Medicare Part B Colony Stimulating Factors Prior Authorization Criteria

FDA APPROVED INDICATIONS AND DOSAGE[1-7,11-13]

Agent(s)	Indication(s)	Dosage
Fulphila™ (pegfilgrastim-jmdb)	• 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 Limitations of Use: Fulphila is not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation	**Nonmyeloid malignancies:** 6 mg subcutaneously once per chemotherapy cycle. Do not administer Fulphila between 14 days before and 24 hours after administration of cytotoxic chemotherapy
Granix® (tbo-filgrastim)	• Adult and pediatric patients 1 month and older for the reduction in the duration of severe neutropenia in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia	**Nonmyeloid malignancies:** 5 mcg/kg/day as a subcutaneous injection. Give the first dose no earlier than 24 hours following myelosuppressive chemotherapy. Do not administer Granix within 24 hours prior to chemotherapy. Continue dosing until expected neutrophil nadir is passed and count has recovered to normal range
Leukine® (sargramostim)	• To shorten 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) • Mobilization of hematopoietic progenitor cells into peripheral blood for collection by leukapheresis in adult patients with cancer undergoing autologous	**AML:** 250 mcg/m^2/day intravenously over a 4-hour period starting approximately on day 11 or 4 days after completion of induction chemotherapy if the day 10 bone marrow is hypoplastic with < 5% blasts. Continue until ANC > 1500 cells/mm^3 for 3 consecutive days or max of 42 days. Do not administer Leukine within 24 hours preceding or following receipt of chemotherapy or radiotherapy **Autologous peripheral blood progenitor cell mobilization and collection:** 250 mcg/m^2/day intravenously over 24 hours or

 Effective: xx/xx/xx

	hematopoietic stem cell transplantation	subcutaneously once daily. Continue through period of peripheral blood progenitor cell collection
	• Acceleration of myeloid reconstitution following autologous peripheral blood progenitor cell or bone marrow transplantation 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	**Autologous peripheral blood progenitor cell transplantation:** 250 mcg/m^2/day intravenously over 24 hours or subcutaneously once daily immediately following infusion of progenitor cells and continuing until an ANC > 1500 cells/mm^3 for 3 consecutive days. Do not administer Leukine within 24 hours preceding or following receipt of chemotherapy or radiotherapy **Autologous bone marrow transplantation:** 250 mcg/m^2/day intravenously over a 2-hours period beginning two to four hours after bone marrow infusion, and not less than 24 hours after the last dose of chemotherapy or radiotherapy. Do not administer Leukine until the post marrow infusion ANC is less than 500 cells/mm^3. Continue Leukine until an ANC greater than 1500 cells/mm^3 for 3 consecutive days is attained. Do not administer Leukine within 24 hours preceding or following receipt of chemotherapy or radiotherapy
	• Acceleration of myeloid reconstitution in adult and pediatric patients 2 years of age and older undergoing allogeneic bone marrow transplantation from HLA-matched related donors	**Allogeneic bone marrow transplantation:** 250 mcg/m^2/day intravenously over 2 hours beginning 2-4 hours after bone marrow infusion, and not less than 24 hours after last dose of chemotherapy or radiation. Do not administer Leukine until the post marrow infusion ANC is < 500 cells/mm^3. Continue until ANC > 1500 cells/mm^3 for 3 consecutive

