

Department:	Pharmacy Management	Original Approval:	01/20/2016
Policy #:	PM137	Last Approval:	12/12/2018
Title:	Filgrastim Products		
Approved By:	UM Committee		

REQUIRED CLINICAL DOCUMENTATION FOR REVIEW.

Documentation required to determine medical necessity for Filgrastim products p): History and/or physical examination notes and relevant specialty consultation notes that address the problem and need for the service: -Diagnosis -Prescribed by or in consultation with an oncologist or hematologist or a physician that specializes in transplantation -Medication list (current and past) to include start and end dates of all chemotherapy agents -Age -Labs/diagnostics -Weight -Dosing and duration requested - Initial/extended approval.

BACKGROUND

Neupogen

Neupogen, a granulocyte colony stimulating factor (G-CSF), is indicated for the following: 1) to 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; 2) to reduce the time to neutrophil recovery and the duration of fever following induction or consolidation chemotherapy treatment of adults with acute myeloid leukemia (AML); 3) to reduce the duration of neutropenia and neutropenia-related clinical sequelae (e.g., febrile neutropenia) in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by marrow transplantation; 4) for the mobilization of hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis; 5) for chronic administration to 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; and 6) to increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome).¹ Nivestym and Zarxio are two products that are biosimilars to Neupogen.^{1,2,9} These have the same indications except do not have an indication regarding hematopoietic syndrome of acute radiation syndrome. Depending on the indication, filgrastim is given by subcutaneous (SC) bolus injection, by short intravenous (IV) infusion (15 to 30 minutes), or by continuous SC or continuous IV infusion.¹ Data support the use of filgrastim in many other conditions. Granix is another filgrastim product.¹⁰

Neupogen is available in single use vials and prefilled syringes. The single-use vials contain either 300 mcg (1 mL) of Neupogen (300 mcg/mL) or 480 mcg (1.6 mL) of Neupogen (300 mcg/mL). The single-use syringes contain either 300 mcg (0.5 mL) of Neupogen (600 mcg/mL) or 480 mcg (0.8 mL) of Neupogen (600 mcg/mL). Zarxio is available in single-use prefilled syringes. The single-use syringes contain either 300 mcg (0.5 mL) of Zarxio or 480 mcg (0.8 mL) of Zarxio. The Zarxio prefilled syringe is not designed to allow for direct administration of doses of less than 0.3 mL. The spring mechanism of the needle guard affixed to the 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 less than 0.3 mL for direct administration to patients. Nivestym is available in single-dose vials (300 mcg/mL and 480 mcg/1.6 mL) and as prefilled syringes (300 mcg/0.5 mL and 480/0.8 mL). The spring mechanism of the needle guard affixed to the 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 less than 0.3 mL for direct administration to patients. Thus, the direct administration to patients requiring doses of less than 0.3 mL (180 mcg) is not recommended for syringes; patients should be directed to the single-dose vial.

DEFINITIONS

None.

INDICATIONS/CRITERIA

Medicaid Members	Neupogen is the preferred Filgrastim on the WA HCA Single Preferred Drug list. Zarxio and Nivestym are not considered for approval unless member has tried and failed the preferred product (Neupogen). <i>Continue to criteria for approval below.</i>
Medicare Members	<i>Step-utilization of Part D drugs not required.</i>

Coverage of Neupogen is recommended in those who meet the following criteria:

FDA-Approved Indications

1. Patients with Cancer Receiving Myelosuppressive Chemotherapy.

Criteria. *The patient must meet the following criteria (A AND B):*

- A)** The agent is prescribed by, or in consultation with, an oncologist or hematologist; AND
- B)** The patient meets ONE of the following conditions (i, ii, iii, or iv):
 - i.** The patient is receiving myelosuppressive anti-cancer medications that are associated with a high risk of febrile neutropenia (the risk of febrile neutropenia is at least 20% based on the chemotherapy regimen); OR
 - ii.** The patient is receiving myelosuppressive anti-cancer medications that are associated with a risk of febrile neutropenia but the risk is less than 20% based on the chemotherapy regimen and the patient has one or more risk factors for febrile neutropenia according to the prescribing physician (e.g., aged ≥ 65 years; prior chemotherapy or radiation therapy; persistent neutropenia; bone marrow involvement by tumor; recent surgery and/or open wounds; liver and/or renal dysfunction; poor performance status; or human immunodeficiency virus [HIV] infection); OR
 - iii.** The patient has had a neutropenic complication from prior chemotherapy and did not receive prophylaxis with a colony stimulating (e.g., filgrastim products [Neupogen, Zarxio, Granix, Nivestym], pegfilgrastim products [Neulasta, Fulphila]), and Leukine®

