

**Clinical Policy: Blood Formation, Coagulation, and Thrombosis Agents:  
Colony Stimulating Factors**

Reference Number: OH.PHAR.PPA.25

Effective Date: 01.20

Last Review Date: 07.20

Line of Business: Medicaid

[Coding Implications](#)

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

**BLOOD AGENTS: HEMATOPOIETIC AGENTS – COLONY-STIMULATING FACTORS**

CLINICAL PA REQUIRED “PREFERRED”	PA REQUIRED “NON-PREFERRED”
GRANIX <sup>®</sup> (tbo-filgrastim) UDENYCA <sup>®</sup> (pegfilgrastim-cbqv); ZIEXTENZO <sup>™</sup> (pegfilgrastim-mez)	FULPHILA <sup>™</sup> (pegfilgrastim-jmdb) LEUKINE <sup>®</sup> (sargramostim) NEULASTA <sup>®</sup> (pegfilgrastim) NEUPOGEN <sup>®</sup> (filgrastim) NIVESTYM <sup>™</sup> (filgrastim-aafi) ZARXIO <sup>®</sup> (filgrastim-sndz)

**Description**

The following are colony-stimulating factors requiring clinical prior authorization: tbo-filgrastim (Granix<sup>®</sup>) and pegfilgrastim-cbqv (Udenyca<sup>®</sup>)

The following are colony-stimulating factors requiring prior authorization: filgrastim (Neupogen<sup>®</sup>) filgrastim-sndz (Zarxio<sup>®</sup>), filgrastim-aafi (Nivestym<sup>™</sup>), pegfilgrastim (Neulasta<sup>®</sup>), pegfilgrastim-jmdb (Fulphila<sup>™</sup>), and sargramostim (Leukine<sup>®</sup>).

**FDA Approved Indication(s)**

**Filgrastim product(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).

Neupogen, Nivestym, and Zarxio are indicated to:

- Decrease the incidence of infection, as manifested by FN, in patients with non-myeloid 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 non-myeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation (BMT)
- Mobilize autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis
- 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

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Neupogen is also indicated to increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome [H-ARS])

**Pegfilgrastim product(s):**

Neulasta, Fulphila, and Udenyca are indicated to decrease the incidence of infection, as manifested by FN, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of FN.

Neulasta is also indicated to increase survival in patients acutely exposed to myelosuppressive doses of radiation (H-ARS)

Limitation(s) of use: Neulasta, Fulphila, and Udenyca are not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation.

**Sargramostim product(s):**

Leukine is indicated to:

- Reduce the time to neutrophil recovery and to reduce the incidence of severe and life-threatening infections and infections resulting in death following induction chemotherapy in adult patients 55 years and older with acute myeloid leukemia (AML)
- Mobilize hematopoietic progenitor cells into peripheral blood for collection by leukapheresis and autologous transplantation in adult patients
- Accelerate myeloid reconstitution following autologous peripheral blood progenitor cell (PBPC) or BMT in adult and pediatric patients 2 years of age and older with non-Hodgkin's lymphoma (NHL), acute lymphoblastic leukemia (ALL) and Hodgkin's lymphoma (HL)
- Accelerate myeloid reconstitution following allogeneic BMT in adult and pediatric patients 2 years of age and older
- Treat delayed neutrophil recovery or graft failure after autologous or allogeneic BMT in adult and pediatric patients 2 years of age and older
- Increase survival in adult and pediatric patients from birth to 17 years of age acutely exposed to myelosuppressive doses of radiation (H-ARS)

**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 Buckeye Health Plan, an affiliate of Centene Corporation® that Granix; Udenyca; Fulphila; Leukine; Neulasta; Neupogen; Nivestym; Zarxio is **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria**

**A. Acute Myeloid Leukemia (must meet all):**

1. Diagnosis of AML;
2. Prescribed for use following induction therapy for AML;
3. Age  $\geq$  55 years;

4. For non-preferred medication requests, meets one of the following (a or b):
  - a. Member has failed therapeutic trials of 14 days with preferred medications
  - b. Member is unable to use a medication not requiring prior approval due to one of the following (i, ii, or iii):
    - i. Allergy
    - ii. Contraindication or drug interaction
    - iii. History of unacceptable/toxic side effects
5. Dose does not exceed the following:
  - a. Leukine: 250 mcg/m<sup>2</sup> IV daily
  - b. Granix, Neupogen, Zarxio, Nivestym: 30 mcg/kg per day [IV] or 24 mcg/kg per day [SC]

**Approval Duration: 14 days or duration of chemotherapy**

**B. Hematopoietic Syndrome of Acute Radiation Syndrome [H-ARS] (must meet all):**

1. Prescribed for use following suspected or confirmed acute exposure to myelosuppressive doses of radiation;
  2. For non-preferred medication requests, meets one of the following (a or b):
    - a. Member has failed therapeutic trials of 14 days with preferred medications
    - b. Member is unable to use a medication not requiring prior approval due to one of the following (i, ii, or iii):
      - i. Allergy
      - ii. Contraindication or drug interaction
      - iii. History of unacceptable/toxic side effects
  3. Dose does not exceed the following:
    - a. Granix, Neupogen, Nivestym, Zarxio: 10 mcg/kg per day [SC]
    - b. Udenyca, Neulasta, Fulphila: two (2) 6 mg doses administered one week apart
    - c. Leukine: 12 mcg/kg daily (See Section V for specific weight-based dosing)
- Approval Duration: 30 days**

