MEDICAL POLICY – 5.01.551
Granulocyte Colony-Stimulating Factor (G-CSF) Use in Adult Patients

Effective Date: April 1, 2018
Last Revised: March 20, 2018
Replaces: N/A

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Introduction

People with certain cancers may be given drugs (chemotherapy) to treat their disease. A side effect of many chemotherapy drugs is destruction of or delay in making immune cells that fight infection. These cells are known as white blood cells, neutrophils, or granulocytes. Neutropenia means a lack of granulocytes (infection-fighting cells). People being treated for cancer may develop neutropenia and fever. When this happens, treatment with antibiotics in the hospital is often necessary in case there is a serious infection. In the 1980s scientists discovered a type of protein called granulocyte-colony stimulating factor (G-CSF) that could stimulate the body to make more granulocytes. It has become a standard practice to give G-CSF drugs in conjunction with certain types of chemotherapy likely to cause neutropenia. These agents can also be given as part of a bone marrow or stem cell transplant or to treat some rare conditions. Recently new forms of these agents, which less costly, have become available; studies show them to be equivalent. The newer agent, Granix® (tbo-filgrastim), is less costly and therefore is preferred for coverage. Granix does not need preapproval for coverage. All other G-CSF agents require preapproval. Depending on the diagnosis, using Granix may be necessary before one of the other drugs is covered.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.
### Policy Coverage Criteria

This policy applies to patients aged **18 years and over**.

<table>
<thead>
<tr>
<th>Targeted Use</th>
<th>Medical Necessity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patients treated with myelosuppressive anti-cancer regimens, at risk of severe febrile neutropenia to decrease the incidence of infection</strong></td>
<td><strong>Granix® (Tbo-filgrastim) may be considered medically necessary as first-line therapy.</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Neupogen® (filgrastim), Zarxio® (filgrastim-sndz), or Neulasta® (pegfilgrastim) / Neulasta Onpro® may be considered medically necessary for second-line therapy when:</strong></td>
</tr>
<tr>
<td></td>
<td>• Granix® (Tbo-filgrastim) has been tried and failed OR</td>
</tr>
<tr>
<td></td>
<td>• There is a contraindication to the use of Granix® (Tbo-filgrastim) OR</td>
</tr>
<tr>
<td></td>
<td>• Patient challenges related to where they live and access to care or a medical inability to self-administer G-CSF may be considered for coverage of the longer acting second-line agents on a case by case basis (see <strong>Geographic Challenge</strong> below).</td>
</tr>
</tbody>
</table>

**For purposes of this policy, the following types of patients are considered to be at risk of severe febrile neutropenia:**

1. Patients that have experienced febrile neutropenia during a previous cycle of treatment with the current chemotherapy regimen

OR

2. Patients receiving chemotherapy regimen that is expected to result in a 20% or higher incidence of FN, based on guidelines from the American Society of Clinical Oncology (see **Appendix**, Smith et al, 2006)

OR

3. Patients with bone marrow impairment

OR

4. Patients that have received 2 or more prior chemotherapy
<table>
<thead>
<tr>
<th>Targeted Use</th>
<th>Medical Necessity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>regimens or extensive radiation</strong></td>
</tr>
<tr>
<td>OR</td>
<td><strong>5. Patients with other serious comorbidities (reviewed on a case basis)</strong></td>
</tr>
<tr>
<td><strong>Geographic Challenge</strong></td>
<td>A geographic challenge is usually an excessive distance the patient would have to travel from their home to the clinic where the G-CSF would be administered. The general standard is a distance greater than 50 roadway miles is considered excessive. Other considerations might include: crossing a body of water or a mountain pass to travel to the clinic, or severe winter driving conditions, and similar situations.</td>
</tr>
<tr>
<td><strong>Note:</strong></td>
<td>Colony-stimulating factors should not be routinely used for afebrile neutropenia (Smith et al, 2006).</td>
</tr>
<tr>
<td></td>
<td><strong>Patients at risk of severe febrile neutropenia</strong></td>
</tr>
<tr>
<td></td>
<td>Neupogen® (filgrastim) and Zarxio® (filgrastim-sndz) may be considered medically necessary as first line therapy for patients at risk of severe febrile neutropenia with the following diagnoses:</td>
</tr>
<tr>
<td></td>
<td>• Acute myeloid leukemia (AML)</td>
</tr>
<tr>
<td></td>
<td>• Patients receiving bone marrow transplantation</td>
</tr>
<tr>
<td></td>
<td>• Patients undergoing peripheral blood progenitor cell collection and therapy</td>
</tr>
<tr>
<td></td>
<td>• Patients with severe chronic neutropenia</td>
</tr>
<tr>
<td></td>
<td><strong>Combination treatment with chemotherapy regimens</strong></td>
</tr>
<tr>
<td></td>
<td>Neulasta® (pegfilgrastim) / Neulasta Onpro® may be considered medically necessary as first-line therapy when used in combination with chemotherapy regimens where it was the only G-CSF product used in published clinical trials.</td>
</tr>
<tr>
<td></td>
<td>• When Neulasta® (pegfilgrastim) / Neulasta Onpro® for this reason, the requesting provider should provide article citations supporting the request.</td>
</tr>
<tr>
<td><strong>Targeted Use</strong></td>
<td><strong>Investigational</strong></td>
</tr>
<tr>
<td>Not listed in this policy</td>
<td><strong>Any other uses of the following G-CSF products not addressed in this policy are considered investigational:</strong></td>
</tr>
</tbody>
</table>
### Targeted Use

