### Colony Stimulating Factors

#### Overrides

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<th>Overrides</th>
<th>Approval Duration</th>
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<tbody>
<tr>
<td>Prior Authorization</td>
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<tr>
<td>Quantity Limit</td>
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#### Medications

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<thead>
<tr>
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<tbody>
<tr>
<td>Fulphila (pegfilgrastim-jmdb)</td>
<td>May be subject to quantity limit</td>
</tr>
<tr>
<td>Granix (tbo-filgrastim)</td>
<td>N/A</td>
</tr>
<tr>
<td>Leukine (sargramatim)</td>
<td>N/A</td>
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<tr>
<td>Neulasta (pegfilgrastim)</td>
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<tr>
<td>Neupogen (filgrastim)</td>
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<tr>
<td>Nivestym (filgrastim-aafi)</td>
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<td>Nyvepria (pegfilgrastim-apgf)</td>
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<td>Udenyca (pegfilgrastim-cbqy)</td>
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<tr>
<td>Zarxio (filgrastim-sndz)</td>
<td>N/A</td>
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<tr>
<td>Ziestenzo (pegfilgrastim-bmez)</td>
<td>May be subject to quantity limit</td>
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#### APPROVAL CRITERIA

I. *In addition to criteria outlined below, requests for Granix, Leukine, Neupogen, Nivestym, must also meet the following criteria:

   A. Individual has had a trial and inadequate response or intolerance to Zarxio; OR
   B. Zarxio is not FDA-approved for the prescribed indication and Granix, Leukine, Neupogen or Nivestym is.

   *Step Therapy does not apply to Florida Healthy Kids*

II. Requests for filgrastim (Neupogen), filgrastim-aafi (Nivestym), or filgrastim-sndz (Zarxio) may be approved if the following criteria are met:

   A. Individual with nonmyeloid malignancy is using for primary prophylaxis of Febrile Neutropenia (FN); **AND**
   B. Individual has a risk of FN of 20% or greater based on chemotherapy regimen (**see Appendix**, Table 1);

   **OR**

   C. Individual with nonmyeloid malignancy is using for primary prophylaxis of FN; **AND**
   D. Individual’s risk of developing FN is greater than or equal to 10% and less than 20% based on chemotherapy regimen (**see Appendix**, Table 1) and individual has any risk...
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factors for:

1. Age greater than 65 years (Lyman 2014; Aagaard 2018); **OR**
2. Poor performance status (Eastern Cooperative Oncology Group 3 or 4) or HIV infection (in particular, those with low CD4 counts (≤ 450/µL) but chemotherapy still indicated) (Lyman 2014); **OR**
3. Prior radiation therapy (within previous 1 year) (Terbuch 2018) (Fujiwara 2017) (Shigeta 2015); **OR**
4. Bone marrow involvement by tumor producing cytopenias (Lyman 2014); **OR**
5. Persistent neutropenia (absolute neutrophil count [ANC] less than 1500mm³) (Lyman 2014); **OR**
6. Poor renal function (glomerular filtration rate [GFR] less than 60mL/min) (Lyman 2014; Aagaard 2018); **OR**
7. Liver dysfunction (liver function tests at least 2X upper limit of normal or bilirubin > 2.0 mg/dL) (Lyman 2014; Aagaard 2018); **OR**
8. Recent surgery performed as part of cancer management within previous 30 days (not to include a procedure such as port placement, drain placement, IVC filter, etc.) (Lyman 2014; Aagaard 2018); **OR**
9. History of active infection within previous 60 days (Lyman 2014; Aagaard 2018); **OR**
10. Current open wound and chemotherapy cannot be delayed (Lyman 2014; Aagaard 2018);

**OR**

E. Individual with nonmyeloid malignancy is using for secondary prophylaxis of FN; **AND**

F. Individual has experienced a neutropenic complication from a prior cycle of chemotherapy (for which primary prophylaxis was not received), in which a reduced dose may compromise disease-free or overall survival or treatment outcome (NCCN 2A);

**OR**

G. Individual is using as adjunctive treatment for FN (NCCN 2A); **AND**

H. Individual has been on prophylactic therapy with filgrastim;

**OR**

I. Individual has not received prophylactic therapy with granulocyte colony stimulating factor (NCCN Guidelines Myeloid Growth Factors); **AND**

