Corporate Medical Policy: White Blood Cell Growth Factors **"Notification"** **POLICY EFFECTIVE JULY 1, 2026**

Restricted Product(s):

- pegfilgrastim-unne (Armlupeg®) subcutaneous injection for administration by a healthcare professional
- filgrastim-laha (Filkri®) intravenous infusion or subcutaneous injection for administration by a healthcare professional
- tbo-filgrastim (Granix®) subcutaneous injection for administration by a healthcare professional
- sargramostim (Leukine®) intravenous infusion or subcutaneous injection for administration by a healthcare professional
- pegfilgrastim (Neulasta®, Neulasta® OnPro®) subcutaneous injection for administration by a healthcare professional
- filgrastim (Neupogen®) intravenous infusion or subcutaneous injection for administration by a healthcare professional
- filgrastim-txid (Nypozi®) intravenous infusion or subcutaneous injection for administration by a healthcare professional
- pegfilgrastim-apgf (Nyvepria®) subcutaneous injection for administration by a healthcare professional
- filgrastim-ayow (Releuko®) intravenous infusion or subcutaneous injection for administration by a healthcare professional
- eflapegrastim-xnst (Rolvedon®) subcutaneous injection for administration by a healthcare professional
- efbemalenograstim alfa-vuxw (Ryzneuta®) subcutaneous injection for administration by a healthcare professional
- pegfilgrastim-fpgk (Stimufend®) subcutaneous injection for administration by a healthcare professional
- pegfilgrastim-cbqv (Udenyca®, Udenyca Onbody®) subcutaneous injection for administration by a healthcare professional
- pegfilgrastim-bmez (Ziextenzo®) subcutaneous injection for administration by a healthcare professional

Preferred Filgrastim Products (Unrestricted)	**Non-Preferred Short-Acting/Filgrastim Products**
Nivestym® (filgrastim-aafi) Zarxio® (filgrastim-sndz)	Neupogen® (filgrastim) Filkri® (filgrastim-laha) Granix® (tbo-filgrastim) Nypozi® (filgrastim-txid) Releuko® (filgrastim-ayow)

Preferred Pegfilgrastim Products (Unrestricted)	**Non-Preferred Long-Acting/Pegfilgrastim Products**
Fulphila® (pegfilgrastim-jmdb) Fylnetra® (pegfilgrastim-pbbk)	Neulasta®, Neulasta® OnPro® (pegfilgrastim) Armlupeg® (pegfilgrastim-unne) Nyvepria® (pegfilgrastim-apgf) Stimufend® (pegfilgrastim-fpgk) Udenyca®, Udenyca Onbody® (pegfilgrastim-cbqv) Ziextenzo® (pegfilgrastim-bmez) Rolvedon® (eflapegrastim-xnst) Ryzneuta® (efbemalenograstim alfa-vuxw)

FDA Approved Use:

- Pegfilgrastim containing products (pegfilgrastim [Neulasta®, Neulasta® OnPro®], pegfilgrastim-unne [Armlupeg®], pegfilgrastim-jmdb [Fulphila®], pegfilgrastim-pbbk [Fylnetra®], pegfilgrastim-apgf [Nyvepria®], pegfilgrastim-fpgk [Stimufend®], pegfilgrastim-cbqv [Udenyca®, Udenyca Onbody®], pegfilgrastim-bmez [Ziextenzo®])
  - To decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia
  - To increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Subsyndrome of Acute Radiation Syndrome)
  - Limitations of use: Not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation
- Tbo-filgrastim (Granix®)
  - For reduction in the duration of severe neutropenia in adult and pediatric patients 1 month and older with non-myeloid malignancies receiving myelosuppressive anticancer drugs associated with a clinically significant incidence of febrile neutropenia
- Sargramostim (Leukine®)
  - To shorten 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 adults 55 years and older with acute myeloid leukemia (AML)
  - For the mobilization of hematopoietic progenitor cells into peripheral blood for collection by leukapheresis and autologous transplantation in adults
  - For the acceleration of myeloid reconstitution following autologous bone marrow or peripheral blood progenitor cell transplantation in adult and pediatric patients 2 years of age and older
  - For the acceleration of myeloid reconstitution following allogeneic bone marrow transplantation in adult and pediatric patients 2 years of age and older
  - For the treatment of delayed neutrophil recovery or graft failure after autologous or allogeneic bone marrow transplantation in adult and pediatric patients 2 years of age and older
  - To increase survival in adult and pediatric patients from birth to 17 years of age acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome [H-ARS])
- Filgrastim containing products (filgrastim [Neupogen®], filgrastim-laha [Filkri®], filgrastim-aafi [Nivestym®], filgrastim-txid [Nypozi®], filgrastim-ayow [Releuko®], filgrastim-sndz [Zarxio®])
  - To decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia
  - To reduce the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML)
  - To reduce the duration of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia, in patients with non-myeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation (BMT)