		days is attained. Do not administer Leukine within 24 hours preceding or following receipt of chemotherapy or radiotherapy
	● Treatment of adult and pediatric patients 2 years and older who have undergone allogeneic or autologous bone marrow transplantation in whom neutrophil recovery is delayed or failed	**Bone Marrow Transplantation Failure or Engraftment Delay:** 250 mcg/m2/day for 14 days as 2-hour intravenous infusion. Dose can be repeated after 7 days if neutrophil recover has not occurred. If neutrophil recovery still has not occurred, a third course of 500 mcg/m^2/day for 14 days may be tried after another 7 days off therapy
	● Increase survival in adult and pediatric patients acutely exposed to myelosuppressive doses of radiation [Hematopoietic Syndrome of Acute Radiation Syndrome (H-ARS)]	**H-ARS:** In adult and pediatric patients weighing greater than 40 kg: 7mcg/kg subcutaneously once daily In pediatric patients weighing15 kg to 40 kg: 10 mcg/kg subcutaneously once daily In pediatric patients weighing less than 15 kg: 12 mcg/kg/day subcutaneously once daily Continue Leukine until the ANC remains greater than 1,000 cells/mm^3 for 3 consecutive CBCs or exceeds 10,000 cells/mm^3
Neulasta® (pegfilgrastim)	● 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	**Patients receiving myelosuppressive anti-cancer drugs:** 6 mg subcutaneously once per chemotherapy cycle. Do not administer 14 days before and 24 hours after cytotoxic chemotherapy
	● Increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Subsyndrome of Acute Radiation Syndrome)	**Acute Radiation Syndrome:** Two doses, 6 mg each, administered subcutaneously one week apart. Administer the first dose as soon as possible after suspected or

	Limitation of Use: Neulasta is not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation	confirmed exposure of radiation levels > 2 gray (Gy). Administer the 2nd dose 1 week after the first dose
Neupogen® (filgrastim)	● Decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever	**Nonmyeloid malignancies:** 5 mcg/kg/day by subcutaneous injection, short IV infusion, or continuous IV infusion. Adjust dose based on ANC nadir. Administer daily for up to 2 weeks or until ANC has reached 10,000/mm^3. Use should be discontinued if ANC surpasses 10,000/mm^3
	● Reduce the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML)	**AML:** 5 mcg/kg/day by subcutaneous injection, short IV infusion, or continuous IV infusion. Adjust dose based on ANC nadir. Administer daily for up to 2 weeks or until ANC has reached 10,000/mm^3. Use should be discontinued if ANC surpasses 10,000/mm^3
	● Reduce the duration of neutropenia and neutropenia-related clinical sequelae (e.g., febrile neutropenia) in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation	**Bone Marrow Transplantation:** 10 mcg/kg/day after bone marrow transplant as IV infusion for no longer than 24 hours. First dose should be given at least 24 hours after cytotoxic chemotherapy and marrow infusion. Dose titration recommended based on labeling
	● Mobilization of hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis	**Autologous Peripheral Blood Progenitor Cell Collection:** 10 mcg/kg/day by subcutaneous injection. Give at least 4 days before first leukapheresis and continue to the last leukapheresis. Dose modifications based on WBC and discontinue when WBC is > 100,000/mm^3 **Congenital neutropenia**:

	• Reduce the incidence and duration of sequelae of neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia	6 mcg/kg subcutaneously twice daily Dose adjust based on patient clinical course and ANC **Idiopathic/Cyclic neutropenia:** 5 mcg/kg/day subcutaneously Dose adjust based on patient clinical course and ANC
	• Increase survival in patients acutely exposed to myelosuppressive doses of radiation (hematopoietic syndrome of acute radiation syndrome)	**Acute Radiation Syndrome:** 10 mcg/kg subcutaneously daily until ANC remains greater than 1,000/mm^3 for 3 consecutive CBCs or exceeds 10,000/mm^3 after a radiation-induced nadir
Nivestym™ (filgrastim-aafi)	• Decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever	**Nonmyeloid malignancies:** 5 mcg/kg/day by subcutaneous injection, short IV infusion, or continuous IV infusion. Adjust dose based on ANC nadir. Administer daily for up to 2 weeks or until ANC has reached 10,000/mm^3. Use should be discontinued if ANC surpasses 10,000/mm^3
	• Reduce the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML)	**AML:** 5 mcg/kg/day by subcutaneous injection, short IV infusion, or continuous IV infusion. Adjust dose based on ANC nadir. Administer daily for up to 2 weeks or until ANC has reached 10,000/mm^3. Use should be discontinued if ANC surpasses 10,000/mm^3
	• Reduce the duration of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation (BMT)	**Bone Marrow Transplantation:** 10 mcg/kg/day after bone marrow transplantation as IV infusion for no longer than 24 hours. First dose should be given at least 24 hours after
	• 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	cytotoxic chemotherapy and marrow infusion **Autologous Peripheral Blood Progenitor Cell Collection:** 10 mcg/kg/day by subcutaneous injection. Give at least 4 days before first leukapheresis and continue to last. Dose modifications based on WBC and discontinue when WBC is > 100,000/mm^3 **Congenital neutropenia**: 6 mcg/kg subcutaneously twice daily Dose adjust based on patient clinical course and ANC **Idiopathic/Cyclic neutropenia:** 5 mcg/kg/day subcutaneously Dose adjust based on patient clinical course and ANC
Nyvepria™ (pegfilgrastim- apgf)	● 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 Limitations of Use: Nyvepria is not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation	**Nonmyeloid malignancies:** 6 mg subcutaneously once per chemotherapy cycle. Do not administer between 14 days before and 24 hours after administration of cytotoxic chemotherapy See prescribing information for dosing in pediatric patients weighing less than 45 mg
Udenyca® (pegfilgrastim-cbqv)	● Decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia Limitations of Use: Udenyca is not indicated for the mobilization of peripheral blood	**Nonmyeloid malignancies:** 6 mg subcutaneously once per chemotherapy cycle. Do not administer between 14 days before and 24 hours after administration of cytotoxic chemotherapy See prescribing information for dosing in pediatric patients weighing less than 45 mg

