Clinical Policy: Filgrastim (Neupogen), Filgrastim-sndz (Zarxio), Tbo-filgrastim (Granix), Filgrastim-aafi (Nivestym), Filgrastim-ayow (Releuko), Filgrastim-txid (Nypozi), Filgrastim-laha (Filkri)

Reference Number: CP.PHAR.297
Effective Date: 12.01.16
Last Review Date: 08.25
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Filgrastim (Neupogen®) and its biosimilars, filgrastim-sndz (Zarxio®), filgrastim-aafi (Nivestym™), filgrastim-ayow (Releuko®), filgrastim-txid (Nypozi™), tbo-filgrastim (Granix®), and filgrastim-laha (Filkri®), are human granulocyte colony-stimulating factors.

FDA Approved Indication(s)

Granix is indicated to reduce the duration of severe neutropenia in adult and pediatric patients 1 month and older with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia (FN).

Filkri, Neupogen, Nivestym, Nypozi, Releuko, and Zarxio are indicated to:

- Mobilize autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis (*excluding Filkri*).
- Decrease the incidence of infection, as manifested by FN, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever.
- Reduce the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML).
- Reduce the duration of neutropenia and neutropenia-related clinical sequelae, e.g., FN, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation (BMT).
- Reduce the incidence and duration of sequelae of severe neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia.

Filkri, Neupogen, Nypozi, Releuko, and Zarxio are also indicated to increase survival in patients acutely exposed to myelosuppressive doses of radiation (hematopoietic syndrome of acute radiation syndrome).

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Filkri, Granix, Neupogen, Nivestym, Nypozi, Releuko, and Zarxio are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Chemotherapy-Induced Neutropenia (must meet all)**:**

1. Diagnosis of non-myeloid malignancy (i.e., solid tumor and lymphoid malignancies) or AML;
2. Prescribed for use following myelosuppressive chemotherapy;
3. For Filkri, Neupogen, Nivestym, Nypozi, Releuko, or Granix requests, member meets one of the following (a, b, or c): ≠
   ≠*For Illinois HIM requests, the step therapy requirements below do not apply as of 1/1/2026 per IL HB 5395, unless biosimilar is interchangeable per FDA Purple Book.*
   a. Member must use Zarxio*;
      **Prior authorization may be required for Zarxio*
   b. If member has intolerance or contraindication to Zarxio, member must use Nivestym*, unless contraindicated or clinically significant adverse effects are experienced;
      **Prior authorization may be required for Nivestym*
   c. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E)*;
4. The requested medication will not be prescribed concurrently with other colony stimulating factors (e.g., pegfilgrastim, Leukine®) within any chemotherapy cycle;
5. For members receiving palliative chemotherapy, provider attestation that chemotherapy dose reduction has been considered;
6. Documentation of member's current weight (in kg);
7. Dose does not exceed 30 mcg/kg per day [IV] or 24 mcg/kg per day [SC] (*see Appendix F for dose rounding guidelines*).

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

B. Bone Marrow Transplantation (must meet all)**:**

1. Diagnosis of non-myeloid malignancy (i.e., solid tumor and lymphoid malignancies);
2. Member is undergoing myeloablative chemotherapy followed by BMT;
3. For Filkri, Neupogen, Nivestym, Nypozi, Releuko, or Granix requests, member meets one of the following (a, b, or c): ≠
   ≠*For Illinois HIM requests, the step therapy requirements below do not apply as of 1/1/2026 per IL HB 5395, unless biosimilar is interchangeable per FDA Purple Book.*
   a. Member must use Zarxio*;
      **Prior authorization may be required for Zarxio*
   b. If member has intolerance or contraindication to Zarxio, member must use Nivestym*, unless contraindicated or clinically significant adverse effects are experienced;
      **Prior authorization may be required for Nivestym*

c. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E)*;

4. The requested medication will not be prescribed concurrently with other colony stimulating factors (e.g., pegfilgrastim, Leukine) within any chemotherapy cycle;
5. Documentation of member's current weight (in kg);
6. Dose does not exceed 10 mcg/kg per day [IV] (*see Appendix F for dose rounding guidelines*).