  - To mobilize autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis
  - To 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
  - To increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome)
- Eflapegrastim-xnst (Rolvedon®)
  - To decrease the incidence of infection, as manifested by febrile neutropenia, in adults with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with clinically significant incidence of febrile neutropenia
  - Limitations of use: Not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation
- Efbemalenograstim alfa-vuxw (Ryzneuta®)
  - To decrease the incidence of infection, as manifested by febrile neutropenia, in adults with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with clinically significant incidence of febrile neutropenia
  - Limitations of use: Not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation

Criteria for Medical Necessity:

The restricted product(s) may be considered medically necessary when the following criteria are met:

1. The request is for **Neulasta**, **Neulasta OnPro**, **Armlupeg**, **Nyvepria**, **Rolvedon**, **Ryzneuta**, **Stimufend**, **Udenyca**, **Udenyca Onbody**, or **Ziextenzo**:
   a. If the request is for Neulasta (pegfilgrastim), Rolvedon (eflapegrastim-xnst), Ryzneuta (efbemalenograstim alfa-vuxw), or non-preferred pegfilgrastim biosimilars (e.g., Armlupeg [pegfilgrastim-unne], Nyvepria [pegfilgrastim-apgf], Stimufend [pegfilgrastim-fpgk], Udenyca [pegfilgrastim-cbqv], Ziextenzo [pegfilgrastim-bmez]), then both of the following criteria are met:
      i. The patient has a documented serious adverse event that required medical intervention to both preferred biosimilar pegfilgrastim products (i.e., Fulphila [pegfilgrastim-jmdb], Fylnetra [pegfilgrastim-pbbk]) that is not anticipated with the requested product; **AND**
      ii. The prescriber has completed and submitted an FDA MedWatch Adverse Event Reporting Form **(the prescriber must provide a copy of the completed MedWatch form. Authorizations will not be considered unless the form is completed and submitted to the FDA)**; **AND**
   b. If the request is for Neulasta OnPro or Udenyca Onbody, the patient has an inability to physically or cognitively adhere to the treatment schedule including all of the following:
      i. Inability to self-administer the medication; **AND**
      ii. Lack of caregiver or support system for assistance with medication administration; **AND**

c. The requested agent will be used for **Primary Prophylaxis** for prevention of Febrile Neutropenia (FN); **AND**
    i. The patient is on a chemotherapy regimen with an intermediate risk of FN (10-20%). In patients whose risk of developing febrile neutropenia is greater than or equal to 10% and less than 20% based on chemotherapy regimen, the use of primary prophylaxis should be reserved for those patients with one or more of the following significant risk factors for FN**:
        1. Age greater than 65 years; **OR**
        2. Poor performance status (ECOG 3 or 4, but chemotherapy still indicated); **OR**
        3. Preexisting neutropenia (e.g., resulting from bone marrow damage or tumor infiltration [ANC < 1500 mm^3]); **OR**
        4. Previous episodes of FN; **OR**
        5. Liver dysfunction (i.e., elevated bilirubin ≥ 1.0 or liver enzymes ≥ 2x upper limit of normal); **OR**
        6. The presence of open wounds or active infections when chemotherapy cannot be delayed to accommodate recovery; **OR**
        7. Renal dysfunction with creatinine clearance of < 50 mL/min; **OR**
        8. Poor nutritional status (baseline albumin ≤ 3.5 g/dL or BMI < 20); **OR**
        9. HIV infection (active) requiring ongoing antiviral therapy; **OR**
        10. High tumor volume and/or high symptom burden from disseminated or unresectable malignancy; **OR**
        11. Multiple serious comorbid conditions in addition to the treated malignancy; **OR**
    ii. The patient is on a chemotherapy regimen with a high risk of FN (≥20%); **OR**
    iii. The patient is on chemotherapy regimen with an < 10% overall risk of FN; **AND**
        1. The patient is at significant risk for serious medical consequences of FN, including death; **AND**
        2. Chemotherapy is being used as a curative or adjuvant therapy; **OR**
d. The requested agent will be used for **Secondary Prophylaxis** for prevention of FN; **AND**
    i. The patient has had a previous neutropenic episode or dose-limiting event from a prior chemotherapy cycle and one of the following:
        1. The patient has history of white blood cell growth factor (colony stimulating factor) use while on a chemotherapeutic regimen; **OR**
        2. The patient has no history of white blood cell growth factor (colony stimulating factor) use [please see criteria for primary prophylaxis]; **OR**
e. The patient has been acutely exposed to **myelosuppressive doses of radiation** to increase survival; **OR**
f. The patient has an indication that is supported by ALL requirements in NCCN 1 or 2A recommended use for the requested agent **[medical record documentation required]**; **OR**