	progenitor cells for hematopoietic stem cell transplantation	
Zarxio® (filgrastim-sndz)	● Decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anticancer 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., febrile neutropenia, in patients with nonmyeloid 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	**Nonmyeloid malignancies:** 5 mcg/kg/day by subcutaneous injection, short IV infusion, or continuous IV infusion. Adjust dose based on ANC nadir. Use should be discontinued if ANC surpasses 10,000/mm^3 **AML:** 5 mcg/kg/day by subcutaneous injection, short IV infusion, or continuous IV infusion. Adjust dose based on ANC nadir. Use should be discontinued if ANC surpasses 10,000/mm^3 **Bone Marrow Transplantation:** 10 mcg/kg/day after bone marrow transplant as IV infusion for no longer than 24 hours. First dose should be given at least 24 hours after cytotoxic chemotherapy and marrow infusion **Autologous Peripheral Blood Progenitor Cell Collection:** 10 mcg/kg/day subcutaneously. Give at least 4 days before first leukapheresis and continue to last. Discontinue when WBC > 100,000/mm^3 **Congenital neutropenia**: 6 mcg/kg subcutaneously twice daily Dose adjust based on patient clinical course and ANC **Idiopathic/Cyclic neutropenia:** 5 mcg/kg/day subcutaneously Dose adjust based on patient clinical course and ANC

Ziextenzo™ (pegfilgrastim-bmez)	• 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	**Patients with cancer receiving myelosuppressive chemotherapy:** 6 mg administered once per chemotherapy cycle. For dosing in pediatric patients weighing less than 45 kg refer to prescribing information

CLINICAL RATIONALE

Hematopoietic growth factors are defined by their ability to promote proliferation and differentiation of hematopoietic progenitors into mature blood cells. Colony-stimulating factors are hematopoietic growth factors responsible for the regulation of growth and differentiation of cells in the myeloid and erythroid lineages. Myeloid growth factors (MGFs), which includes granulocyte colony-stimulating factor (G-CSF) and granulocyte macrophage colony-stimulating factor (GM-CSF), are primarily used to reduce the incidence of neutropenia in patients with solid tumors receiving myelosuppressive chemotherapy.[8]

For patients with neutropenia, the risk of serious infection increases as the absolute neutrophil count (ANC) falls to the clinically significant range of < 500/mcL or an anticipated decline to ≤ 500/mcL in the next 48 hours. Febrile neutropenia (FN) is defined as clinically significant neutropenia AND a fever of ≥ 101°F (≥ 38.3°C) orally or ≥ 100.4°F (≥ 38.0°C) over 1 hour, is a major dose limiting toxicity of chemotherapy that often requires prolonged hospitalization and broad-spectrum antibiotic use. Occurrences of severe neutropenia or FN can prompt chemotherapy dose reductions and/or treatment delays for subsequent chemotherapy cycles and compromise clinical outcome.[8]