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

C. Peripheral Blood Progenitor Cell Collection (must meet all)**:**

1. Prescribed for the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis;
2. The prescribed drug will be initiated before leukapheresis (e.g., prescribed for 6 to 7 days with leukapheresis on days 5, 6 and 7);
3. For Filkri, Neupogen, Nivestym, Nypozi, Releuko, or Granix requests, member meets one of the following (a, b, or c): ≠

   ≠*For Illinois HIM requests, the step therapy requirements below do not apply as of 1/1/2026 per IL HB 5395, unless biosimilar is interchangeable per FDA Purple Book.*

   a. Member must use Zarxio*;
      **Prior authorization may be required for Zarxio*
   b. If member has intolerance or contraindication to Zarxio, member must use Nivestym*, unless contraindicated or clinically significant adverse effects are experienced;
      **Prior authorization may be required for Nivestym*
   c. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E)*;
4. The requested medication will not be prescribed concurrently with other colony stimulating factors (e.g., pegfilgrastim, Leukine) within any chemotherapy cycle;
5. Documentation of member's current weight (in kg);
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 10 mcg/kg per day [IV or SC] (*see Appendix F for dose rounding guidelines*);
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approved duration: 1 month

D. Chronic Neutropenia (must meet all)**:**

1. Prescribed for use in symptomatic (e.g., fever, infections, oropharyngeal ulcers) severe chronic neutropenia caused by congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia;
2. For Filkri, Neupogen, Nivestym, Nypozi, Releuko, or Granix requests, member meets one of the following (a, b, or c): ≠

≠For Illinois HIM requests, the step therapy requirements below do not apply as of 1/1/2026 per IL HB 5395, unless biosimilar is interchangeable per FDA Purple Book.

a. Member must use Zarxio*;
**Prior authorization may be required for Zarxio*
b. If member has intolerance or contraindication to Zarxio, member must use Nivestym*, unless contraindicated or clinically significant adverse effects are experienced;
**Prior authorization may be required for Nivestym*
c. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E)*;

3. The requested medication will not be prescribed concurrently with other colony stimulating factors (e.g., pegfilgrastim, Leukine) within any chemotherapy cycle;
4. Documentation of member's current weight (in kg);
5. Dose does not exceed: 30 mcg/kg per day [IV] or 24 mcg/kg per day [SC] (*see Appendix F for dose rounding guidelines*).

Approved duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

E. Acute Radiation Syndrome (must meet all)**:**

1. Prescribed for use following suspected or confirmed acute exposure to myelosuppressive doses of radiation;
2. For Filkri, Neupogen, Nivestym, Nypozi, Releuko, or Granix requests, member meets one of the following (a, b, or c): ≠

≠For Illinois HIM requests, the step therapy requirements below do not apply as of 1/1/2026 per IL HB 5395, unless biosimilar is interchangeable per FDA Purple Book.

a. Member must use Zarxio*;
**Prior authorization may be required for Zarxio*
b. If member has intolerance or contraindication to Zarxio, member must use Nivestym*, unless contraindicated or clinically significant adverse effects are experienced;
**Prior authorization may be required for Nivestym*
c. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E)*;

3. The requested medication will not be prescribed concurrently with other colony stimulating factors (e.g., pegfilgrastim, Leukine) within any chemotherapy cycle;
4. Documentation of member's current weight (in kg);
5. Dose does not exceed 10 mcg/kg per day [SC] (*see Appendix F for dose rounding guidelines*).