2. The request is for **Neupogen**, **Filkri**, **Granix**, **Nypozi**, or **Releuko**:
    a. If the request is for Neupogen (filgrastim) or non-preferred filgrastim biosimilars (e.g., Filkri [filgrastim-laha], Granix [tbo-filgrastim], Nypozi [filgrastim-txid], Releuko [filgrastim-ayow]), then <u>both</u> of the following criteria are met:

i. The patient has a documented serious adverse event that required medical intervention to both preferred biosimilar filgrastim products (i.e., Nivestym [filgrastim-aafi], Zarxio [filgrastim-sndz]) that is not anticipated with the requested product; **AND**
ii. The prescriber has completed and submitted an FDA MedWatch Adverse Event Reporting Form **(the prescriber must provide a copy of the completed MedWatch form. Authorizations will not be considered unless the form is completed and submitted to the FDA)**; **AND**

b. The requested agent will be used for **Primary Prophylaxis** for prevention of Febrile Neutropenia (FN); **AND**
   i. The patient is on a chemotherapy regimen with an intermediate risk of FN (10-20%). In patients whose risk of developing febrile neutropenia is greater than or equal to 10% and less than 20% based on chemotherapy regimen, the use of primary prophylaxis should be reserved for those patients with one or more of the following significant risk factors for FN**:
      1. Age greater than 65 years; **OR**
      2. Poor performance status (ECOG 3 or 4, but chemotherapy still indicated); **OR**
      3. Preexisting neutropenia (e.g., resulting from bone marrow damage or tumor infiltration [ANC < 1500 mm^3]); **OR**
      4. Previous episodes of FN; **OR**
      5. Liver dysfunction (i.e., elevated bilirubin ≥ 1.0 or liver enzymes ≥ 2x upper limit of normal); **OR**
      6. The presence of open wounds or active infections when chemotherapy cannot be delayed to accommodate recovery; **OR**
      7. Renal dysfunction with creatinine clearance of < 50 mL/min; **OR**
      8. Poor nutritional status (baseline albumin ≤ 3.5 g/dL or BMI < 20); **OR**
      9. HIV infection (active) requiring ongoing antiviral therapy; **OR**
      10. High tumor volume and/or high symptom burden from disseminated or unresectable malignancy; **OR**
      11. Multiple serious comorbid conditions in addition to the treated malignancy; **OR**
   ii. The patient is on a chemotherapy regimen with a high risk of FN (>20%); **OR**
   iii. The patient is on chemotherapy regimen with an < 10% overall risk of FN; **AND**
      1. The patient is at significant risk for serious medical consequences of FN, including death; **AND**
      2. Chemotherapy is being used as a curative or adjuvant therapy; **OR**

c. The requested agent will be used for **Secondary Prophylaxis** for prevention of FN; **AND**
   i. The patient has had a previous neutropenic episode or dose-limiting event from a prior chemotherapy cycle and one of the following:
      1. The patient has history of white blood cell growth factor (colony stimulating factor) use while on a chemotherapeutic regimen; **OR**
      2. The patient has no history of white blood cell growth factor (colony stimulating factor) use [please see criteria for primary prophylaxis]; **OR**

d. The requested agent will be used for the **Treatment of FN**; **AND**
   i. The patient has one of the following risk factors for the development of febrile neutropenia:

1. Sepsis syndrome; **OR**
2. Patient is greater than 65 years of age; **OR**
3. Absolute neutrophil count (ANC) <100 cells/mm^3; **OR**
4. Prolonged neutropenia expected (>10 days); **OR**
5. Pneumonia or other clinically documented infections; **OR**
6. Invasive fungal infection; **OR**
7. Hospitalization at the time of fever; **OR**
8. Prior episode of febrile neutropenia; **OR**

e. The requested agent will be used for **Severe Chronic Neutropenia**; **AND**
   i. The patient has at least one symptom (i.e., fever, infections, or ulcers); **AND**
   ii. Laboratory findings are consistent with severe chronic neutropenia (i.e., CBC with differential, platelet counts, and bone marrow morphology and karyotype); **OR**