[sargramostim injection]) and a reduced dose or frequency of chemotherapy may compromise treatment outcome; OR

- iv. The patient who has received chemotherapy has febrile neutropenia and has at least one risk factor for poor clinical outcomes or for developing infection-associated complications according to the prescribing physician³⁻⁴ (e.g., sepsis syndrome; age > 65 years; severe neutropenia [absolute neutrophil count {ANC} < 100 cells/mm³]; neutropenia expected to be > 10 days in duration; invasive fungal infection; other clinically documented infections).

Filgrastim is indicated for this condition to 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 and fever.¹⁻⁴ The National Comprehensive Cancer Network (NCCN) guidelines for myeloid growth factors (version 1.2018) recommend Neupogen, along with other CSFs, for prophylactic use if the patient is receiving anti-cancer medications that are associated with a high (> 20%) incidence of severe neutropenia with fever.³ Consider CSF therapy for patients with an intermediate (10% to 20%) probability of developing febrile neutropenia based on risk factors. The NCCN guidelines also recommend therapy with a CSF in other scenarios in those given myelosuppressive chemotherapy.

Dosing in Patients with Cancer (Adults and Children) Receiving Myelosuppressive Chemotherapy.

Dosing must meet the following: The starting dose is 5 mcg per kg per day by SC or IV injection for up to 2 weeks.¹⁻² Doses may be increased in increments of 5 mcg per kg according to the duration and severity of the absolute neutrophil count (ANC) nadir after chemotherapy.

The recommended starting dose of Filgrastim is 5 mcg/kg/day given as a single daily injection by SC injection, by short IV infusion (15 to 30 minutes), or by continuous IV infusion.¹⁻² Dose increases in increments of 5 mcg/kg may be considered for each chemotherapy cycle and is according to the duration and severity of the ANC nadir. It is recommended to stop if the ANC increases beyond 10,000 cells/mm³. Filgrastim is given at least 24 hours after cytotoxic chemotherapy, and should not be given within the 24-hour period before chemotherapy. A transient increase in the neutrophil count is usually seen 1 to 2 days after starting Filgrastim. To ensure a sustained therapeutic response, these agents are given daily for up to 2 weeks or until the ANC reaches 10,000 cells/mm³ following the expected chemotherapy-induced neutrophil nadir. The duration of therapy needed may depend on the myelosuppressive potential of the chemotherapy regimen that is used. According to the NCCN guidelines for myeloid growth factors, the SC route is preferred.³ Filgrastim is started the next day up to 3 to 4 days after completion of chemotherapy and treatment continues through post-nadir recovery. Because the duration of neutropenia often increases with each cycle of chemotherapy, longer periods of therapy with a CSF may be required for later chemotherapy cycles than for early cycles.¹⁻²

Initial Approval/Extended Approval.

- A) Initial Approval. Initial approval is for up to 6 months.
- B) Extended Approval. Extended approval is for up to 6-month intervals if the patient continues to receive myelosuppressive chemotherapy.

Duration of Therapy in Patients with Cancer (Adults and Children) Receiving Myelosuppressive Chemotherapy. Therapy may be continued as long as the patient is receiving myelosuppressive chemotherapy.

Labs/Diagnostics. None required.

2. Adults with Acute Myeloid Leukemia (AML) Receiving Chemotherapy.

Criteria. *The patient must meet the following criteria:* The agent is prescribed by, or in consultation with, an oncologist or hematologist.

Filgrastim is indicated to reduce the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of adults with AML.¹⁻² In the professional opinion of specialist physicians reviewing the data, we have adopted this criterion.