**Investigational**

- Granix® (Tbo-filgrastim)
- Neulasta® (pegfilgrastim) / Neulasta Onpro®
- Neupogen® (filgrastim)
- Zarxio® (Filgrastim-sndz)

### Coding

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td></td>
</tr>
<tr>
<td>96377</td>
<td>Application of on-body injector (includes cannula insertion) for timed subcutaneous injection (Neulasta Onpro®) (Both injector and drug are inclusive)</td>
</tr>
<tr>
<td>HCPCS</td>
<td></td>
</tr>
<tr>
<td>J1442</td>
<td>Injection, filgrastim (G-CSF) (Neupogen®), 1 microgram</td>
</tr>
<tr>
<td>J1447</td>
<td>Injection, tbo-filgrastim (Granix®), 1 microgram</td>
</tr>
<tr>
<td>J2505</td>
<td>Injection, pegfilgrastim (Neulasta®), 6 mg</td>
</tr>
<tr>
<td>Q5101</td>
<td>Injection, filgrastim, (G-CSF), biosimilar (Zarxio®), 1 microgram</td>
</tr>
</tbody>
</table>

**Note:** CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

### Related Information

This policy addresses the following four granulocyte colony-stimulating factors:

**Granix® (Tbo-filgrastim)**

A non-glycosylated recombinant methionyl human granulocyte colony-stimulating growth factor (r-metHuG-CSF) manufactured by recombinant DNA technology using the bacterium strain E.coli K802. It is identical in amino acid sequence to filgrastim but is produced by a different manufacturer using a slightly different process. Granix® (Tbo-filgrastim) was reviewed by the FDA independent of the original BLA for filgrastim and was assigned the prefix “Tbo” to differentiate the two. Both are produced in vitro using genetically engineered strains of E. coli.
Granix® (Tbo-filgrastim) is indicated to reduce the duration of severe neutropenia in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia because it was independently labelled as a separate drug by FDA it has slightly different labelled indications from Neupogen, however, it has identical labelling and indications for FN.

**Neulasta® (pegfilgrastim) / Neulasta Onpro®**

A covalent conjugate of recombinant methionyl human G-CSF (filgrastim) and monomethoxypolyethylene glycol. Neulasta® (pegfilgrastim) /Neulasta Onpro® is indicated to decrease the incidence of infection, as manifested by FN, in patients with non-myeloid malignancies receiving myelosuppressive chemotherapy associated with a clinically significant incidence of febrile neutropenia.