Approved duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

F. Myelodysplastic Syndrome (off-label) (must meet all)**:**

1. Diagnosis of myelodysplastic syndrome with symptomatic anemia without del (5q) abnormality;

2. Current (within the past 30 days) serum erythropoietin level ≤ 500 mU/mL;
3. Member previously has no response to either an erythropoiesis-stimulating agent (e.g., epoetin alfa, darbepoetin) or Reblozyl®;
4. Prescribed in combination with an erythropoiesis-stimulating agent (e.g., epoetin alfa);
5. For Filkri, Neupogen, Nivestym, Nypozi, Releuko, or Granix requests, member meets one of the following (a, b, or c): ≠

   ≠For Illinois HIM requests, the step therapy requirements below do not apply as of 1/1/2026 per IL HB 5395, unless biosimilar is interchangeable per FDA Purple Book.

   a. Member must use Zarxio*;
      **Prior authorization may be required for Zarxio*
   b. If member has intolerance or contraindication to Zarxio, member must use Nivestym*, unless contraindicated or clinically significant adverse effects are experienced;
      **Prior authorization may be required for Nivestym*
   c. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E)*;
6. The requested medication will not be prescribed concurrently with other colony stimulating factors (e.g., pegfilgrastim, Leukine) within any chemotherapy cycle;
7. Documentation of member's current weight (in kg);
8. Request meets one of the following (a or b):
   a. Dose does not exceed 2 mcg/kg twice a week [SC] (*see Appendix F for dose rounding guidelines*);
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approved duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

G. Wilms Tumor (off-label) (must meet all)**:**
1. Diagnosis of Wilms tumor (nephroblastoma);
2. Request is for supportive care for member receiving a regimen of cyclophosphamide and etoposide, or cyclophosphamide, doxorubicin, and vincristine in Regimen M and Regimen I (*see Appendix D*);
3. For Filkri, Neupogen, Nivestym, Nypozi, Releuko, or Granix requests, member meets one of the following (a, b, or c): ≠

   ≠For Illinois HIM requests, the step therapy requirements below do not apply as of 1/1/2026 per IL HB 5395, unless biosimilar is interchangeable per FDA Purple Book.

   a. Member must use Zarxio*;
      **Prior authorization may be required for Zarxio*
   b. If member has intolerance or contraindication to Zarxio, member must use Nivestym*, unless contraindicated or clinically significant adverse effects are experienced;
      **Prior authorization may be required for Nivestym*
   c. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E)*;

4. The requested medication will not be prescribed concurrently with other colony stimulating factors (e.g., pegfilgrastim, Leukine) within any chemotherapy cycle;
5. Documentation of member's current weight (in kg);
6. Request meets one of the following (a or b):
   a. Dose does not exceed 30 mcg/kg per day [IV] or 24 mcg/kg per day [SC] (*see Appendix F for dose rounding guidelines*);
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approved duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

H. Other diagnoses/indications (must meet all)**:**

1. For Filkri, Neupogen, Nivestym, Nypozi, Releuko, or Granix requests, member meets one of the following (a, b, or c): [≠]
   [≠]*For Illinois HIM requests, the step therapy requirements below do not apply as of 1/1/2026 per IL HB 5395, unless biosimilar is interchangeable per FDA Purple Book.*
   a. Member must use Zarxio*;
      **Prior authorization may be required for Zarxio*
   b. If member has intolerance or contraindication to Zarxio, member must use Nivestym*, unless contraindicated or clinically significant adverse effects are experienced;
      **Prior authorization may be required for Nivestym*
   c. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E)*;
2. One of the following (a or b):
   a. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (i or ii):
      i. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
      ii. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
   b. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 2a above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Peripheral Blood Progenitor Cell Collection

1. Re-authorization is not permitted. Members must meet the initial approval criteria.

Approval duration: Not applicable

B. All Other Indications in Section I (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy;
3. For Filkri, Neupogen, Nivestym, Nypozi, Releuko, or Granix requests, member meets one of the following (a, b, or c): ≠
   ≠*For Illinois HIM requests, the step therapy requirements below do not apply as of 1/1/2026 per IL HB 5395, unless biosimilar is interchangeable per FDA Purple Book.*
   a. Member must use Zarxio*;
      **Prior authorization may be required for Zarxio*
   b. If member has intolerance or contraindication to Zarxio, member must use Nivestym*, unless contraindicated or clinically significant adverse effects are experienced;
      **Prior authorization may be required for Nivestym*
   c. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E*);
4. The requested medication will not be prescribed concurrently with other colony stimulating factors (e.g., pegfilgrastim, Leukine) within any chemotherapy cycle;
5. Documentation of member's current weight (in kg);
6. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed the FDA-approved maximum recommended dose for the relevant indication in Section V (*see Appendix F for dose rounding guidelines*);
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