Dosing in AML. *Dosing must meet the following:* The starting dose is 5 mcg per kg per day by SC or IV injection for up to 2 weeks and starting 24 hours after the last dose of chemotherapy until neutrophil recovery¹⁻² that is usually for a maximum of 35 days. Doses may be increased in increments of 5 mcg per kg according to the duration and severity of the absolute neutrophil count (ANC) nadir after chemotherapy.

The recommended starting dose of filgrastim is 5 mcg/kg/day given as a single daily injection by SC injection, by short IV infusion (15 to 30 minutes), or by continuous IV infusion.¹⁻² Dose increases in increments of 5 mcg/kg may be considered for each chemotherapy cycle and is according to the duration and severity of the ANC nadir. It is recommended to stop filgrastim if the ANC increases beyond 10,000 cells/mm³. Filgrastim is given at least 24 hours after cytotoxic chemotherapy, and should not be given within the 24-hour period before chemotherapy. A transient increase in the neutrophil count is usually seen 1 to 2 days after starting filgrastim. To ensure a sustained therapeutic response, these agents are given daily for up to 2 weeks or until the ANC reaches 10,000 cells/mm³ following the expected chemotherapy-induced neutrophil nadir. The duration of therapy needed may depend on the myelosuppressive potential of the chemotherapy regimen that is used. Filgrastim is given following induction chemotherapy and for consolidation chemotherapy (i.e., post-remission chemotherapy).

Initial Approval/Extended Approval.

- A) Initial Approval.** Initial approval is for up to 6 months.
- B) Extended Approval.** Extended approval is at 6-month intervals.

Duration of Therapy in AML. Therapy may be continued as long as the patient is receiving chemotherapy. Some patients will receive an autologous or allogeneic hematopoietic stem cell transplantation and may require Neupogen after peripheral blood progenitor cell (PBPC) collection. See Criteria 4 below.

Labs/Diagnostics. None required.

3. Patients with Cancer Receiving Bone Marrow Transplant (BMT).

Criteria. *The patient must meet the following criteria:* The agent is prescribed by, or in consultation with, a hematologist, an oncologist, or a physician that specializes in transplantation.

Filgrastimis indicated 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 BMT.¹⁻² This criterion is recommended based on the professional opinion of specialized and other physicians.

Dosing in BMT. *Dosing must meet the following:* 10 mcg per kg per day given as an IV infusion no longer than 24 hours. During the period of neutrophil recovery, the dose should be titrated according to the absolute neutrophil count (ANC). Doses up to 30 mcg per kg per day have been used.¹⁻² Alternative dosing will be assessed individually on a case-by-case basis.

The recommended dose of filgrastim after BMT is 10 mcg/kg/day given as an IV infusion for no longer than 24 hours.¹⁻² The first dose is given at least 24 hours after cytotoxic chemotherapy and at least 24 hours after bone marrow infusion. During the period of neutrophil recovery, the daily dosage of filgrastim is titrated according to the neutrophil response. Recommendations for dosage adjustments during neutrophil recovery are as follows: 1) when the ANC is > 1,000 cells/mm³ for 3 consecutive days, reduce the dose to 5 mcg/kg/day; 2) then, if the ANC remains > 1,000 cells/mm³ for 3 or more consecutive days, discontinue filgrastim; and 3) then, if ANC decreases to < 1,000 cells/mm³ resume at 5 mcg/kg/day. If the ANC decreases to < 1,000 cells/mm³, at any time during the 5 mcg/kg/day administration, increase the dose to 10 mcg/kg/day, and then follow the previous steps. In the pivotal trials establishing efficacy of filgrastim in patients with cancer receiving BMT, the dose of these agents was 10 mcg/kg/day or 30 mcg/kg/day.

Initial Approval/Extended Approval.

- A) *Initial Approval.* Approve for 1 month.
- B) *Extended Approval.* Not applicable.

Duration of Therapy in BMT. Use is short-term after BMT (up to one month). Alternative durations will be assessed individually on a case-by-case basis.

Labs/Diagnostics. None required.