**Neupogen® (filgrastim)**

A recombinant human granulocyte colony-stimulating factor produced by Amgen, Inc. It is recombinant methionyl human granulocyte colony-stimulating factor (r-metHuG-CSF, which is a 175 amino acid protein identical to the endogenous growth factor except for an inserted N-terminal methionine and the lack of glycosylation). Neupogen® (filgrastim) is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs in one of the following categories:

1. Cancer patients receiving myelosuppressive chemotherapy
2. Patients with acute myeloid leukemia (AML) receiving induction or consolidation chemotherapy
3. Cancer patients receiving bone marrow transplantation
4. Patients undergoing Peripheral Blood Progenitor Cell Collection and Therapy
5. Patients with Severe Chronic Neutropenia

Patients in these categories are associated with a significant incidence of severe febrile neutropenia (FN).
Zarxio® (filgrastim-sndz)

A 175 amino acid human granulocyte colony-stimulating factor (G-CSF) manufactured by recombinant DNA technology. Zarxio® (filgrastim-sndz) is produced by Escherichia coli (E coli) bacteria into which has been inserted the human granulocyte colony-stimulating factor gene. Zarxio has a molecular weight of 18,800 daltons. The protein has an amino acid sequence that is identical to the natural sequence predicted from human DNA sequence analysis, except for the addition of an N-terminal methionine necessary for expression in E coli. Because Zarxio is produced in E coli, the product is non-glycosylated and thus differs from G-CSF isolated from a human cell.

Summary of Labeled Indications for G-CSF Products:

<table>
<thead>
<tr>
<th></th>
<th>Myelosuppressive Chemotherapy</th>
<th>Acute Myeloid Leukemia</th>
<th>Bone Marrow Transplant</th>
<th>Progenitor Cell Collection</th>
<th>Severe Chronic Neutropenia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Granix®</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neulasta®</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neupogen®</td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Zarxio®</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

Contraindications

**Neulasta®** is not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation.

**Neupogen®** and **Neulasta®** are contraindicated in patients with known hypersensitivity to E coli-derived proteins, filgrastim, or any component of the product.

**Granix®** has no labeled contraindications.

**Zarxio®** is contraindicated in patients with a history of serious allergic reactions to human granulocyte colony-stimulating factors such as filgrastim or pegfilgrastim products.
Benefit Application

Granix® and Neupogen® may be covered under either the medical benefit (if administered by a provider) or pharmacy benefit (if administered by the patient or a nonprofessional caregiver).

Evidence Review

Efficacy

Neupogen® (filgrastim) has been shown to be safe and effective in accelerating the recovery of neutrophil counts following a variety of chemotherapy regimens. In a phase III clinical trial in small cell lung cancer, the benefits of filgrastim over placebo were shown to be prevention of infection as manifested by febrile neutropenia, decreased hospitalization, and decreased IV antibiotic usage. No difference in survival or disease progression was demonstrated. Filgrastim is also indicated for use in adjunct to acute myeloid leukemia (AML) chemotherapy induction and consolidation. In a phase III clinical trial it was found to effectively reduce the duration of neutropenia, leading to significant clinical benefits by reducing the duration of fever, requirement for parenteral anti-infectives; and the duration of hospitalization. Filgrastim also has an indication for use in severe chronic neutropenia, in which a phase III clinical trial showed that the use of filgrastim resulted in a stimulation of bone marrow production and maturation of neutrophils, an increase in circulating neutrophils, and a reduction in the infection-related events. Filgrastim is also indicated for the use of stem cell harvest in donors.

Granix® (tbo-filgrastim) has been shown to be superior to placebo in duration of severe neutropenia (DSN) with a statistically significant reduction in DSN (1.1 days vs. 3.8 days, p < 0.0001). These results are from a phase III clinical trial in chemotherapy-naïve patients with high-risk stage II, stage III, or stage IV breast cancer.

Neulasta® (pegfilgrastim) has been shown safe and effective in accelerating the recovery of neutrophil counts. In a phase III study comparing pegfilgrastim to placebo, the incidence of hospitalizations (1% vs. 14%) and IV anti-infective use (2% vs. 10%) for the treatment of febrile neutropenia was lower in the pegfilgrastim treated patients compared to the placebo treated patients.
Comparative Effectiveness

In a Phase III study comparing pegfilgrastim to filgrastim as support for commonly used chemotherapy regimens, a single subcutaneous injection of pegfilgrastim provided adequate and safe neutrophil support comparable with daily subcutaneous injections of filgrastim in patients receiving commonly used standard-dose mild-to-moderate myelosuppressive chemotherapy regimens.

A Phase III clinical trial comparing pegfilgrastim to filgrastim for cytokine-alone mobilization of autologous hematopoietic stem and progenitor cells found that the total CD34+ cell yield was equivalent for both filgrastim- and pegfilgrastim-mobilized patients (80% vs. 91%, p = 0.44).