f. The requested agent will be used for **HIV/AIDS**; **AND**
   i. The patient's absolute neutrophil count is ≤ 750 cells/mm^3; **OR**
   ii. The patient has drug-induced neutropenia (i.e., zidovudine, ganciclovir); **OR**

g. The requested agent will be used for **Myelodysplastic Syndrome**; **AND**
   i. The patient has a history of recurrent or resistant infections with an ANC ≤ 500 cells/mm^3; **OR**
   ii. The requested agent is being used for the treatment of refractory anemia to increase erythropoietic activity; **AND**
      1. The patient is concurrently on an erythropoietic agent (Epogen, Procrit); **AND**
      2. Serum erythropoietin level ≤ 500 mU/mL; **AND**
      3. Adequate iron stores with ≥20% transferrin saturation or serum ferritin ≥100 ng/mL; **OR**

h. The patient has been diagnosed with **Acute Myeloid Leukemia (AML)**; **AND**
   i. The patient is receiving induction or consolidation chemotherapy (for improvement of fever duration and time for neutrophil recovery); **OR**

i. The patient has been diagnosed with a **Non-myeloid Malignancy**; **AND**
   i. The patient is undergoing myeloablative chemotherapy followed by autologous or allogeneic bone marrow transplantation (BMT); **OR**

j. The patient has been diagnosed with **aplastic anemia**; **OR**

k. The requested agent will be used for the **mobilization of autologous hematopoietic progenitor cells** into the peripheral blood for collection by leukapheresis; **OR**

l. The patient has been acutely exposed to **myelosuppressive doses of radiation** to increase survival; **OR**

m. The patient has an indication that is supported by ALL requirements in NCCN 1 or 2A recommended use for the requested agent **[medical record documentation required]**; **OR**

3. The request is for **Leukine**; **AND**
    a. The requested agent will be used for **Primary Prophylaxis** for prevention of Febrile Neutropenia (FN); **AND**
        i. The patient is on a chemotherapy regimen with an intermediate risk of FN (10-20%). In patients whose risk of developing febrile neutropenia is greater than or equal to 10% and less than 20% based on chemotherapy regimen, the use of primary prophylaxis should be reserved for those patients with one or more of the following significant risk factors for FN**:
            1. Age greater than 65 years; **OR**
            2. Poor performance status (ECOG 3 or 4, but chemotherapy still indicated); **OR**
            3. Preexisting neutropenia (e.g., resulting from bone marrow damage or tumor infiltration [ANC < 1500 mm^3]); **OR**
            4. Previous episodes of FN; **OR**
            5. Liver dysfunction (i.e., elevated bilirubin ≥ 1.0 or liver enzymes ≥ 2x upper limit of normal); **OR**
            6. The presence of open wounds or active infections when chemotherapy cannot be delayed to accommodate recovery; **OR**
            7. Renal dysfunction with creatinine clearance of < 50 mL/min; **OR**
            8. Poor nutritional status (baseline albumin ≤ 3.5 g/dL or BMI < 20); **OR**
            9. HIV infection (active) requiring ongoing antiviral therapy; **OR**
            10. High tumor volume and/or high symptom burden from disseminated or unresectable malignancy; **OR**
            11. Multiple serious comorbid conditions in addition to the treated malignancy; **OR**
        ii. The patient is on a chemotherapy regimen with a high risk of FN (>20%); **OR**
        iii. The patient is on chemotherapy regimen with an < 10% overall risk of FN; **AND**
            1. The patient is at significant risk for serious medical consequences of FN, including death; **AND**
            2. Chemotherapy is being used as a curative or adjuvant therapy; **OR**
    b. The requested agent will be used for **Secondary Prophylaxis** for prevention of FN; **AND**
        i. The patient has had a previous neutropenic episode or dose-limiting event from a prior chemotherapy cycle and one of the following:
            1. The patient has history of white blood cell growth factor (colony stimulating factor) use while on a chemotherapeutic regimen; **OR**
            2. The patient has no history of white blood cell growth factor (colony stimulating factor) use [please see criteria for primary prophylaxis]; **OR**
    c. The requested agent will be used for the **Treatment of FN**; **AND**
        i. The patient has one of the follow risk factors for the development of febrile neutropenia:
            1. Sepsis syndrome; **OR**
            2. Patient is greater than 65 years of age; **OR**
            3. Absolute neutrophil count (ANC) <100 cells/mm^3; **OR**
            4. Prolonged neutropenia expected (>10 days); **OR**

