This policy does not apply to health plans or member categories that do not have pharmacy benefits, nor does it apply to Medicare. Note that market specific restrictions or transition-of-care benefit limitations may apply.

CRX-ALL-0446-19
1. Age greater than 65 years; OR
2. Poor performance status (Eastern Cooperative Oncology Group 3 or 4) or HIV infection (in particular, those with low CD4 counts); OR
3. Prior chemotherapy or radiation therapy; OR
4. Bone marrow involvement by tumor producing cytopenias; OR
5. Persistent neutropenia (absolute neutrophil count [ANC] less than 1500 mm$^3$); OR
6. Poor renal function (glomerular filtration rate [GFR] less than 60 mL/min); OR
7. Liver dysfunction (liver function tests at least 2X upper limit of normal); OR
8. Recent surgery and/or the presence of open wounds;

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; 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 10$^9$/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;

OR

K. Individual has a diagnosis of acute lymphocytic leukemia (ALL); AND
L. Individual is using after completion of the first few days of initial induction chemotherapy or first post-remission course of chemotherapy (AHFS, NCCN Guidelines Acute Lymphoblastic Leukemia);

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CRX-ALL-0446-19
Market Applicability

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<th>Market</th>
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</table>

2. Poor performance status (Eastern Cooperative Oncology Group 3 or 4) or HIV infection (in particular, those with low CD4 counts); OR
3. Prior chemotherapy or radiation therapy; OR
4. Bone marrow involvement by tumor producing cytopenias; OR
5. Persistent neutropenia (absolute neutrophil count [ANC] less than 1500mm³); OR
6. Poor renal function (glomerular filtration rate [GFR] less than 60mL/min); OR
7. Liver dysfunction (liver function tests at least 2X upper limit of normal); OR
8. Recent surgery and/or the presence of open wounds;

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;

OR

J. Individual has a diagnosis of acute lymphocytic leukemia (ALL); AND
K. Individual is using after completion of the first few days of initial induction chemotherapy or first post-remission course of chemotherapy (AHFS, NCCN Guidelines Acute Lymphoblastic Leukemia);

OR

L. Individual is receiving dose dense therapy (treatment given more frequently, such as every 2 weeks instead of every 3 weeks) for adjuvant treatment of breast cancer (ASCO Smith 2015);
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CRX-ALL-0446-19
5. Persistent neutropenia (absolute neutrophil count [ANC] less than 1500mm$^3$); OR
6. Poor renal function (glomerular filtration rate [GFR] less than 60mL/min); OR
7. Liver dysfunction (liver function tests at least 2X upper limit of normal); OR
8. Recent surgery and/or the presence of open wounds;

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, pegfilgrastim, 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).

State Specific Mandates

<table>
<thead>
<tr>
<th>State name</th>
<th>Date effective</th>
<th>Mandate details (including specific bill if applicable)</th>
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<tr>
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Key References:

4. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2018; Updated periodically.