4. Patients (Adults and Children) Undergoing Peripheral Blood Progenitor Cell (PBPC) Collection and Therapy.

Criteria. *Patient must meet the following criteria:* Filgrastim is prescribed by, or in consultation with, an oncologist, a hematologist, or a physician that specializes in transplantation.

Filgrastim is indicated for the mobilization of hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.¹⁻² Mobilization allows for the collection of increased numbers of

progenitor cells capable of engraftment compared with collection by leukapheresis without mobilization or bone marrow harvest. After myeloablative chemotherapy, the transplantation of an increased number of progenitor cells can lead to a more rapid engraftment, which may result in a decreased need for supportive care. The scenarios where filgrastim are utilized includes patients with cancer or healthy donors undergoing mobilization of PBPC, as well as patients with cancer post autologous PBPC transplantation.^{1-3,5-6} This criterion is recommended based on the professional opinion of specialized and other physicians.

Dosing in Patients (Adults and Children) Undergoing PBPC Collection and Therapy. Dosing must meet ONE of the following (A, B, OR C):

- A)** Patients with Cancer or Healthy Donors Undergoing Mobilization for PBPC: 10 mcg per kg per day SC, either as a bolus or continuous infusion for 5 to 7 days. Some patients may require up to 32 mcg per kg per day SC. Dosing can be once daily or twice daily.³ Alternate dosing will be assessed individually on a case-by-case basis.

The recommended dosage of filgrastim for the mobilization of autologous PBPC is 10 mcg/kg/day as a SC injection.¹⁻² Filgrastim is given for at least 4 days before the first leukapheresis procedure and continued until the last leukapheresis. The optimal duration of filgrastim administration and leukapheresis schedule have not been established, but filgrastim is usually administered for 6 to 7 days with leukapheresis on Days 5, 6, and 7 and was safe and effective in patients with cancer who were undergoing PBPC collection for autologous transplantation.¹⁻² Discontinue Filgrastim if the white blood cell count increases to > 100,000 cells/mm³. Other sources indicate 5 days of filgrastim 10 mcg per kg per day is adequate⁵⁻⁶ but some patients may require a longer duration of therapy (see duration of therapy section). Twice daily dosing may be utilized in certain circumstances.³

- B)** Patients Undergoing Mobilization of PBPC Who Are Poor Mobilizers: 12.5 to 50 mcg per kg per day IV or SC.⁶ Dosing can be once daily or twice daily.³ Alternate dosing will be assessed individually on a case-by-case basis.

Poor mobilizers (e.g., patients who fail to mobilize an adequate number of stem cells on the first attempt; patients with Hodgkin's lymphoma, non-Hodgkin's lymphoma, and preleukemic syndromes; recent chemotherapy or radiation), may use filgrastim or use other regimens that add Leukine to filgrastim, add Mozobil® (plerixafor injection), or mobilization with chemotherapy plus filgrastim.^{3,6}

- C)** Patients with Cancer Post Autologous PBPC Transplantation: 5 to 24 mcg per kg per day after reinfusion of the collected cells until a sustainable ANC is attained.¹⁻² Dosing can be once daily or twice daily.³ Alternative dosing will be assessed individually on a case-by-case basis.

In clinical trials of filgrastim for mobilization of hematopoietic progenitor cells, filgrastim was given to patients at doses of 5 to 24 mcg/kg/day after reinfusion of the collected cells until a sustainable ANC \geq 500 cells/mm³ was reached.¹⁻² Another recommendation for supportive care in patients post autologous stem cell or cord blood transplant, is to give filgrastim 5 mcg/kg/day

beginning \geq 5 days post-transplant until recovery of ANC (e.g., $> 1,500$ cells/mm³ for 2 consecutive days).³

Initial Approval/Extended Approval.

Patients with Cancer or Healthy Donors Undergoing Mobilization of PBPC.

- A) ***Initial Approval.*** For unrelated healthy donors, 5 days of therapy with filgrastim 10 mcg per kg per day are used.^{1-2,5-6} For patients with cancer, 5 to 7 days of filgrastim 10 mcg per kg per day are usually given once daily; twice daily dosing may be used. Alternative regimens will be assessed individually on a case-by-case basis and may be extended for some patients (e.g., patients who are poor mobilizers).
- B) ***Extended Approval.*** Not applicable.