5. Pneumonia or other clinically documented infections; **OR**
6. Invasive fungal infection; **OR**
7. Hospitalization at the time of fever; **OR**
8. Prior episode of febrile neutropenia; **OR**

d. The requested agent will be used for **Severe Chronic Neutropenia**; **AND**
   i. The patient has at least one symptom (i.e., fever, infections, or ulcers); **AND**
   ii. Laboratory findings are consistent with severe chronic neutropenia (i.e., CBC with differential, platelet counts, and bone marrow morphology and karyotype); **OR**
e. The requested agent will be used for **HIV/AIDS**; **AND**
   i. The patient's absolute neutrophil count is ≤750 cells/mm^3; **OR**
   ii. The patient has drug-induced neutropenia (i.e., zidovudine, ganciclovir); **OR**
f. The requested agent will be used for **Myelodysplastic Syndrome**; **AND**
   i. The patient has a history of recurrent or resistant infections with an ANC ≤500 cells/mm^3; **OR**
   ii. The requested agent is being used for the treatment of refractory anemia to increase erythropoietic activity; **AND**
      1. The patient is concurrently on an erythropoietic agent (Epogen, Procrit); **AND**
      2. Serum erythropoietin level ≤500 mU/mL; **AND**
      3. Adequate iron stores with ≥20% transferrin saturation or serum ferritin ≥100 ng/mL; **OR**
g. The patient has been diagnosed with **Acute Myeloid Leukemia (AML)**; **AND**
   i. The patient is receiving induction or consolidation chemotherapy (for improvement of fever duration and time for neutrophil recovery); **OR**
h. The patient has been diagnosed with a **Non-myeloid Malignancy**; **AND**
   i. The patient is undergoing myeloablative chemotherapy followed by autologous or allogeneic bone marrow transplantation (BMT); **OR**
i. The patient has been diagnosed with **aplastic anemia**; **OR**
j. The medication will be used for the **mobilization of autologous hematopoietic progenitor cells** into the peripheral blood for collection by leukapheresis; **OR**
k. The patient has undergone an **allogeneic or autologous BMT** and has a delayed or failed engraftment; **OR**
l. The patient has been diagnosed with **malignant melanoma**; **OR**
m. The patient has been diagnosed with **radiation exposure**; **AND**
   i. The patient received radiation therapy in the absence of chemotherapy; **AND**
   ii. The patient experienced prolonged delays in treatment secondary to neutropenia; **OR**
   iii. The patient was irradiated with doses greater than 2 Gy (hematopoietic syndrome of acute radiation syndrome); **OR**
n. The patient has an indication that is supported by ALL requirements in NCCN 1 or 2A recommended use for the requested agent **[medical record documentation required]**; **AND**

4. The requested quantity (dose) and treatment duration is within FDA labeled dosing for the requested indication or NCCN 1 or 2A compendia supported dosing for the requested indication; **AND**
5. The requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below); **AND**
6. If the request is for Armlupeg, Filkri, Granix, Neulasta, Neulasta OnPro, Neupogen, Nypozi, Nyvepria, Releuko, Rolvedon, Ryzneuta, Stimufend, Udenyca, Udenyca Onbody, or Ziextenzo:
    a. For requests for injection or infusion administration of the requested medication in an **inpatient or outpatient hospital setting,** Site of Care Criteria applies (outlined below)*

Duration of Approval: 24 weeks

**Chemotherapy risk category is defined per Carelon Febrile Neutropenia Risk Guidelines.

NOTE:
Use of White Blood Cell Growth Factors may be considered medically necessary for clinical indications not listed above when the drug is prescribed for the treatment of **cancer** either:

1. In accordance with FDA label, when clinical benefit has been established and it is not determined to be investigational as defined in the Blue Cross NC Corporate Medical Policy (CMP), "Investigational (Experimental) Services." Please refer to CMP "Investigational (Experimental) Services" for a summary of evidence standards from nationally recognized compendia.; **OR**
2. In accordance with specific strong endorsement or support by nationally recognized compendia (e.g., National Comprehensive Cancer Network, NCCN), when such recommendation is based on the highest level of evidence (Level 1, 2A), and/or uniform consensus of clinical appropriateness has been reached.

