th>ICD-10</th>
<th>ICD-10 Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>D61.81</td>
<td>Pancytopenia</td>
</tr>
<tr>
<td>C64.1</td>
<td>Malignant neoplasm of right kidney, except renal pelvis</td>
</tr>
<tr>
<td>C64.2</td>
<td>Malignant neoplasm of left kidney, except renal pelvis</td>
</tr>
<tr>
<td>C64.9</td>
<td>Malignant neoplasm of unspecified kidney, except renal pelvis</td>
</tr>
<tr>
<td>D70.1</td>
<td>Agranulocytosis secondary to cancer chemotherapy</td>
</tr>
<tr>
<td>D70.9</td>
<td>Neutropenia, unspecified</td>
</tr>
<tr>
<td>T45.1X5A</td>
<td>Adverse effect of antineoplastic and immunosuppressive drugs initial encounter</td>
</tr>
<tr>
<td>T45.1X5D</td>
<td>Adverse effect of antineoplastic and immunosuppressive drugs subsequent encounter</td>
</tr>
<tr>
<td>T45.1X5S</td>
<td>Adverse effect of antineoplastic and immunosuppressive drugs sequela</td>
</tr>
<tr>
<td>T66.XXXA</td>
<td>Radiation sickness, unspecified, initial encounter</td>
</tr>
<tr>
<td>T66.XXXD</td>
<td>Radiation sickness, unspecified, subsequent encounter</td>
</tr>
<tr>
<td>T66.XXXS</td>
<td>Radiation sickness, unspecified, sequela</td>
</tr>
<tr>
<td>W88.1</td>
<td>Exposure to radioactive isotopes</td>
</tr>
<tr>
<td>W88.8</td>
<td>Exposure to other ionizing radiation</td>
</tr>
<tr>
<td>Z41.8</td>
<td>Encounter for other procedures for purposes other than remedying health state</td>
</tr>
<tr>
<td>Z48.290</td>
<td>Encounter for aftercare following bone marrow transplant</td>
</tr>
<tr>
<td>Z51.11</td>
<td>Encounter for antineoplastic chemotherapy</td>
</tr>
</tbody>
</table>
ICD-10 | ICD-10 Description 
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Z51.12 | Encounter for antineoplastic immunotherapy 
Z51.89 | Encounter for other specified aftercare 
Z52.011 | Autologous donor, stem cells 
Z76.89 | Persons encountering health services in other specified circumstances 
Z94.81 | Bone marrow transplant status 
Z94.84 | Stem cells transplant status 

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: [http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx](http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx). Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA):

| --- | --- | --- |

<table>
<thead>
<tr>
<th>Jurisdiction</th>
<th>Applicable State/US Territory</th>
<th>Contractor</th>
</tr>
</thead>
<tbody>
<tr>
<td>E (1)</td>
<td>CA, HI, NV, AS, GU, CNMI</td>
<td>Noridian Healthcare Solutions, LLC</td>
</tr>
<tr>
<td>F (2 &amp; 3)</td>
<td>AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ</td>
<td>Noridian Healthcare Solutions, LLC</td>
</tr>
<tr>
<td>5</td>
<td>KS, NE, IA, MO</td>
<td>Wisconsin Physicians Service Insurance Corp (WPS)</td>
</tr>
<tr>
<td>Jurisdiction</td>
<td>Applicable State/US Territory</td>
<td>Contractor</td>
</tr>
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<td>------------------------------------------------</td>
</tr>
<tr>
<td>6</td>
<td>MN, WI, IL</td>
<td>National Government Services, Inc. (NGS)</td>
</tr>
<tr>
<td>H (4 &amp; 7)</td>
<td>LA, AR, MS, TX, OK, CO, NM</td>
<td>Novitas Solutions, Inc.</td>
</tr>
<tr>
<td>8</td>
<td>MI, IN</td>
<td>Wisconsin Physicians Service Insurance Corp (WPS)</td>
</tr>
<tr>
<td>N (9)</td>
<td>FL, PR, VI</td>
<td>First Coast Service Options, Inc.</td>
</tr>
<tr>
<td>J (10)</td>
<td>TN, GA, AL</td>
<td>Palmetto GBA, LLC</td>
</tr>
<tr>
<td>M (11)</td>
<td>NC, SC, WV, VA (excluding below)</td>
<td>Palmetto GBA, LLC</td>
</tr>
<tr>
<td>L (12)</td>
<td>DE, MD, PA, NJ, DC (includes Arlington &amp; Fairfax counties and the city of Alexandria in VA)</td>
<td>Novitas Solutions, Inc.</td>
</tr>
<tr>
<td>K (13 &amp; 14)</td>
<td>NY, CT, MA, RI, VT, ME, NH</td>
<td>National Government Services, Inc. (NGS)</td>
</tr>
<tr>
<td>15</td>
<td>KY, OH</td>
<td>CGS Administrators, LLC</td>
</tr>
</tbody>
</table>