J. Individual has a high risk for infection-associated complications as demonstrated by any of the following (NCCN 2A):

1. Expected prolonged (greater than 10 days) and profound (less than 0.1 x 10⁹/L) neutropenia; **OR**
2. Age greater than 65 years; **OR**
3. Pneumonia or other clinically documented infections; **OR**
4. Hypotension and multi organ dysfunction (sepsis syndrome); **OR**
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2. Poor performance status (Eastern Cooperative Oncology Group 3 or 4) or HIV infection (in particular, those with low CD4 counts (≤ 450/µL) but chemotherapy still indicated) (Lyman 2014); OR
3. Prior radiation therapy (within previous 1 year) (Terbuch 2018) (Fujiwara 2017) (Shigeta 2015); OR
4. Bone marrow involvement by tumor producing cytopenias (Lyman 2014); OR
5. Persistent neutropenia (absolute neutrophil count [ANC] less than 1500mm³) (Lyman 2014); OR
6. Poor renal function (glomerular filtration rate [GFR] less than 60mL/min) (Lyman 2014; Aagaard 2018); OR
7. Liver dysfunction (liver function tests at least 2X upper limit of normal or bilirubin > 2.0 mg/dL) (Lyman 2014; Aagaard 20218); OR
8. Recent surgery performed as part of cancer management within previous 30 days (not to include a procedure such as port placement, drain placement, IVC filter, etc.) (Lyman 2014; Aagaard 2018); OR
9. History of active infection within previous 60 days (Lyman 2014; Aagaard 2018); OR
10. Current open wound and chemotherapy cannot be delayed (Lyman 2014; Aagaard 2018);

OR
E. Individual with nonmyeloid malignancy is using for secondary prophylaxis of FN;
AND
F. Individual has experienced a neutropenic complication from a prior cycle of chemotherapy (for which prophylaxis was not received), in which a reduced dose may compromise disease-free or overall survival or treatment outcome (NCCN 2A);

OR
G. Individual is using as adjunctive treatment for FN; AND
H. Individual has not received prophylactic therapy with pegfilgrastim (NCCN 2A); AND
I. Individual has a high risk for infection-associated complications as demonstrated by any of the following:
   1. Expected prolonged (greater than 10 days) and profound (less than 0.1 x 10⁹/L) neutropenia; OR
   2. Age greater than 65 years; OR
   3. Pneumonia or other clinically documented infections; OR
   4. Hypotension and multi organ dysfunction (sepsis syndrome); OR
   5. Invasive fungal infection; OR
   6. Prior episode of febrile neutropenia; OR
   7. Hospitalized at the time of the development of fever;

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G. Individual is using shortly after the completion of induction or repeat induction of chemotherapy of AML;

**OR**

H. Individual has a diagnosis of myelodysplastic syndromes (MDS); **AND**
I. Individual has severe neutropenia (ANC less than or equal to 500 mm³) or experiencing recurrent or resistant infections (NCCN Guidelines Myelodysplastic Syndromes; AHFS);

**OR**

J. Individual is 18 years or older; **AND**
K. Individual is using for the mobilization of hematopoietic progenitor cells into peripheral blood for collection by leukapheresis and autologous transplantation

**OR**

L. Individual is 2 years of age and older; **AND**
M. Individual is using for the acceleration of myeloid reconstitution following autologous or allogenic bone marrow transplantation or peripheral blood progenitor cell transplantation;

**OR**

N. Individual is 2 years of age and older; **AND**
O. Individual is using for the treatment of delayed neutrophil recovery or graft failure after autologous or allogenic bone marrow transplantation;

**OR**

P. Individual is using to increase survival in adult and pediatric individuals (from birth to 17 years of age) acutely exposed to myelosuppressive doses of radiation (such as Hematopoietic Syndrome of Acute Radiation Syndrome (H-ARS));

**OR**

Q. Individual is 18 years of age or younger; **AND**
R. Individual is diagnosed with relapsed/refractory high-risk neuroblastoma; **AND**
S. Individual is using in combination with dinutuximab (Unituxin), 13-cis-retinoic acid (i.e. isotretinoin) and interleukin-2 (IL-2) (i.e. aldesleukin); **AND**
T. Individual achieved a partial response to first-line multi-agent, multi-modality therapy (i.e. induction combination chemotherapy, or myeloablative consolidation chemotherapy followed by autologous stem cell transplant).

V. Requests for tbo-filgrastim (Granix) may be approved if the following criteria are met:

A. Individual with non-myeloid malignancy is using for primary prophylaxis of FN; **AND**
B. Individual has a risk of FN of 20% or greater based on chemotherapy regimen (see Appendix, Table 1);

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OR
C. Individual with nonmyeloid malignancy is using for primary prophylaxis of FN; AND
D. Individual’s risk of developing FN is greater than or equal to 10% and less than 20% based on chemotherapy regimen and individual has any risk factors for FN:

1. Age greater than 65 years (Lyman 2014; Aagaard 2018); OR
2. Poor performance status (Eastern Cooperative Oncology Group 3 or 4) or HIV infection (in particular, those with low CD4 counts (≤ 450/µL)) but chemotherapy still indicated (Lyman 2014); OR
3. Prior radiation therapy (within previous 1 year) (Torbuch 2018) (Fujiwara 2017) (Shigeta 2015); OR
4. Bone marrow involvement by tumor producing cytopenias (Lyman 2014); OR
5. Persistent neutropenia (absolute neutrophil count [ANC] less than 1500mm³) (Lyman 2014); OR
6. Poor renal function (glomerular filtration rate [GFR] less than 60mL/min) (Lyman 2014; Aagaard 2018); OR
7. Liver dysfunction (liver function tests at least 2X upper limit of normal or bilirubin > 2.0 mg/dL) (Lyman 2014; Aagaard 2018); OR
8. Recent surgery performed as part of cancer management within previous 30 days (not to include a procedure such as port placement, drain placement, IVC filter, etc.) (Lyman 2014; Aagaard 2018); OR
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10. Current open wound and chemotherapy cannot be delayed (Lyman 2014; Aagaard 2018);