The National Comprehensive Cancer Network (NCCN) Supportive Care: Hematopoietic Growth Factors: Management of Neutropenia guidelines are based on the risk of febrile neutropenia associated with chemotherapy. When considering prophylactic use of MGFs, patients should be placed into one of following three risk categories based on disease type, chemotherapy regimen (high-dose, dose-dense, or standard-dose therapy), patient risk factors, and treatment intent (curative vs palliative): overall high-risk group (> 20% risk of FN), intermediate-risk group (10-20% risk), or low-risk group (< 10% risk). Patients at high risk for febrile neutropenia AND those with intermediate risk along with at least 1 additional risk factor should be treated with G-CSF.[8]

Risk for developing FN should be assessed prior to the first chemotherapy cycle and before each subsequent cycle. If a patient had FN or a dose-limiting neutropenic event (a nadir or a day-of-treatment count impacting the planned dose of chemotherapy) in a previous treatment cycle, with the same dose and schedule planned for the current cycle, this patient is now in the high-risk group. If the patient experiences such an episode despite receiving MGF, the recommendation is a dose reduction or change in treatment regimen unless there is an impact on patient survival. When choosing among MGFs for prophylactic treatment of FN, filgrastim (or any of the biosimilars to filgrastim), tbo-filgrastim, and pegfilgrastim (or any of the biosimilars to pegfilgrastim) are considered NCCN Category 1 recommendations. Sargramostim is no longer recommended in patients with solid tumors receiving myelosuppressive chemotherapy. There is insufficient data to support the dose and schedule for weekly regimens of pegfilgrastim (or the biosimilars to pegfilgrastim); therefore, use of peg-filgrastim or its biosimilars in patients receiving weekly chemotherapy cannot be recommended.[8]

Filgrastim, pegfilgrastim, and sargramostim are FDA-approved for the treatment of patients presenting with acute exposure to myelosuppressive doses of radiation. NCCN endorses the use of any of the biosimilars to filgrastim or pegfilgrastim as well as tbo-filgrastim in this setting as well.[8]

MGFs are commonly administered in both the autologous and allogenic hematopoietic cell transplant (HCT) settings, either for mobilization of hematopoietic progenitor cells or as supportive care after transplantation. Mobilization of peripheral blood progenitor cells by G-CSF-containing regimens has largely replaced bone marrow collection for HCT due to ease of collection, avoidance of general anesthesia, and more rapid

recovery of blood counts. Most data on mobilization of hematopoietic progenitor cells in the autologous setting are focused of filgrastim. While some studies suggest that single-dose pegfilgrastim may have similar efficacy, there are limited high-quality data supporting the use of pegfilgrastim in this setting. Therefore, pegfilgrastim and its biosimilars are not recommended by NCCN for mobilization at this time.[8]

Consensus is lacking o the use of MGFs in the post-transplant setting. Filgrastim administration after high-dose chemotherapy and autologous HCT has been shown to expedite neutrophil recover in prospective randomized trials. Data are conflicting on G-CSF use as a supportive care measure for allogeneic transplant recipients, with some studies associating G-CSF with worse clinical outcomes. However, G-CSF has been used routinely to facilitate the recovery of blood counts after umbilical cord blood transplant, because there is a significant delay in the rate and kinetics of neutrophil and platelet engraftment after cord blood transplant as compared to marrow or mobilized PBPC grafts.[8]

While filgrastim biosimilars have been accepted as equivalent options to filgrastim for FN prophylaxis, there is discussion among medical professionals regarding their equivalency in hematopoietic cell mobilization. Therefore, while it is reasonable to substitute with filgrastim biosimilars the clinician should be aware of any complications presented in the literature or in their patients. NCCN recommends single-agent filgrastim as preferred with a 2A recommendation and the biosimilars to filgrastim along with tbo-filgrastim as 2B recommendations. The world marrow donor association (WMDA) does recommend the use of filgrastim biosimilars for the mobilization of peripheral blood progenitor cells in healthy donors in the allogenic HCT setting.[8]