C. Other diagnoses/indications (must meet all)**:**

1. For Filkri, Neupogen, Nivestym, Nypozi, Releuko, or Granix requests, member meets one of the following (a, b, or c): ≠
   ≠*For Illinois HIM requests, the step therapy requirements below do not apply as of 1/1/2026 per IL HB 5395, unless biosimilar is interchangeable per FDA Purple Book.*
   a. Member must use Zarxio*;
      **Prior authorization may be required for Zarxio*
   b. If member has intolerance or contraindication to Zarxio, member must use Nivestym*, unless contraindicated or clinically significant adverse effects are experienced;
      **Prior authorization may be required for Nivestym*

c. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E)*;

2. One of the following (a or b):
   a. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (i or ii):
      i. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
      ii. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
   b. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 2a above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AML: acute myeloid leukemia
ANC: absolute neutrophil count
BMT: bone marrow transplantation
FDA: Food and Drug Administration
FN: febrile neutropenia
G-CSF: granulocyte colony-stimulating factor

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): history of serious allergic reactions to human granulocyte colony-stimulating factors such as filgrastim products or pegfilgrastim products
- Boxed warning(s): none reported

Appendix D: General Information

- Zarxio and Filkri are not recommended in patients requiring direct administration of less than 0.3 mL due to the potential for dosing errors. The spring-mechanism of the needle guard apparatus affixed to the prefilled syringe interferes with the visibility of the graduation markings on the syringe barrel corresponding to 0.1 mL and 0.2 mL. The

visibility of these markings is necessary to accurately measure doses of Zarxio and Filkri less than 0.3 mL (180 mcg).

- Neutropenia is defined as an absolute neutrophil count (ANC) of < 500 neutrophils/mcL or an ANC of < 1,000 neutrophils/mcL and a predicted decline to ≤ 500 neutrophils/mcL over the next 48 hours. Neutropenia can progress to FN, defined as a single temperature of ≥ 38.8ºC orally or ≥ 38.0ºC over 1 hour.
- The development of febrile neutropenia is a common dose-limiting toxicity of many chemotherapy regimens. This risk is directly related to the intensity of the chemotherapy regimen. Chemotherapy regimens that have an incidence of febrile neutropenia greater than 20% in clinical trials in chemotherapy naïve patients are considered by the National Comprehensive Cancer Network (NCCN) panel at high risk. Prophylaxis with myeloid growth factors is recommended at this level of risk (Category 1 recommendation). NCCN Compendium recommend prophylaxis be considered in intermediate-risk (10-20% overall risk of FN) and low-risk (< 10% overall risk of FN) patients (Category 2A recommendation). In addition to chemotherapy regimens, other risk factors such as: treatment-related, patient related, cancer-related, and co-morbidities have also been associated with an increased risk of febrile neutropenia. Therefore, the type of chemotherapy regimen is only one component of the risk assessment.
- For chemotherapy patients, continuing filgrastim until the ANC has reached 10,000/mm^3 following the expected chemotherapy-induced neutrophil nadir (as specified in the G-CSF package insert), is known to be safe and effective. However, a shorter duration of administration that is sufficient to achieve clinically adequate neutrophil recovery is a reasonable alternative, considering issues of patient convenience and cost.[5]
- There are insufficient data to support the use of filgrastim to treat febrile neutropenia in patients who have received prophylactic Neulasta.
- In a randomized, double-blind, multi-center safety and efficacy study of 218 breast cancer patients receiving chemotherapy with a high risk of neutropenia, Zarxio was non-inferior to Neupogen on the primary endpoint of duration of severe neutropenia (1.17 days for Zarxio and 1.20 days for Neupogen).
- NCCN guidelines for myelodysplastic syndrome list filgrastim with a category 2A recommendation for use as initial treatment of symptomatic anemia in lower risk disease with no del (5q), serum erythropoietin levels ≤500 mU/mL, and ring sideroblasts ≥15%. Filgrastim may also be considered for the treatment of symptomatic anemia in lower risk disease with serum erythropoietin levels ≤500 mU/mL, and ring sideroblasts <15% when these is no response or erythroid response followed by loss of response to epoetin or darbepoetin alone (category 2A recommendation).
- For patients with a latex allergy, Granix (tbo-filgrastim) and Nivestym (filgrastim-aafi) are considered to be latex free. For Neupogen (filgrastim), Nypozi (filgrastim-txid), and Zarxio (filgrastim-sndz), the presence of latex cannot definitively be ruled out. Filkri (filgrastim-laha) should not be used in these patients as the needle cap on the prefilled syringe contains latex.
- According to the ASCO, 2006 Clinical Practice Guideline for the Use of White Blood Cell Growth Factors, dose reduction or delay remains an appropriate strategy for the palliative treatment of cancer, as there is no evidence that dose maintenance or escalation improves clinically important outcomes in this setting. The 2015 updates to this guideline