In a trial that compared fixed dose pegfilgrastim to daily filgrastim following autologous stem cell transplantations, it was found that there was no difference in outcomes in terms of safety and efficacy in a single dose of pegfilgrastim compared to 8 days of filgrastim.

In a single-blind, randomized, crossover trial comparing tbo-filgrastim to filgrastim, equivalence was demonstrated for the serum concentration profile, for the ANC profile, and for the CD34+ cell count, which is a marker for the ability of the GCSF to mobilize stem cells.

Safety

In clinical trials, the most common adverse events for peg-filgrastim, filgrastim, and pegfilgrastim was bone pain, which is often severe enough to require opioid analgesia. All three agents carry the risk of more serious adverse events, such as: splenic rupture, acute respiratory distress syndrome, serious allergic reactions, precipitation of severe sickle cell crisis in patients with sickle cell disorders, and the potential for tumor growth stimulatory effects on malignant cells.

Choosing Wisely Guidelines

ASCO guidelines recommend using white cell stimulating factors when the risk of febrile neutropenia, secondary to a recommended chemotherapy regimen, is greater than 20 percent and equally effective treatment programs that do not require white cell stimulating factors are unavailable (see Appendix).
Exceptions should be made when using regimens that have a lower chance of causing febrile neutropenia if it is determined that the patient is at high risk for this complication (due to age, medical history, or disease characteristics).

2015 Update

Added criteria and description for Zarxio® (filgrastim-sndz), a biosimilar to Neupogen that was recently approved by the FDA. A literature search from 7/1/14-10/31/15 did not identify any new evidence that would change the criteria for Neupogen, Neulasta, or Granix. This policy was reviewed by the Pharmacy and Therapeutics Committee November 19, 2015.

2016 Update

A literature search from 7/1/15-12/31/16 did not identify any new evidence that would change policy coverage.

2018 Update

A literature search from 1/1/17-1/30/18 did not identify any new evidence that would change policy coverage.

References

5. Granix Prescribing Information. North Wales, PA: Cephalon (Teva); 2013. Available at: November 12, 2015 27, 2014.


Appendix

Regimens with predicted risk of Febrile Neutropenia greater than 20% (Source: Smith, 2006)