Patients with Cancer Post Autologous PBPC Transplantation.

- A) ***Initial Approval.*** 14 days or until the absolute neutrophil count (ANC) is $> 1,500$ cells/mm³ for 3 consecutive days. Usually the duration of therapy is 9 to 11 days but has ranged from 7 to 63 days. Alternative regimens will be assessed individually on a case-by-case basis.
- B) ***Extended Approval.*** Not applicable.

Duration of Therapy in PBPC.

Patients with Cancer or Healthy Donors Undergoing Mobilization of PBPC. 5 days of filgrastim. Alternative durations will be assessed individually on a case-by-case basis and may be extended for some patients (e.g., patients who are poor mobilizers).

The National Marrow Donor Program protocol gives filgrastim for 4 consecutive days (in patients weighing < 35 kg) or 5 consecutive days in unrelated donors (allogeneic transplantation).⁵ In some instances, patients may require a longer duration of therapy (e.g., patients with cancer heavily pretreated with chemotherapy, healthy patients in which a higher number of cells are needed due to the type of transplantation).

Patients with Cancer Post Autologous PBPC Transplantation. 14 days of filgrastim. Approve for another 14 days if ANC is not at a sustainable level. Most patients have a response after 28 days of filgrastim. Alternative durations will be assessed individually on a case-by-case basis.

Labs/Diagnostics. None required.

5. Patients (Adults and Children) with Severe Chronic Neutropenia (e.g., Congenital Neutropenia, Cyclic Neutropenia, Idiopathic Neutropenia).

Criteria. *The patient must meet the following criteria:* The agent is prescribed by, or in consultation with, a hematologist.

Filgrastim is indicated for chronic administration to 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.^{1-3,7-8} The criteria is recommended based on the professional opinion of specialized and other physicians.

Dosing in Severe Chronic Neutropenia. Dosing must meet the following: The starting dose in congenital neutropenia is 6 mcg per kg twice daily (BID) by SC injection.^{1-3,7} For idiopathic or cyclic neutropenia, the starting dose is 5 mcg per kg SC once daily. The dose is adjusted based on the clinical response and the ANC. Alternative dosing will be assessed individually on a case-by-case basis.

The recommended starting dose in congenital neutropenia is 6 mcg/kg BID by SC injection.¹⁻² The recommended starting dose in patients with idiopathic or cyclic neutropenia is 5 mcg/kg as a single daily SC injection. In patients with severe chronic neutropenia, chronic daily administration is required. The dosage is individualized based on the patient's clinical course and the ANC. In the severe chronic neutropenia post-marketing surveillance study, the median daily doses of filgrastim were: 6 mcg/kg (congenital neutropenia); 2.1 mcg/kg (cyclic neutropenia); and 1.2 mcg/kg (idiopathic neutropenia). In rare instances, patients with congenital neutropenia have required doses of filgrastim \geq 100 mcg/kg/day. Many different doses have been used long-term. ANC should not be used as the sole indication of efficacy.^{1,3,7} Some data show that patients with idiopathic and cyclic neutropenia generally respond to low-dose daily, alternative day, or thrice-per-week filgrastim (1 to 3 mcg per kg per day SC).³ Patients with congenital neutropenia generally require higher doses of 3 to 10 mcg per kg per day.

Initial Approval/Extended Approval.

- A) Initial Approval. Initial approval is for up to 6 months.
- B) Extended Approval. Extended approval is for up to 6 months.

Duration of Therapy in Patients with Severe Chronic Neutropenia. Therapy is chronic.

Labs/Diagnostics. None required.

6. Radiation Syndrome (Hematopoietic Syndrome of Acute Radiation Syndrome).

Criteria. The patient must meet the following criteria: The agent is prescribed by, or in consultation with, a physician with expertise in treating acute radiation syndrome.