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

1. Diagnosis of non-myeloid malignancy;
2. Prescribed for use following myelosuppressive chemotherapy;
3. For non-preferred medication requests, must meet one of the following (a or b):
  - a. Member has failed therapeutic trials of 14 days with preferred medications
  - b. Member is unable to use a medication not requiring prior approval due to one of the following (i, ii, or iii):
    - i. Allergy
    - ii. Contraindication or drug interaction
    - iii. History of unacceptable/toxic side effects
4. Dose does not exceed the following:
  - a. Granix, Neupogen, Zarxio, Nivestym: 30 mcg/kg per day [IV] or 24 mcg/kg per day [SC]
  - b. Udenyca, Neulasta, Fulphila: 6 mg (1 syringe) per chemotherapy cycle

**Approval Duration: 14 days or duration of chemotherapy regimen**

**D. Bone Marrow Transplantation (BMT)**

1. **Filgrastim products** (must meet a, b, c, and d):
  - a. Diagnosis of non-myeloid malignancy;
  - b. Member is undergoing myeloablative chemotherapy following BMT;
  - c. For non-preferred medication requests, must meet one of the following (i or ii):
    - i. Member has failed therapeutic trails of 14 days with preferred medications
    - ii. Member is unable to use a medication not requiring prior approval due to one of the following (1, 2, or 3):
      - 1) Allergy
      - 2) Contraindication or drug interaction
      - 3) History of unacceptable/toxic side effects
  - d. Dose does not exceed 10 mcg/kg per day [IV or SC]
2. **Leukine** (must meet a, b, c, and d):
  - a. Prescribed for use in one of the following settings (i, ii, or iii):
    - i. Following autologous BMT in members with NHL, ALL, or HL for acceleration of myeloid reconstitution;
    - ii. Following allogeneic BMT for acceleration of myeloid reconstitution;
    - iii. Following BMT where engraftment is delayed or has failed;
  - b. Age  $\geq$  2 years;
  - c. For non-preferred medication requests, must meet one of the following (i or ii):
    - i. Member has failed therapeutic trails of 14 days with preferred medications
    - ii. Member is unable to use a medication not requiring prior approval due to one of the following (1, 2, or 3):
      - 1) Allergy
      - 2) Contraindication or drug interaction
      - 3) History of unacceptable/toxic side effects
  - d. Dose does not exceed 500 mcg/m<sup>2</sup> IV daily

**Approval Duration:**

- **Undergoing myeloablative chemotherapy prior to allogeneic or autologous bone marrow transplantation – 14 days or duration of chemotherapy regimen**
- **Myeloid Engraftment for BMT – 30 days**

**E. Severe, Chronic Neutropenia (filgrastim products only)** (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 non-preferred medication requests, must meet one of the following (a or b):
  - a. Member has failed therapeutic trails of 14 days with preferred medications
  - b. Member is unable to use a medication not requiring prior approval due to one of the following (I, ii, or iii):
    - i. Allergy
    - ii. Contraindication or drug interaction
    - iii. History of unacceptable/toxic side effects
  - c. Dose does not exceed: 30 mcg/kg per day [IV] or 24 mcg/kg per day [SC]

**Approval Duration: 30 days or duration of chemotherapy regimen**

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**II. Diagnoses/Indications for which coverage is NOT authorized:**

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.PMN.53 for Medicaid or evidence of coverage documents.

**III. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

FDA: Food and Drug Administration

PA: Prior Authorization

ER: Extended Release

*Appendix B: Therapeutic Alternatives*

*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.*

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Granix (tbofilgrastim),	<b>Myelosuppressive chemotherapy</b> 5 mcg/kg SC or IV QD	5 mcg/kg/day
pegfilgrastimcbqv (Udenyca)	<b>Myelosuppressive chemotherapy</b> 6 mg administered SC once per chemotherapy cycle. Do not administer between 14 days before and 24 hours after administration of cytotoxic chemotherapy. Weight based dosing for pediatric patients < 45 kg	6 mg/dose

*Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.*

*Appendix C: Contraindications/Boxed Warnings*

- See package insert; clinical pharmacology or other appropriate clinical reference.

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- IV. Dosage and Administration:** varies by drug product. See package insert; clinical pharmacology or other appropriate clinical reference for FDA approved dosing and administration.
  
- V. Product Availability:** varies by drug product. See package insert; clinical pharmacology or other appropriate clinical reference for product availability.
  
- VI. References.** Refer to package insert.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	10.19	
Added Ziextenzo (pegfilgrastim-mez) to list of Clinical PA Required “Preferred” agents	07.20	

**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



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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.

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**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.

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