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Acronym</th>
<th>FN (%)</th>
<th>Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin + Paclitaxel</td>
<td></td>
<td>21</td>
<td>Bladder</td>
</tr>
<tr>
<td>Methotrexate + Vinblastine + Doxorubicin + Cisplatin</td>
<td>MVAC</td>
<td>&gt; 20</td>
<td>Bladder</td>
</tr>
<tr>
<td>Docetaxel</td>
<td></td>
<td>21</td>
<td>Breast</td>
</tr>
<tr>
<td>Docetaxel + Trastuzumab</td>
<td></td>
<td>&gt; 20</td>
<td>Breast</td>
</tr>
<tr>
<td>Dose-dense Doxorubicin + Cyclophosphamide followed by Paclitaxel</td>
<td>DD AC followed by T</td>
<td>&gt; 20</td>
<td>Breast</td>
</tr>
<tr>
<td>Doxorubicin + Cyclophosphamide followed by Docetaxel</td>
<td>AC followed by Docetaxel</td>
<td>5-25</td>
<td>Breast</td>
</tr>
<tr>
<td>Docetaxel followed by Doxorubicin + Cyclophosphamide</td>
<td>Docetaxel followed by AC</td>
<td>40</td>
<td>Breast</td>
</tr>
<tr>
<td>Regimen</td>
<td>Acronym</td>
<td>FN (%)</td>
<td>Cancer</td>
</tr>
<tr>
<td>------------------------------------------------------------------------</td>
<td>------------------</td>
<td>--------</td>
<td>----------------------</td>
</tr>
<tr>
<td>Doxorubicin + Docetaxel</td>
<td></td>
<td>33-48</td>
<td>Breast</td>
</tr>
<tr>
<td>Doxorubicin + Paclitaxel</td>
<td></td>
<td>21-32</td>
<td>Breast</td>
</tr>
<tr>
<td>Docetaxel + Doxorubicin + Cyclophosphamide</td>
<td>TAC</td>
<td>22-25</td>
<td>Breast</td>
</tr>
<tr>
<td>Dose-dense Cyclophosphamide + Epirubicin + Fluorouracil</td>
<td>DD FEC</td>
<td>71</td>
<td>Breast</td>
</tr>
<tr>
<td>Dose-dense Doxorubicin followed by Paclitaxel followed by Cyclophosphamide</td>
<td></td>
<td>&gt; 20</td>
<td>Breast</td>
</tr>
<tr>
<td>Dose-dense Epirubicin + Cyclophosphamide</td>
<td></td>
<td>&gt; 20</td>
<td>Breast</td>
</tr>
<tr>
<td>Cyclophosphamide + Epirubicin + Fluorouracil + Docetaxel</td>
<td>FEC-D</td>
<td>25-46</td>
<td>Breast</td>
</tr>
<tr>
<td>Fractionated cyclophosphamide + Vincristine + Docorubicin + Dexamethasone + Rituximab</td>
<td>Hyper CVAD + Rituximab</td>
<td>&gt; 20</td>
<td>Burkitt’s Lymphoma</td>
</tr>
<tr>
<td>Paclitaxel + Cisplatin</td>
<td></td>
<td>28</td>
<td>Cervical</td>
</tr>
<tr>
<td>Docetaxel + Cisplatin + Fluorouracil</td>
<td></td>
<td>&gt; 20</td>
<td>Esophageal/Gastric</td>
</tr>
<tr>
<td>Bleomycin + Vincristine + Cisplatin followed by Cisplatin + Ifosfamide + Etoposide</td>
<td>BOP followed by VIP</td>
<td>46</td>
<td>Germ Cell</td>
</tr>
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<td>Vinblastine + Ifosfamide + Cisplatin</td>
<td>VeIP</td>
<td>67-71</td>
<td>Germ Cell</td>
</tr>
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<td>30</td>
<td>Head &amp; Neck</td>
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<td>54</td>
<td>Hodgkin’s</td>
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<td>Hodgkin’s</td>
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<td>Ifosfamide + Mesna + Gemcitabine + Vinorelbine</td>
<td>IGEV</td>
<td>28</td>
<td>Hodgkin’s</td>
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<td>Kidney</td>
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<td>26</td>
<td>Lung</td>
</tr>
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<td>Dacarbazine + Cisplatin + Vinblastine</td>
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<td>Melanoma</td>
</tr>
<tr>
<td>Dacarbazine + Cisplatin + Vinblastine + IL-2, interferon alfa</td>
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</tr>
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<td>Leucovorin-primed Fluorouracil</td>
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<td>Leucovorin-primed Fluorouracil + Cisplatin</td>
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<td>40</td>
<td>Metastatic gastric cancer</td>
</tr>
<tr>
<td>Regimen</td>
<td>Acronym</td>
<td>FN (%)</td>
<td>Cancer</td>
</tr>
<tr>
<td>------------------------------------------------------------------------</td>
<td>----------------------------------------------</td>
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<td>-------------------------</td>
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<td>Leucovorin-primed Fluorouracil + Irinotecan</td>
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<td>Decitabine</td>
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<td>Myelodysplastic</td>
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<td>R-CHOP-14</td>
<td>&gt; 20</td>
<td>NHL</td>
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<td>Mesna + Ifosfamide + Novantrone + Etoposide</td>
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<td>NHL</td>
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<td>Cisplatin + Cytarabine + Dexamthasone</td>
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<td>NHL/CLL</td>
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<td>NHL/CLL</td>
</tr>
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<td>Dose-dense Doxorubicin or Mitoxantrone + Cyclophosphamide + Vindesine + Bleomycin</td>
<td>DD ACBVP</td>
<td>78</td>
<td>NHL/CLL</td>
</tr>
<tr>
<td>Ifosfamide + Carboplatin + Etoposide</td>
<td>ICE</td>
<td>11.5-24</td>
<td>NHL/CLL</td>
</tr>
<tr>
<td>Rituximab + Ifosfamide + Carboplatin + Etoposide</td>
<td>R-ICE</td>
<td>11.5-24</td>
<td>NHL/CLL</td>
</tr>
<tr>
<td>Mechlorethamine + Doxorubicin + Vinblastine + Vincristine + Bleomycin + Etoposide + Prednisolone</td>
<td>Stanford V</td>
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<td>NHL/CLL</td>
</tr>
<tr>
<td>Mechlorethamine + Vincristine + Procarbazine + Prednisone + Etoposide + Bleomycin + Vinblastine +</td>
<td>MOPPEB-VCAD</td>
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<td>NHL/CLL</td>
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<tr>
<td>Regimen</td>
<td>Acronym</td>
<td>FN (%)</td>
<td>Cancer</td>
</tr>
<tr>
<td>------------------------------------------------------------------------</td>
<td>---------</td>
<td>--------</td>
<td>------------------</td>
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<tr>
<td>Lomustine + Doxorubicin + Vinodesine</td>
<td>FC</td>
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<tr>
<td>Fludarabine + Cyclophosphamide</td>
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<td>33.7</td>
<td>NHL/CLL</td>
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<td>Fludarabine + Cyclophosphamide + Rituximab</td>
<td>FCR</td>
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<td>NHL/CLL</td>
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<tr>
<td>Docetaxel + Carboplatin</td>
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<tr>
<td>Etoposide + Cisplatin</td>
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<td>54</td>
<td>NSCLC</td>
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<td>Cisplatin + Vinorelbine + Cetuximab</td>
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<td>NSCLC</td>
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<td>Vinorelbine + Ifosfamide + Gemcitabine</td>
<td>VIG</td>
<td>25</td>
<td>NSCLC</td>
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<tr>
<td>Topotecan</td>
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<td>&gt; 20</td>
<td>Ovarian</td>
</tr>
<tr>
<td>Docetaxel</td>
<td></td>
<td>33</td>
<td>Ovarian</td>
</tr>
<tr>
<td>Paclitaxel</td>
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<td>22</td>
<td>Ovarian</td>
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<td>Doxorubicin + Cyclophosphamide + Etoposide</td>
<td>ACE</td>
<td>24-57</td>
<td>SCLC</td>
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<tr>
<td>Topotecan</td>
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<td>28</td>
<td>SCLC</td>
</tr>
<tr>
<td>Ifosfamide + Carboplatin + Etoposide</td>
<td>ICE</td>
<td>24</td>
<td>SCLC</td>
</tr>
<tr>
<td>Vincristine + Ifosfamide + Carboplatin + Etoposide</td>
<td>VICE</td>
<td>70</td>
<td>SCLC</td>
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<tr>
<td>Dose-dense Doxorubicin + Cyclophosphamide + Etoposide</td>
<td>DD ACE</td>
<td>34-56</td>
<td>SCLC</td>
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<tr>
<td>Dose-dense Ifosfamide + Carboplatin + Etoposide</td>
<td>DD ICE</td>
<td>&gt; 20</td>
<td>SCLC</td>
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<tr>
<td>Dose-dense Cyclophosphamide + Doxorubicin + Vincristine followed by Cisplatin + Etoposide</td>
<td>DD CAV followed by PE</td>
<td>&gt; 20</td>
<td>SCLC</td>
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<tr>
<td>Mesna + Doxorubicin + Ifosfamide + Dacarbazine</td>
<td>MAID</td>
<td>&gt; 20</td>
<td>Soft Tissue Sarcoma</td>
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<td>Doxorubicin</td>
<td></td>
<td>&gt; 20</td>
<td>Soft Tissue Sarcoma</td>
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<tr>
<td>Ifosfamide + Doxorubicin</td>
<td></td>
<td>&gt; 20</td>
<td>Soft Tissue Sarcoma</td>
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<tr>
<td>Vinblastine + Ifosfamide + Cisplatin</td>
<td>VeIP</td>
<td>&gt; 20</td>
<td>Testicular</td>
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<tr>
<td>Etoposide + Ifosfamide + Cisplatin</td>
<td>VIP</td>
<td>&gt; 20</td>
<td>Testicular</td>
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<tr>
<td>Bleomycin + Etoposide + Cisplatin</td>
<td>BEP</td>
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<td>Testicular</td>
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<td>Paclitaxel + Ifosfamide + Cisplatin</td>
<td>TIP</td>
<td>&gt; 20</td>
<td>Testicular</td>
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<tr>
<td>Paclitaxel + Carboplatin</td>
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<td>25</td>
<td>Urothelial</td>
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<tr>
<td>Methotrexate + Vinblastine + Doxorubicin + Cisplatin</td>
<td>MVAC</td>
<td>26</td>
<td>Urothelial</td>
</tr>
<tr>
<td>Dose-dense Methotrexate + Vinblastine + Doxorubicin + Cisplatin</td>
<td>DD MVAC</td>
<td>&gt; 20</td>
<td>Urothelial</td>
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</tbody>
</table>
### History