Neupogen is indicated to increase survival in patients acutely exposed to myelosuppressive dose of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome).¹ The recommended dose of Neupogen is 10 mcg/kg as a single daily SC injection for patients exposed to myelosuppressive radiation doses. Administer Neupogen as soon as possible after suspected or confirmed exposure to radiation doses greater than 2 gray. Continue Neupogen therapy until the absolute neutrophil count remains greater than 1,000/mm³ for 3 consecutive days. It is notable that due to ethical and feasibility reasons, studies investigating the efficacy of Neupogen could not be done in humans with acute radiation syndrome. Approval of Neupogen for this use was based on efficacy studies performed in animals and data supporting the use of Neupogen for other approved indications.¹ Other sources also cite filgrastim being used for this scenario.^{9-10,19}

Dosing in Patients with Radiation Syndrome (Hematopoietic Syndrome of Acute Radiation Syndrome).
Dosing must meet the following: 10 mcg per kg per day SC.¹

The recommended dose of Neupogen is 10 mcg/kg as a single daily SC injection for patients exposed to myelosuppressive doses of radiation.¹ Filgrastim is given as soon as possible after suspected or confirmed exposure to radiation doses of greater than 2 grays. The patient's absorbed radiation dose (i.e., level of radiation exposure) is estimated based on information from public health authorities, biodosimetry if available, or clinical findings such as time to onset of vomiting or lymphocyte depletion kinetics. A baseline complete blood count (CBC) is obtained, and then serial CBCs are done approximately every third day until the ANC remains > 1,000 cells/mm³ for three consecutive CBCs. Administration of filgrastim is not delayed if a CBC is not readily available. Administration of filgrastim is continued until the ANC remains > 1,000 cells/mm³ for three consecutive CBCs or exceeds 10,000 cells/mm³ after a radiation-induced nadir.

Initial Approval/Extended Approval.

- A) Initial Approval. Initial approval is for 1 month.
- B) Extended Approval. Approve at 1-month intervals.

Duration of Therapy in Radiation Syndrome (Hematopoietic Syndrome of Acute Radiation Syndrome).
Usually only one course is needed until the ANC is adequate.

Labs/Diagnostics required. None required.

Other Uses with Supportive Evidence

7. Neutropenia Associated with Human Immunodeficiency Virus (HIV) or Acquired Immunodeficiency Syndrome (AIDS) in Adults.

Criteria. Patient must meet the following criteria: The agent is prescribed by, or in consultation with, a physician that specializes in infectious diseases, a hematologist, or a physician that specializes in the management of HIV/AIDS.

Neutropenia occurs in patients with HIV and may be caused by medications or due to the disease process. Studies have assessed use of filgrastim for the treatment of neutropenia in this patient population.¹²⁻¹⁵ In one open-label, non-comparative, multicenter study involving 200 HIV-positive patients filgrastim reversed neutropenia in 98% of patients with a median reversal time of 2 days.¹³ In another multicenter, randomized, controlled, open-label trial, use of daily filgrastim or intermittent filgrastim reduced the incidence of severe neutropenia or death compared with control patients who had advanced HIV infection.¹² Additionally, those receiving filgrastim developed fewer bacterial infections.

Dosing for Neutropenia in Adults with HIV or AIDS. Dosing must meet the following: Neupogen 5 to 10 mcg per kg SC once per day.

Initial Approval/Extended Approval.

- A) Initial Approval. Initial approval is for 4 months.
- B) Extended Approval. Extended approval is at 4-month intervals.

Duration of Therapy for Neutropenia in Adults with HIV or AIDS. Use may be long-term due to the nature of the disease and/or the need to continue medication therapy.

Labs/Diagnostics. None required.

8. Treatment of Myelodysplastic Syndrome (MDS) in Adults.

Criteria. Patient must meet the following criteria: The agent is prescribed by, or in consultation with, an oncologist or hematologist.

The NCCN guidelines on MDS (version 1.2019) recommend filgrastim for use in certain patients with MDS (e.g., neutropenic patients with recurrent or resistant infections, combination use with epoetin alfa or Aranesp® [darbepoetin alfa injection]).¹⁶ In one trial, 39% (n = 48/123 assessable patients) of patients with MDS treated with erythropoietin plus G-CSF achieved an erythroid response. Also, 29% (n = 25/85) of transfusion-dependent patients became transfusion independent.¹⁷ Other data are available.¹⁸

Dosing in MDS. Dosing must meet the following: The dose range is 1 to 2 mcg per kg given 1 to 2 times per week SC¹⁶ or 5 mcg per kg once daily SC or IV.¹⁷

Initial Approval/Extended Approval.