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
pegfilgrastim (Neulasta®, Neulasta® OnPro®) subcutaneous (SC) injection	• Decrease incidence of infection, as manifested by febrile neutropenia (FN), in patients with cancer	• SC: 6 mg once per chemotherapy cycle (weight-based dosing to be used	J2506	FN: 288

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
pegfilgrastim-unne (Armlupeg®) subcutaneous (SC) injection	receiving myelosuppressive chemotherapy	according to labeling for pediatric patients < 45 kg). Do not administer between 14 days prior and 24 hours after cytotoxic chemotherapy.	C9399** J3490** J3590** J9999**	Exposure to myelosuppressive doses of radiation: 48
pegfilgrastim-apgf (Nyvepria®) subcutaneous (SC) injection	• Increase survival in patients acutely exposed to myelosuppressive doses of radiation	• SC: 2 doses (6 mg each) administered one week apart (weight-based dosing to be used according to labeling for pediatric patients < 45 kg). First dose to be administered as soon as possible following suspected or confirmed exposure to myelosuppressive doses of radiation.	Q5122	
pegfilgrastim-fpgk (Stimufend®) subcutaneous (SC) injection			Q5127	
pegfilgrastim-cbqv (Udenyca®, Udenyca Onbody®) subcutaneous (SC) injection			Q5111	
pegfilgrastim-bmez (Ziextenzo®) subcutaneous (SC) injection			Q5120	

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
filgrastim (Neupogen®) intravenous (IV) infusion or subcutaneous (SC) injection	• Decrease incidence of infection, as manifested by FN, in patients with cancer receiving myelosuppressive chemotherapy • Reduce neutrophil recovery time and fever duration after induction and/or consolidation chemotherapy for AML • Reduce FN in patients with cancer undergoing BMT • Autologous peripheral blood progenitor cell collection and therapy • Reduce sequelae of severe neutropenia in congenital neutropenia, cyclic or idiopathic neutropenia • Increase survival in patients acutely exposed to myelosuppressive doses of radiation	• IV or SC: Starting dose of 5 mcg/kg/day	J1442	99999
filgrastim-laha (Filkri®) intravenous (IV) infusion or subcutaneous (SC) injection		• IV or SC: Starting dose of 5 mcg/kg/day • IV: 10 mcg/kg/day	C9399** J3490** J3590** J9999**	
filgrastim-txid (Nypozi®) intravenous (IV) infusion or subcutaneous (SC) injection		• SC: 10 mcg/kg/day, administered for at least 4 days before first leukapheresis procedure and continued until last procedure • Congenital neutropenia: Starting dose of 6 mcg/kg SC twice daily • Cyclic or idiopathic neutropenia: Starting dose of 5 mcg/kg SC daily	Q5148	
filgrastim-ayow (Releuko®) intravenous (IV) infusion or subcutaneous (SC) injection		• SC: 10 mcg/kg/day	Q5125	

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
tbo-filgrastim (Granix®) subcutaneous (SC) injection	Reduce duration of severe neutropenia in non-myeloid malignancies receiving myelosuppressive anticancer drugs associated with a clinically significant incidence of FN	SC: 5 mcg/kg per day. First dose to be administered no sooner than 24 hours after myelosuppressive chemotherapy, and not within 24 hours prior to chemotherapy.	J1447	99999

sargramostim (Leukine®)
 	
intravenous (IV) infusion or subcutaneous (SC) injection
	• Neutrophil recovery following chemotherapy for AML
	
	• Mobilization of peripheral blood progenitor cells by leukapheresis and autologous transplantation
	
	• Myeloid reconstitution after autologous or allogeneic BMT
	
	• Delayed neutrophil recovery or graft failure after autologous or allogeneic BMT
	
	• Increase survival in patients acutely exposed to myelosuppressive doses of radiation
		• IV: 250 mcg/m^2/day
		
		• IV: 250 mcg/m^2/day
		• SC: 250 mcg/m^2 once daily
		
		• IV: 250 mcg/m^2/day
		
		• IV: 250 mcg/m^2/day for 14 days
		
		• SC: Once daily
		  ○ Adult and pediatric >40 kg: 7 mcg/kg
		  ○ Pediatric 15-40 kg: 10 mcg/kg
		  ○ Pediatric <15 kg: 12 mcg/kg
			J2820	99999

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
eflapegrastim-xnst (Rolvedon®) subcutaneous (SC) injection	Decrease incidence of infection, as manifested by FN, in adult patients with cancer receiving myelosuppressive chemotherapy	SC: 13.2 mg once per chemotherapy cycle. Do not administered between 14 days prior and 24 hours after cytotoxic chemotherapy.	J1449	3,168
efbemalenograstim alfa-vuxw (Ryzneuta®) subcutaneous (SC) injection	Decrease incidence of infection, as manifested by FN, in adult patients with cancer receiving myelosuppressive chemotherapy	SC: 20 mg once per chemotherapy cycle. Do not administered between 14 days prior and 24 hours after cytotoxic chemotherapy.	J9361	960