found no new data supporting the use of colony-stimulating factors (CSFs) to maintain dose-intensity in the treatment of metastatic disease, and the review found no demonstrable benefit in the use of myeloid growth factors to in patients with metastatic lung, small-cell lung, colorectal, hormone-refractory prostate, or breast cancer. To date, there have been no improvements in disease-free or OS reported for any common cancer with the use of CSFs to maintain dose-intensity, instead of dose reduction. The ASCO Panel recognizes that there may be individual patients who will not tolerate effective doses of chemotherapy without CSFs. Medical Oncologists making the decision to use prophylactic MGFs, or not, may need to consider not only the optimal chemotherapy regimen, but also the individual member risk factors and the intention of treatment; that is, curative, prolongation of life, or symptom control and palliation.

- For mobilization of hematopoietic progenitor cells in the autologous setting, NCCN myeloid growth factor treatment guidelines include a dosing range from 10 to 32 mcg/kg/day by subcutaneous injection, in daily or twice-daily dosing, when used as a single-agent growth factor.
- Chemotherapy regimens used in the treatment of Wilms Tumor for which filgrastim supportive care may be considered:
  - Regimen M: 9 doses of vincristine, 5 doses of dactinomycin, 5 doses of doxorubicin (cumulative dose 150 mg/m2), 4 courses of 5 daily doses of cyclophosphamide, and 4 courses of 5 daily doses of etoposide over 24 weeks. Dactinomycin and doxorubicin are given together, and cyclophosphamide and etoposide are given together.
  - Regimen I: 9 doses of vincristine, 4 doses of doxorubicin (cumulative dose 180 mg/m2), 7 courses of 3 to 5 daily doses of cyclophosphamide, and 3 courses of 5 daily doses of etoposide. Doxorubicin and 3 daily doses of cyclophosphamide are given together, and 5 daily doses of cyclophosphamide and etoposide are given together.

Appendix E: States with Regulations against Redirections in Cancer

State	Step Therapy Prohibited?	Notes
FL	Yes	For stage 4 metastatic cancer and associated conditions.
GA	Yes	For stage 4 metastatic cancer. Redirection does not refer to review of medical necessity or clinical appropriateness.
IA	Yes	For standard of care stage 4 cancer drug use, supported by peer-reviewed, evidence-based literature, and approved by FDA.
IN	Yes	For advanced, metastatic cancer and associated conditions
LA	Yes[≠]	For stage 4 advanced, metastatic cancer or associated conditions. [≠]Exception if clinically equivalent therapy, contains identical active ingredient(s), and proven to have same efficacy.
MS	Yes	For advanced metastatic cancer and associated conditions
NV	Yes	Stage 3 and stage 4 cancer patients for a prescription drug to treat the cancer or any symptom thereof of the covered person
OH	Yes	For stage 4 metastatic cancer and associated conditions
OK	Yes	For advanced metastatic cancer and associated conditions
PA	Yes	For stage 4 advanced, metastatic cancer

