MDWise PRIOR AUTHORIZATION PROTOCOL FOR WHITE BLOOD CELL STIMULATORS

**Neupogen® (filgrastim):** 300 mcg/mL vial, 300 mcg/0.5 mL prefilled syringe; 480 mcg/1.6 mL vial, 480 mcg/0.8 mL prefilled syringe

**Mozobil® (plerixafor):** 24mg/1.2ml single use vial

**Leukine® (sargramostim):** 250 mcg lyophilized powder for injection vial, 500 mcg/mL solution multi-dose vial *

**Neulasta® (pegfilgrastim):** 6 mg/0.6mL prefilled syringe

**INITIAL APPROVAL:**
- The request for the medication is for an FDA approved indication, and/or is used for a medical condition that is supported by the medical compendium (Micromedex, American Hospital Formulary Service (AHFS), Drug Points, Drug Package Insert) as defined in the Social Security Act 1927 and/or per the National Comprehensive Cancer Network (NCCN) or the American Society of Clinical Oncology (ASCO) standard of care guidelines.

- If the medication request is for Neulasta and is being ordered for a patient requiring dose dense chemotherapy (i.e. for a documented diagnosis of breast cancer) no prior trials of any other white blood cell stimulator is needed for that patient.

- However for all other medication requests for Neulasta, the patient has a documented treatment failure (i.e. failure to reach and/or maintain target ANC, prolonged febrile neutropenia, unplanned hospitalization, infection requiring prolonged anti-infectives) which is consistent with pharmacy claims data, with an adequate trial (including dates, doses of therapy) of Neupogen and/or has another documented medical reason (intolerance, hypersensitivity, or dose dense chemotherapy, etc) for not taking Neupogen to treat their medical condition.

- If the medication request is for Mozobil, the patient has a documented treatment failure (i.e. failure to reach and/or maintain target therapeutic goal) which is consistent with pharmacy claims data, with an adequate trial (including dates, doses of therapy) of Neupogen. In addition, documentation must be submitted that the patient is using Mozobil in combination with a granulocyte-colony stimulating factor (G-CSF) agent (i.e. Neupogen or Neulasta)

- Prescribed dosing of medication is within FDA approved indications and/or is supported by the medical compendium as defined by the Social Security Act and/or per the NCCN or ASCO standard of care guidelines.

If all of the above conditions are met, the request will be approved for up to 12 weeks or as recommended per FDA approved indications and/or as defined by the medical compendium as defined above and/or per the NCCN or ASCO standard of care guidelines; if all of the above criteria are not met, the request is referred to a Medical Director for medical necessity review.

**REAUTHORIZATION OF MEDICATION:**
- The prescribing physician has provided documentation as to the clinical benefits of the medication supporting continued treatment, OR the medication is being continued in accordance with the recommended time as defined by FDA drug package insert, and/or per recommendations of the medical compendium as described above, and/or per the NCCN or ASCO standard of care guidelines.

- Prescribed dosing of medication is within FDA approved indications and/or supported by the medical compendium as defined by the Social Security Act and/or per the NCCN or ASCO standard of care guidelines.

If all of the above conditions are met, the request will be approved for up to 12 weeks or as recommended per FDA approved indications and/or as defined by the medical compendium as defined above and/or per the NCCN or ASCO standard of care guidelines; if all of the above criteria are not met then, based on professional judgment, the Pharmacist reviewer will issue a denial for the medication requested.

**FDA APPROVED INDICATIONS AND DOSING:**

**Neupogen® (filgrastim)**

**Adult dosing:**

- **Patients Receiving Myelosuppressive Chemotherapy:** The recommended starting dose of Neupogen® is 5 mcg/kg/day, administered as a single daily injection SC bolus injection, by short IV infusion (15 to 30 minutes), or by continuous SC or continuous IV infusion. Doses may be increased in increments of 5 mcg/kg for each chemotherapy cycle, according to the duration and severity of the ANC nadir. Therapy with Neupogen® should be discontinued if the ANC surpasses 10,000/mm³ after the expected chemotherapy-induced neutrophil nadir.

- **Cancer Patients Receiving Bone Marrow Transplant (BMT):** The recommended dose of Neupogen® following BMT is 10 mcg/kg/day given as an IV infusion of 4 to 24 hours, or as a continuous 24 hour SC infusion. The daily dose of Neupogen® should be titrated against the neutrophil response as follows:
<table>
<thead>
<tr>
<th>Absolute Neutrophil Count</th>
<th>Neupogen® Dose Adjustment</th>
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<tbody>
<tr>
<td>When ANC &gt; 1000/mm³ for 3 consecutive days</td>
<td>Reduce to 5 mcg/kg/day</td>
</tr>
<tr>
<td>Then: If ANC remains &gt; 1000/mm³ for 3 consecutive days</td>
<td>Discontinue Neupogen®</td>
</tr>
<tr>
<td>Then: If ANC decreases &lt; 1000/mm³</td>
<td>Resume at 5 mcg/kg/day</td>
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If ANC decreases to at any time during the 5 mcg/kg/day administration, Neupogen® should be increased to 10 mcg/kg/day, and the above steps should then be followed.