***Maximum units allowed for duration of approval**
****Non-specific assigned HCPCS codes, must submit requested product NDC**

Other codes applicable to this policy may include:
HCPCS Codes: S0353, S0354
ICD-10 Codes: C00.0-C49.9, C4A.0-C4A.9, C50.011-C79.9, C7A.00-C7A.8, C7B.00-C7B.8, C80.0-C86.6, C88.2-C96.Z, D00.00-D09.9, Z51.11, Z51.12

***Site of Care Medical Necessity Criteria [NOTE: Not applicable for sargramostim (Leukine) requests]**

1. For requests for injection or infusion administration in an **inpatient setting**, the injection or infusion may be given if the above medical necessity criteria are met AND the inpatient admission is NOT for the sole purpose of administering the injection or infusion; **OR**
2. For requests for injection or infusion administration in an **outpatient hospital setting**, the injection or infusion may be given if the above medical necessity criteria are met AND ONE of the following must be met:
    a. History of a severe adverse event following the injection or infusion of the requested medication (i.e., anaphylaxis, seizure, thromboembolism, myocardial infarction, renal failure); **OR**
    b. Conditions that cause an increased risk for severe adverse event (i.e., unstable renal function, cardiopulmonary conditions, unstable vascular access); **OR**
    c. History of mild adverse events that have not been successfully managed through mild pre-medication (e.g., diphenhydramine, acetaminophen, steroids, fluids, etc.); **OR**

   d. Inability to physically and cognitively adhere to the treatment schedule and regimen complexity; **OR**
   e. New to therapy, defined as initial injection or infusion OR less than 3 months since initial injection or infusion; **OR**
   f. Re-initiation of therapy, defined as ONE of the following:
      i. First injection or infusion after 6 months of no injections or infusions for drugs with an approved dosing interval less than 6 months duration; **OR**
      ii. First injection or infusion after at least a 1-month gap in therapy outside of the approved dosing interval for drugs requiring every 6 months dosing duration; **OR**
   g. Requirement of a change in the requested restricted product formulation; **AND**
3. If the Site of Care Medical Necessity Criteria in #1 or #2 above are not met, the injection or infusion will be administered in a **home-based infusion** or physician office setting with or without supervision by a certified healthcare professional.

References: all information referenced is from FDA package insert unless otherwise noted below.

Policy Implementation/Update Information: Criteria and treatment protocols are reviewed annually by the Blue Cross NC P&T Committee, regardless of change. This policy is reviewed in Q3 annually.

July 2026: Criteria change: Added Site of Care medical necessity criteria for the following products: Armlupeg, Filkri, Granix, Neulasta, Neulasta OnPro, Neupogen, Nypozi, Nyvepria, Releuko, Rolvedon, Ryzneuta, Stimufend, Udenyca, Udenyca Onbody, and Ziextenzo. **Policy notification given 5/1/2026 for effective date 7/1/2026**.
April 2026: Criteria update: Added new to market product Filkri (filgrastim-laha) with corresponding criteria as a non-preferred short-acting/filgrastim white blood cell growth factor product with requirement of trial and failure of both Nivestym and Zarxio. Added associated dosing table updates and HCPCS codes C9399, J3490, J3590, and J9999 for Filkri.
January 2026: Criteria change: Added new to market product Armlupeg (pegfilgrastim-unne) with corresponding criteria as a non-preferred long-acting/pegfilgrastim white blood cell growth factor product with requirement of trial and failure of both Fulphila and Fylnetra. Added associated dosing table updates and HCPCS codes C9399, J3490, J3590, and J9999 for Armlupeg. Adjusted formatting of dosing table for clarity.
January 2026: Criteria change: Changed requirement for trial and failure of preferred pegfilgrastim biosimilar products to include Fylnetra in addition to existing preferred Fulphila; adjusted non-preferred pegfilgrastim biosimilar products to include Nyvepria, Stimufend, Udenyca/Udenyca Onbody and Ziextenzo. Added Nyvepria (pegfilgrastim-apgf) to restricted products; removed Fylnetra (pegfilgrastim-pbbk) from restricted products (now unrestricted). **Policy notification given 10/1/2025 for effective date 1/1/2026**.
April 2025: Coding change (Nypozi): Added HCPCS code Q5148 for Nypozi to dosing reference table effective 4/1/2025; deleted C9173, J3490, J3590, and J9999 termed 3/31/2025.
January 2025: Coding change (Nypozi): Added HCPCS code C9173 for Nypozi to dosing reference table effective 1/1/2025; deleted C9399 termed 12/31/2024.