State	Step Therapy Prohibited?	Notes
TN	Yes^	For stage 4 advanced metastatic cancer, metastatic blood cancer, and associated conditions ^Exception if step therapy is for AB-rated generic equivalent, interchangeable biological product, or biosimilar product to the equivalent brand drug
TX	Yes	For stage 4 advanced, metastatic cancer and associated conditions

*Appendix F: Dose Rounding Guidelines**

Weight-based Dose Range	Vial Quantity Recommendation
≤ 314.99 mcg	1 vial of 300 mcg/1 mL
315-503.99 mcg	1 vial of 480 mcg/1.6 mL
315-629.99 mcg	2 vials of 300 mcg/1 mL
630-944.99 mcg	3 vials of 300 mcg/1 mL
945-1,007.99 mcg	2 vials of 480 mcg/1.6 mL
1,008-1,511.99 mcg	3 vials of 480 mcg/1.6 mL

**This is part of a dose rounding guideline on select drug classes as part of an initiative conducted on a larger scale with multiple references and prescriber feedback.*

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Filgrastim (Neupogen), filgrastim-sndz (Zarxio) , filgrastim-aafi (Nivestym), filgrastim-ayow (Releuko), filgrastim-txid (Nypozi), filgrastim-laha (Filkri)	Chemotherapy-induced neutropenia	5 mcg/kg SC or IV QD Dose may be increased in increments of 5 mcg/kg for each chemotherapy cycle, according to the duration and severity of the ANC nadir Do not administer 24 hours before and after chemotherapy	30 mcg/kg/day [IV] or 24 mcg/kg/day [SC]
	Chronic neutropenia	Congenital: 6 mcg/kg SC BID Idiopathic or cyclic: 5 mcg/kg SC QD	30 mcg/kg/day [IV] or 24 mcg/kg/day [SC]
	BMT	10 mcg/kg IV infusion QD	10 mcg/kg/day
	Peripheral blood progenitor cell collection (*excluding Filkri)*	10 mcg/kg SC bolus or continuous infusion QD	10 mcg/kg/day
	Patients acutely exposed to	10 mcg/kg SC QD	10 mcg/kg/day

Drug Name	Indication	Dosing Regimen	Maximum Dose
	myelosuppressive doses of radiation		
Tbo-filgrastim (Granix)	Myelosuppressive chemotherapy	5 mcg/kg SC or IV QD	5 mcg/kg/day

VI. Product Availability

Drug	Availability
Filgrastim (Neupogen)	Single-dose prefilled syringes for injection: 300 mcg/0.5 mL, 480 mcg/0.8 mL Single-dose vials for injection: 300 mcg/mL, 480 mcg/1.6 mL
Filgrastim-sndz (Zarxio)	Single-dose prefilled syringes for injection: 300 mcg/0.5 mL, 480 mcg/0.8 mL Single-dose vials for injection: 300 mcg/mL, 480 mcg/1.6 mL
Filgrastim-aafi (Nivestym)	Single-dose prefilled syringes for injection: 300 mcg/0.5 mL, 480 mcg/0.8 mL Single-dose vials for injection: 300 mcg/mL, 480 mcg/1.6 mL
Filgrastim-ayow (Releuko)	Single-dose prefilled syringes for injection: 300 mcg/0.5 mL, 480 mcg/0.8 mL Single-dose vials for injection: 300 mcg/mL, 480 mcg/1.6 mL
Filgrastim-txid (Nypozi)	Single-dose prefilled syringes for injection: 300 mcg/0.5 mL, 480 mcg/0.8 mL
Tbo-filgrastim (Granix)	Single-dose prefilled syringes for injection: 300 mcg/0.5 mL, 480 mcg/0.8 mL Single-dose vials for injection: 300 mcg/mL, 480 mcg/1.6 mL
Filgrastim-laha (Filkri)	Single-dose prefilled syringes for injection: 300 mcg/0.5 mL, 480 mcg/0.8 mL