<table>
<thead>
<tr>
<th>Date</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>03/10/14</td>
<td>New policy. This policy is added to the Prescription Drug section and covers three granulocyte colony-stimulating factors: tbo-filgrastim (Granix®), filgrastim (Neupogen®) and pegfilgrastim (Neulasta®). All are considered medically necessary when criteria are met for conditions and per treatment guidelines outline in this policy. Policy approved with a hold for provider notification; it will be effective August 30, 2014.</td>
</tr>
<tr>
<td>08/11/14</td>
<td>Coding update. HCPCS codes J1442, J1446 and J2505 added to the policy.</td>
</tr>
<tr>
<td>10/13/14</td>
<td>Interim update. Policy reformatted to clarify details of step therapy in the use of GCSF; criteria added for making exceptions due to geographical issues.</td>
</tr>
<tr>
<td>02/10/15</td>
<td>Coding update. HCPCS code J1446 removed from policy; this is not being reviewed at this time.</td>
</tr>
<tr>
<td>02/09/16</td>
<td>Interim Review. Policy scope clarified to apply only to adults, age 18 and over.</td>
</tr>
<tr>
<td>10/01/16</td>
<td>Policy moved into new format; no change to policy statements.</td>
</tr>
<tr>
<td>04/01/17</td>
<td>Annual Review, approved March 14, 2017. No changes to criteria made. Added a new reference to the bibliography section (#15).</td>
</tr>
<tr>
<td>03/01/18</td>
<td>Annual Review, approved February 27, 2018. Minor change made to criteria. Deletion of first cycle of chemotherapy within the criteria. HCPCS code J1447 added to policy.</td>
</tr>
<tr>
<td>03/09/18</td>
<td>Coding update, added CPT code 96377.</td>
</tr>
<tr>
<td>04/01/18</td>
<td>Interim Review, approved March 20, 2018. Added “Neulasta Onpro®” for clarity.</td>
</tr>
</tbody>
</table>