American Society of Clinical Oncologist (ASCO) guidelines on the use of white blood cell growth factors recommend the use of CSF for primary prophylaxis when the risk of FN is ≥20% and no other equally effective and safe regimen that does not require CSFs is available. Similar to NCCN guidelines, high risk determination is based on several factors including age, medical history, disease characteristics, and myelotoxicity of the chemotherapy regimen. ASCO also recommends immediate administration of CSFs when there are lethal doses of total-body radiotherapy given (with the exception of doses high enough to lead to certain death as a result of organ injury). Use for secondary prophylaxis is recommended when a patient had a neutropenic complication from a prior cycle of chemotherapy and a reduced dose and/or treatment delay will compromise disease-free/overall survival or treatment outcome. CSFs are also supported for use after chemotherapy to mobilize peripheral-blood progenitor cells, after autologous or allogeneic stem-cell transplantation to reduce the duration of severe neutropenia, and can be considered in diffuse aggressive lymphoma in those age ≥ 65 years who are treated with curative chemotherapy especially when the patient has comorbidities. The choice of agent [pegfilgrastim, filgrastim, tbo-filgrastim, and filgrastim-sndz (and other biosimilars, as they become available)] depends on convenience, cost, and clinical situation.[9]

COMPENDIA SUPPORTED INDICATIONS

Myelodysplastic syndrome (MDS)

MDS represent myeloid clonal hemopathies with relatively heterogenous spectrums of presentation. The major clinical problems in these disorders are morbidities caused by patients' cytopenias and the potential for MDS to evolve into acute myeloid leukemia (AML).[10] NCCN guidelines note that CSF products are not recommended for routine infection prophylaxis, but should be considered for use in recurrent or resistant infections in neutropenic patients. NCCN compendia supports filgrastim, filgrastim-sndz, and tbo-filgrastim in MDS.[10] The American Society of Clinical Oncology (ASCO) recommendations for the use of white blood cell growth factors note that CSFs can increase the absolute neutrophil count in neutropenic patients with MDS. However, data supporting the routine use of long-term continuous use of CSFs is lacking. Intermittent administration of CSFs may be considered in a subset of patients with severe neutropenia and recurrent infection.[9]

Therapeutic Use of CSFs in Neutropenia

Compared to prophylactic use, there is less evidence supporting the therapeutic use of MGFs for febrile neutropenia as an adjunct to antibiotics. It has been found that there is no difference in mortality outcomes; however, there is evidence to support shorter hospitalization stays, faster neutrophil recovery, shorter duration of grade 4 neutropenia, and antibiotic therapy with treatment. The National

Comprehensive Cancer Network (NCCN) guidelines recommend patients who have FN and who are already receiving prophylactic G-CSFs continue with the same G-CSF. Those who received prophylactic pegfilgrastim or its biosimilars should not be treated with additional MGF. NCCN recommends those who have FN and are not on prophylactic CSF that an evaluation for risk factors for infection-related complications or poor clinical outcome be completed. NCCN lists the following as factors for consideration: age > 65 years, sepsis syndrome, ANC < 100 neutrophils/mcL, anticipated prolonged (> 10 days) neutropenia, pneumonia, invasive fungal infections or other clinically documented infections, hospitalization, and a prior episode of FN. If risk factors are present, then MGFs should be considered. Filgrastim (or its biosimilars), tbo-filgrastim, or sargramostim may be administered in the therapeutic setting. Pegfilgrastim and its biosimilars have only been studied for prophylactic use and are not recommended for therapeutic use at this time.[8] ASCO guidelines suggest CSFs be considered in patients with fever and neutropenia who are at high risk for infection-associated complication or who have prognostic factors predictive of poor clinical outcomes.[9]

Safety[1-7,11-13]