VII. References

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Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J1442	Injection, filgrastim (G-CSF), excludes biosimilars, 1 microgram
J1447	Injection, tbo-filgrastim, 1 microgram
Q5101	Injection, filgrastim-sndz, biosimilar, (Zarxio), 1 microgram
Q5110	Injection, filgrastim-aafi, biosimilar, (Nivestym), 1 microgram
Q5125	Injection, filgrastim-ayow, biosimilar, (Releuko), 1 mcg
Q5148	Injection, filgrastim-txid (Nypozi), biosimilar, 1 microgram

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2021 annual review: added NCCN compendium supported off-label use in Wilms tumor; references reviewed and updated.	05.05.21	08.21
Added Nevada to Appendix E.	08.03.21	
RT4: added Releuko to policy; revised redirection bypass language to indicate it applies more generally for a State with regulations against step therapy in certain oncology settings.	03.10.22	
3Q 2022 annual review: removed general description of "stage IV or metastatic" cancer for states with regulations against redirections; applied redirection bypass for State with regulations against step therapy to all indications; added requirement that requested medication will not be prescribed concurrently with other colony stimulating factors (e.g., pegfilgrastim, Leukine) within any chemotherapy cycle; clarified non-myeloid malignancy refers to solid tumor and lymphoid malignancies; added unclassified biologics HCPCS code for Releuko; reference reviewed and updated. Added HCPCS code for Releuko [C9096].	04.20.22	08.22
Added HCPCS code [Q5125]. Template changes applied to other diagnoses/indications and continued therapy section.	09.09.22	
3Q 2023 annual review: for MDS added requirement per NCCN to be prescribed in combination with an erythropoiesis-stimulating agent; removed inactive HCPCS codes C9096, C9399, J3590; per May SDC if member is unable to use Zarxio, added stepwise redirection to use Nivestym; references reviewed and updated; updated Appendix E to include Oklahoma.	04.18.23	08.23
Updated Appendix E to include Mississippi.	06.05.24	
3Q 2024 annual review: per NCCN Compendium for MDS added requirement that member previously has no response to either an	07.08.24	08.24

Reviews, Revisions, and Approvals	Date	P&T Approval Date
erythropoiesis-stimulating agent (e.g., epoetin alfa, darbepoetin) or Reblozyl; for BMT removed SC route of administration per prescribing information; to confirm weight-based dosing added requirement for documentation of member's current weight (in kg); references reviewed and updated. RT4: added Nypozi to policy.		
RT4: added Zarxio single-dose vials to product availability.	08.19.24	
RT4: updated FDA-approved indications for Zarxio to include use in hematopoietic syndrome of acute radiation syndrome per updated prescribing information. HCPCS code added [C9173].	11.19.24	
HCPCS code added [Q5148].	02.13.25	
3Q 2025 annual review: RT4: per updated prescribing information, added Releuko to indications for mobilizing autologous hematopoietic progenitor cells for collection by leukapheresis and to increase survival in patients acutely exposed to myelosuppressive doses of radiation; updated Appendix E with revised language and exception for Tennessee; references reviewed and updated.	04.14.25	08.25
RT4: added Filkri to policy; revised peripheral blood progenitor cell collection initial approval duration for Commercial line of business to 1 month and for all other indications, revised initial approval durations for Medicaid/HIM to 12 months; for continued therapy of peripheral blood progenitor cell collection, added exclusion for re-authorization and that member must meet the initial approval criteria; revised continued therapy Medicaid/HIM approval duration for all other indications to 12 months; removed HCPCS code C9173. Added step therapy bypass for IL HIM per IL HB 5395.	03.11.26	
For Appendix E, added state IN.	03.26.26	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.