**Disclaimer:** This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). ©2018 Premera All Rights Reserved.

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Premera:
• Provides free aids and services to people with disabilities to communicate effectively with us, such as:
  • Qualified sign language interpreters
  • Written information in other formats (large print, audio, accessible electronic formats, other formats)
• Provides free language services to people whose primary language is not English, such as:
  • Qualified interpreters
  • Information written in other languages

If you need these services, contact the Civil Rights Coordinator.

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Civil Rights Coordinator - Complaints and Appeals
PO Box 91102, Seattle, WA 98111
Toll free 855-332-4535, Fax 425-918-5592. TTY 800-842-5357
Email AppealsDepartmentInquiries@Premera.com

You can also file a grievance in person or by mail, fax, or email. If you need help filing a grievance, the Civil Rights Coordinator is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at:
https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:
U.S. Department of Health and Human Services
200 Independence Avenue SW, Room 509F, HHH Building
Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD)
Complaint forms are available at

Getting Help in Other Languages

This Notice has Important Information. This notice may have important information about your application or coverage through Premera Blue Cross. There may be key dates in this notice. You may need to take action by certain deadlines to keep your health coverage or help with costs. You have the right to get this information and help in your language at no cost.
Call 800-722-1471 (TTY: 800-842-5357).

Arabic (Arabic):
عمى هذا الإشعار معلومات هامة. قد يحتوي هذا الإشعار معلومات مهمة بخصوص طبيك أو
العجلة التي تريد الحصول عليها من خلال Premera Blue Cross. قد تكون هناك ترجمة للعاجزة
لمعنى بحالة طبيتك. يحتوي هذا الإشعار على هذه المعلومات والمساعدة بذلك دون فهم أي كلمة. يحصل
800-722-1471 (TTY: 800-842-5357) على

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申请或保险的重要讯息。本通知内可能有重要日期。您可能需要在截止日期
之前採取行动，以保留您的健康保险或费用补贴。您有權利免費以您的母
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This notice contains information about your health benefits and rights under federal and state laws.

This notification may contain important information that you should know to make informed decisions about your health care.

If you have questions about this notice, please contact your customer service representative or call Premera Blue Cross at 1-800-722-1471 (TTY: 800-842-5357).

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