**Patients with Congenital neutropenia:** 6 mcg/kg SC twice daily based on ANC results and clinical course.

**Patients Undergoing Peripheral Blood Progenitor Cell Collection (PBPC) and Therapy:** The recommended dose of Neupogen® for the mobilization of PBPC is 10 mcg/kg/day SV, either as a bolus or a continuous infusion. It is recommended that Neupogen® be given for at least 4 days before the first leukapheresis procedure and continued until the last leukapheresis. Neupogen® dose modification should be considered for those patients who develop a WBC count > 100,000/mm³.

**Patients with Severe Chronic Neutropenia, Idiopathic or Cyclic:** The recommended daily starting dose is 5 mcg/kg as a single injection SC every day.

**Pediatric dosing:**

ASC has no official recommendation, but states that adult doses have been used in pediatric patients; NCCN has no information on pediatric patients.

Based on the Compendia pediatric dosing was available for: Chemotherapy-induced Neutropenia, BMT to reduce the duration of neutropenia and neutropenia-related clinical sequelae in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy prior to BMT, Peripheral Blood Progenitor Cell Transplantation; and Congenital, Cyclic and Idiopathic neutropenia. **Follow adult dosing guidelines for pediatric dosing for aforementioned indications.**

**Leukine® (sargramostim)**

**Adult dosing:**

**Use Following Induction Chemotherapy in Acute Myelogenous Leukemia (AML):** The recommended dose is 250 mcg/m²/day administered intravenously over a 4 hour period starting approximately on day 11 or four days following the completion of induction chemotherapy. Leukine® treatment should be continued until an ANC <1500 cells/mm³ for 3 consecutive days or a maximum of 42 days.

**Use in Mobilization and Following Transplantation of Autologous Peripheral Blood Progenitor Cells:** The recommended dose is 250 mcg/m²/day administered IV over 24 hours or SV once daily. Leukine® treatment should be continued until an ANC <1500 cells/mm³ for 3 consecutive days.

**Use in Myeloid Reconstitution after Autologous or Allogenic Bone Marrow Transplantation:** The recommended dose is 250 mcg/m²/day administered IV over a 2 hour period beginning two to four hours after bone marrow infusion and not less than 24 hours after the last dose of chemotherapy or radiotherapy. Leukine® treatment should be continued until an ANC <1500 cells/mm³ for 3 consecutive days.

**Use in Bone Marrow Transplantation Failure of Engraftment Delay:** The recommended dose is 250 mcg/m²/day for 14 days as a 2 hour IV infusion. The dose can be repeated after 7 days off therapy if engraftment has not occurred.

**Pediatric dosing:**

Safety and efficacy in pediatric patients has not been established; however, available safety data indicate that Leukine does not exhibit any greater toxicity in pediatric patients than in adults.

**Neulasta® (pegfilgrastim)**

**Adult dosing:**

**Chemotherapy-induced Febrile Neutropenia Prophylaxis:** The recommended dose of Neulasta® is a single SC injection of 6 mg administered once per chemotherapy cycle. Neulasta® should not be administered in the period between 14 days before and 24 hours after administration of cytotoxic chemotherapy.
Pediatric dosing:

Safety and efficacy have not been established; the 6 mg fixed-dose single-use syringe formulation should not be used in infants, children, and smaller adolescents weighing less than 45 kg.

****ASCO and NCCN practice guidelines prefer the subcutaneous route of administration for all 3 white blood cell stimulators. Per ASCO guidelines the calculated dose may be rounded off, within reason, to the nearest vial/syringe size to reduce wastage. ******

Mozobil (plerixafor)

Adult dosing:

In combination with granulocyte-colony stimulating factor (G-CSF) to mobilize hematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in patients with non-Hodgkin’s lymphoma (NHL) and multiple myeloma: The recommended dose of Mozobil is 0.24 mg/kg body weight by subcutaneous (SC) injection. Begin treatment with Mozobil after the patient has received G-CSF once daily for four days. Administer Mozobil approximately for 11 hours prior to initiation of apheresis for up to 4 consecutive days.

<table>
<thead>
<tr>
<th>Estimated Creatinine Clearance (mL/min)</th>
<th>Dose</th>
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<tbody>
<tr>
<td>&gt; 50</td>
<td>0.24 mg/kg once daily (not to exceed 40 mg/day)</td>
</tr>
<tr>
<td>&lt; 50</td>
<td>0.16 mg/kg once daily (not to exceed 40 mg/day)</td>
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Safety and efficacy in pediatric patients has not been established have not been established in controlled clinical studies.

References:


Revision/Review Date: MAC 10/12/2011
Associated Policy: Prior Authorization of Medications 236.200

NOTE: Clinical reviewer must override criteria when, in his/her professional judgment, the requested item is medically necessary.