OR
E. Individual with nonmyeloid malignancy is using for secondary prophylaxis of FN; AND
F. Individual has experienced a neutropenic complication from a prior cycle of chemotherapy (for which prophylaxis was not received), in which a reduced dose may compromise disease-free or overall survival or treatment outcome (NCCN 2A);

OR
G. Individual is using as an adjunctive treatment for FN;
AND
H. Individual was previously using Granix (tbo-filgrastim) prophylactically (NCCN 2A);

OR
I. Individual has not received prophylactic therapy with a granulocyte colony stimulating factor (NCCN Guidelines Myeloid Growth Factors);
AND
J. Individual has a high risk for infection-associated complications as demonstrated by any of the following:
   1. Expected prolonged (greater than 10 days) and profound (less than 0.1 x 10^9/L) neutropenia (NCCN 2A); OR
   2. Age greater than 65 years; OR
   3. Pneumonia or other clinically documented infections; OR
   4. Hypotension and multi organ dysfunction (sepsis syndrome); OR
   5. Invasive fungal infection; OR
   6. Prior episode of febrile neutropenia; OR
   7. Hospitalized at the time of the development of fever;

OR
K. Individual is using after a hematopoietic progenitor stem cell transplant (HPCT/HSCT) to promote myeloid reconstitution or when engraftment is delayed or has failed (NCCN 2A);

OR
L. Individual has a diagnosis of myelodysplastic syndrome (MDS); AND
M. Individual has severe neutropenia (ANC less than or equal to 500mm^3) or experiencing recurrent or resistant infections (NCCN 2A);

OR
N. Individual is using to mobilize progenitor cells into peripheral blood for collection by leukapheresis, as an adjunct to peripheral blood/hematopoietic stem cell transplantation (PBSCT/PHSCT) (AHFS).

Colony Stimulating Factors (filgrastim, and their biosimilars, pegfilgrastim and their biosimilars, sargramostim, and tbo-filgrastim) may not be approved for any of the following:

I. Individual is using as prophylaxis for FN, except when criteria above are met; OR
II. Individual is using as treatment in neutropenia in those who are afebrile, except when criteria above are met; OR
III. Individual is using as adjunctive therapy in those with uncomplicated febrile neutropenia, defined as: fever less than 10 days duration, no evidence of pneumonia, cellulitis, abscess, sinusitis, hypotension, multi-organ dysfunction, or invasive fungal infection; and no uncontrolled malignancies; OR
IV. Individual is using for chemosensitization of myeloid leukemias; OR
V. Individual is using for prophylaxis for FN during concomitant chemotherapy and radiation therapy; OR
VI. Individual is continuing use if no response is seen within 28-42 days (individuals who have failed to respond within this time frame are considered non-responders); OR

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VII. Individual is using as a technique to increase the numbers of circulating hematopoietic stem cells as treatment of damaged myocardium.

**Key References:**


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Non-Small Cell Lung Cancer (Advanced)
- Docetaxel
- Intermediate

Non-Small Cell Lung Cancer (Advanced)
- Docetaxel and cisplatin
- Low
  - Abe T 2015; Fossella F 2003; Kubota K 2015; Schiller JH 2002

Non-Small Cell Lung Cancer (Metastatic)
- Carboplatin/cisplatin, pemetrexed, and pembrolizumab
- Low
  - Gandhi 2018; Langer 2016; Rodrigues-Pereira 2011; Scagliotti 2008

Non-Small Cell Lung Cancer (Metastatic, non-squamous)
- Carboplatin, paclitaxel, and atezolizumab ± bevacizumab
- Low
  - Lilenbaurn 2005; Ohe 2007; Socinski 2018; Williamson 2005

Non-Small Cell Lung Cancer (Metastatic, squamous)
- Carboplatin, paclitaxel/nab-paclitaxel, and pembrolizumab
- Low
  - Gadgeel 2018; Lilienbaum 2005; Ohe 2007; Paz-Ares 2018; Williamson 2005

Ovarian Cancer
- Carboplatin and paclitaxel
- Low

Ovarian Cancer (Advanced)
- Topotecan
- Intermediate

Pancreatic Cancer
- FOLFIRINOX
- Intermediate
  - Chloorean 2019; Conroy 2011; Conroy 2005; Hosein 2012; Okusaka 2014; Peddi 2012; Suker 2016; Thibodeau 2018; Tong 2018

Small Cell Lung Cancer (Extensive Stage)
- Carboplatin, etoposide, and atezolizumab
- Low
  - Horn 2018; Kosmidis 1994; Socinski 2009

Soft Tissue Sarcoma (Advanced)
- Doxorubicin
- High
  - Judson I 2014; Lorigan P 2007; Nielsen OS 1998; Seddon B 2017; Tap WD 2017; Tap WD 2020

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Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

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