November 2024: Criteria change: Added new to market product Nypozi (filgrastim-txid) with corresponding criteria as a non-preferred short-acting/filgrastim white blood cell growth factor product with requirement of trial and failure of both Nivestym and Zarxio. Added associated dosing table updates and HCPCS codes C9399, J3490, J3590, and J9999 for Nypozi.
July 2024: Coding change (Ryzneuta): Added HCPCS code J9361 for Ryzneuta to dosing reference table effective 7/1/2024; deleted C9399, J3490, J3590, and J9999 termed 6/30/2024. Adjusted maximum units for Ryzneuta according to coding unit definition for clarity.
April 2024: Criteria change: Changed requirement for trial and failure of preferred pegfilgrastim biosimilar products to include Fulphila and Nyvepria; adjusted non-preferred pegfilgrastim biosimilar products to include Fylnetra, Stimufend, Udenyca/Udenyca Onbody and Ziextenzo. Added Udenyca/Udenyca Onbody (pegfilgrastim-cbqv) and Ziextenzo (pegfilgrastim-bmez) to restricted products; removed Fulphila (pegfilgrastim-jmdb) and Nyvepria (pegfilgrastim-apgf) from restricted products (now unrestricted). Added new to market Udenyca formulation, Udenyca Onbody (pegfilgrastim-cbqv), to policy as non-preferred with same criteria as Neulasta OnPro. **Policy notification given 1/8/2024 for effective date 4/1/2024**.
February 2024: Criteria change: Added new to market product Ryzneuta (efbemalenograstim alfa-vuxw) with corresponding criteria as a non-preferred long-acting white blood cell growth factor product with requirement of trial and failure of both Udenyca and Ziextenzo. Added associated dosing table updates and HCPCS codes C9399, J3490, J3590, and J9999 for Ryzneuta.
October 2023: Criteria update: Adjusted FDA Label Reference table for Stimufend to include dosing and units for hematopoietic subsyndrome of acute radiation syndrome indication, with no change to policy intent.
July 2023: Criteria change: Restructured criteria for Rolvedon as a non-preferred long-acting white blood cell growth factor product with requirement of trial and failure of both Udenyca and Ziextenzo. **Policy notification given 5/2/2023 for effective date 7/1/2023**.
April 2023: Coding update: Added HCPCS codes J1449 for Rolvedon, Q5127 for Stimufend, and Q5130 for Fylnetra to dosing reference table effective 4/1/2023; deleted C9399, J3490, J3590, and J9999 for all three drugs termed 3/31/2023. Updated maximum units for pegfilgrastim products and for Rolvedon per updated code definitions effective 4/1/2023.
March 2023: Criteria update: Changed AIM reference to Carelon with no change to policy intent.
October 2022: Criteria change: Added new to market product Stimufend as a non-preferred pegfilgrastim product and dosing table updates. Added Rolvedon with corresponding criteria and dosing table updates.
October 2022: Coding update: Added HCPCS code Q5125 for Releuko to dosing reference table effective 10/1/2022, deleted C9096, J3490, J3590, and J9999 termed 9/30/2022.
July 2022: Coding update: Added HCPCS code C9096 for Releuko to dosing reference table effective 7/1/2022, deleted C9399 termed 6/30/2022.
June 2022: Criteria change: Added new to market product Fylnetra (pegfilgrastim-pbbk) with corresponding criteria as a non-preferred pegfilgrastim product and dosing table updates. Adjusted criteria for myelodysplastic syndrome for clarity with no change to intent.
June 2022: Coding update: Replaced HCPCS code J2505 with J2506 effective 1/1/2022 for clarity and alignment with Prior Review (Prior Plan Approval) Code List. Adjusted maximum units accordingly based on J2506 code definition.
June 2022: Criteria change: Added new to market product Releuko (filgrastim-ayow) with corresponding criteria as a non-preferred filgrastim product and dosing table updates. Preferred products removed from criteria and dosing table as they are now unrestricted.

February 2022: Criteria change: Added requirement of NCCN 2A or higher evidence rating for supporting compendia. Adjusted chemotherapy risk category definitions corresponding to use of WBC GFs for primary prophylaxis of febrile neutropenia. Added maximum units; medical policy formatting change. **Policy notification given 12/17/2021 for effective date 2/15/2022**.
*Further historical criteria changes and updates available upon request from Medical Policy and/or Corporate Pharmacy.