- **Fulphila (pegfilgrastim-jmdb)** is contraindicated in:
  - Patients with a history of serious allergic reactions to human granulocyte colony-stimulating factors such as pegfilgrastim or filgrastim products
- **Granix (tbo-filgrastim)** is contraindicated in:
  - Patients with a history of serious allergic reactions to filgrastim or pegfilgrastim products
- **Leukine (sargramostim)** is contraindicated in:
  - Patients with hypersensitivity to GM-CSF, yeast-derived products or any component of the product; Excessive leukemic myeloid blasts in bone marrow or peripheral blood (≥ 10%); Concomitant use with chemotherapy and radiotherapy
- **Neulasta (pegfilgrastim)** is contraindicated in:
  - Patients with a history of serious allergic reactions to human granulocyte colony-stimulating factors such as filgrastim or pegfilgrastim
- **Neupogen (filgrastim)** is contraindicated in :
  - Patients with a history of serious allergic reactions to human granulocyte colony-stimulating factors such as filgrastim or pegfilgrastim
- **Nivestym (filgrastim-aafi)** is contraindicated in:
  - Patients with a history of serious allergic reactions to human granulocyte colony-stimulating factors such as filgrastim products or pegfilgrastim products
- **Nyvepria (pegfilgrastim-apgf)** is contraindicated in:
  - Patients with a history of serious allergic reactions to human granulocyte colony-stimulating factors such as pegfilgrastim products or filgrastim products
- **Udenyca (pegfilgrastim-cbqv)** is contraindicated in:
  - Patients with a history of serious allergic reactions to human granulocyte colony-stimulating factors such as filgrastim products or pegfilgrastim products
- **Zarxio (filgrastim-sndz)** is contraindicated in:
  - Patients with a history of serious allergic reactions to human granulocyte colony-stimulating factors such as filgrastim or pegfilgrastim products
- **Ziextenzo (pegfilgrastim-bmez)** is contraindicated in:
  - Patients with a history of serious allergic reactions to human granulocyte colony-stimulating factors such as pegfilgrastim products or filgrastim products

References

1. Neupogen prescribing information. Amgen Inc. January 2021.
2. Neulasta prescribing information. Amgen Inc. January 2021.
3. Leukine prescribing information. Sanofi-Aventis. March 2018.
4. Granix prescribing information. Teva Pharmaceuticals. March 2019.
5. Zarxio prescribing information. Sandoz Inc. August 2019.
6. Fulphila prescribing information. Mylan. May 2019.
7. Nivestym prescribing information. Pfizer Labs. July 2018.
8. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology. Hematopoietic Growth Factors. Version 2.2020.

 Effective: xx/xx/xx

9. Smith TJ, Bohlke K, Lyman GH, et al. American Society of Clinical Oncologists. Recommendations for the Use of WBC Growth Factors: American Society of Clinical Oncology Clinical Practice Guideline Update. Journal of Clinical Oncology 33, no 28 (October 1 2015) 3199-3212.
10. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology. Myelodysplastic syndromes. Version 3.2021.
11. Udenyca prescribing information. Coherus BioSciences Inc. February 2020.
12. Ziextenzo prescribing information. Sandoz Inc. November 2019.
13. Nyvepria prescribing information. Pfizer Oncology. June 2020.

Original Part B Prime Standard criteria approved by P&T UM Committee 12/2020 Annual Review Part B Prime Standard with changes to criteria, approved by P&T UM Committee 03/2021 Mid-Year Review Prime Standard Part B with changes to criteria, approved by P&T UM Committee 12/2021

 Effective: xx/xx/xx

Medicare Part B – Colony Stimulating Factor

Coverage and policy application are contingent on National Coverage Determinations (NCD) and Local Coverage Determinations (LCD). An NCD or LCD that is applicable to the drug or product must be used in lieu of applicable medical necessity criteria. Also, please note that Prior Authorization criteria cannot be stricter than an NCD or LCD with specified step therapy requirements.

TARGET PREFERRED AGENT(S)	TARGET NON-PREFERRED AGENT(S)
Target preferred and non-preferred agent(s) to be determined client	Target preferred and non-preferred agent(s) to be determined client
Filgrastim agents **Granix** (tbo-filgrastim) **Neupogen** (filgrastim) **Nivestym** (filgrastim-aafi) **Zarxio** (filgrastim-sndz) **Pegfilgrastim agents** **Fulphila** (pegfilgrastim-jmdb) **Neulasta** (pegfilgrastim) **Nyvepria** (pegfilgrastim-apgf) **Udenyca** (pegfilgrastim-cbqv) **Ziextenzo** (pegfilgrastim-bmez) **Other CSF agents** **Leukine** (sargramostim)	

Brand (generic)	GPI	Multisource Code	HCPCS/ J Code
Fulphila (pegfilgrastim-jmdb)			
6mg/0.6 mL prefilled syringe	8240157020E520	M, N, O, or Y	Q5108
Granix (tbo-filgrastim)			
300 mcg/0.5 mL prefilled syringe	8240152070E530	M, N, O, or Y	J1447
300 mcg/mL vial	82401520702020	M, N, O, or Y	J1447
480 mcg/0.8 mL prefilled syringe	8240152070E540	M, N, O, or Y	J1447
480 mcg/1.6 mL vial	82401520702030	M, N, O, or Y	J1447
Leukine (sargramostim)			
250 mcg injection	82402050002120	M, N, O, or Y	J2820
Neulasta (pegfilgrastim)			
6mg/0.6 mL prefilled syringe	8240157000E520	M, N, O, or Y	J2505
6mg/0.6 mL prefilled syringe kit (Onpro kit)	8240157000F820	M, N, O, or Y	J2505
Neupogen (filgrastim)			
300 mcg/0.5 mL prefilled syringe	8240152000E545	M, N, O, or Y	J1442
480 mcg/0.8 mL prefilled syringe	8240152000E550	M, N, O, or Y	J1442
300 mcg/mL injection	82401520002010	M, N, O, or Y	J1442
480mcg/1.6 mL vial	82401520002012	M, N, O, or Y	J1442
Nivestym (filgrastim-aafi)			
300 mcg/0.5 mL prefilled syringe	8240152010E520	M, N, O, or Y	Q5110
480 mcg/0.8 mL prefilled syringe	8240152010E530	M, N, O, or Y	Q5110
300 mcg/mL single use vial	82401520102020	M, N, O, or Y	Q5110
480 mcg/mL single use vial	82401520102030	M, N, O, or Y	Q5110
Nyvepria (pegfilgrastim-apgf)			
6 mg/0.6 mL prefilled syringe	8240157002E520	M, N, O, or Y	Q5122
Udenyca (pegfilgrastim-cbqv)			
6 mg/0.6 mL prefilled syringe	8240157010E520	M, N, O, or Y	Q5111

 Effective: xx/xx/xx

Zarxio (filgrastim-sndz)			
300 mcg/0.5 mL prefilled syringe	8240152060E530	M, N, O, or Y	Q5101
480 mcg/0.8 mL prefilled syringe	8240152060E540	M, N, O, or Y	Q5101
Ziextenzo (pegfilgrastim-bmez)			
6 mg/0.6 mL prefilled syringe	8240157005E520	M, N, O, or Y	Q5120

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

Evaluation

Target agent(s) will be approved when ALL of the following are met:

1. The requested agent is being used for ONE of the following:
    a. An FDA approved indication
    OR
    b. An indication in CMS approved compendia

    AND
2. If the client has preferred agents, then ONE of the following:
    a. The requested agent is the preferred agent
    OR
    b. Information has been provided that indicates the patient has been treated with the requested agent in the past 365 days
    OR
    c. There is documentation that the patient has had an ineffective treatment response to the active ingredient(s) of ALL preferred agent(s)
    OR
    d. The patient has a documented intolerance, hypersensitivity, or FDA labeled contraindication to the active ingredient(s) of ALL preferred agent(s)
    OR
    e. The prescriber has submitted documentation indicating ALL preferred agent(s) are likely to be ineffective or are likely to cause an adverse reaction or other harm to the patient

    AND
3. The patient does NOT have any FDA labeled contraindications to the requested agent
    AND
4. The requested quantity (dose) is within FDA labeled dosing or supported in compendia for the requested indication

Length of approval: up to 12 months

 Effective: xx/xx/xx