- A) Initial Approval. Initial approval is for 3 months.
- B) Extended Approval. Approve at 3-month intervals.

Duration of Therapy in MDS. Therapy is usually intermittent.

Labs/Diagnostics. None required.

9. Aplastic Anemia (Adults and Children).

Criteria. The patient must meet the following criteria: The agent is prescribed by, or in consultation with, a hematologist.

Filgrastim has been utilized in the treatment of aplastic anemia, usually in combination with immunosuppressive therapy or with erythropoietin-stimulating products.²⁰⁻²⁴ In one multicenter, randomized, controlled study, patients with anemia associated with aplastic anemia (n = 131) were treated with G-CSF alone or with epoetin alfa.²¹ The response rates at 12 weeks in 110 evaluable patients were between 12.9% and 36.8%.

Dosing in Aplastic Anemia. Dosing must meet the following: 5 mcg per kg per day SC once daily or 1 to 3 times per week SC.¹⁹

Initial Approval/Extended Approval.

- A) *Initial Approval.* Approve for 1 month.
- B) *Extended Approval.* Approval is at 1-month intervals.

Duration of Therapy in Patients with Aplastic Anemia. Therapy is usually intermittent.

Labs/Diagnostics. None required.

10. Drug-Induced (Non-Chemotherapy) Agranulocytosis or Neutropenia.

Criteria. Approve

Filgrastim has been used for agranulocytosis caused by non-cytotoxic medications, primarily described in case series, case reports and literature reviews.^{11,25-32}

Dosing in Drug-Induced (Non-Chemotherapy) Agranulocytosis or Neutropenia. Dosing must meet the following: The dose range is 5 to 10 mcg per kg per day SC or 300 mcg per day SC once daily.

Initial Approval/Extended Approval.

- A) *Initial Approval.* Approve for 1 month.
- B) *Extended Approval.* Approve at 1-month intervals.

Duration of Therapy in Patients with Drug-Induced (Non-Chemotherapy) Agranulocytosis or Neutropenia). Therapy is usually short-term (up to 1 month).

Labs/Diagnostics. None required.

11. Acute Lymphocytic Leukemia (ALL).

Criteria. The patient must meet the following criteria: The agent is prescribed by, or in consultation with, an oncologist or hematologist.

Data notes some benefits in patients with ALL in selected scenarios.^{4,32-33} This criterion is recommended based on the professional opinion of specialized and other physicians.

Dosing in ALL: Dosing must meet the following: The filgrastim dose is in the range of 5 to 10 mcg per kg per day SC.³³⁻³⁴

Initial Approval/Extended Approval.

- A) *Initial Approval.* Approval is for up to 1 month.
- B) *Extended Approval.* Not applicable.

Duration of therapy in patients with ALL. Use is short-term.

Labs/Diagnostics. None required.

12. Radiation-Induced Neutropenia.

Criteria. *Patient must meet the following criteria (A AND B).*^{1,4,35-37}

- A) Filgrastim is prescribed by, or in consultation with, an oncologist, radiologist, or radiation oncologist; AND
- B) The patient is not concurrently receiving chemotherapy.

ASCO guidelines, updated in 2015, state that CSFs may be considered in patients receiving radiation therapy alone if prolonged delays secondary to neutropenia are expected.⁴ However, the filgrastim prescribing information notes that the safety and efficacy of filgrastim have not been evaluated in patients receiving concurrent radiation therapy.¹⁻² Simultaneous use of filgrastim with chemotherapy and radiation therapy should be avoided. The ASCO guidelines state that CSFs should be avoided in patients receiving concomitant chemotherapy and radiation therapy, particularly involving the mediastinum.⁴ The NCCN guidelines for myeloid growth factors (version 1.2018) state the prophylactic use of CSFs in patients given concurrent chemotherapy and radiation is not recommended.³ In one trial that administered radiotherapy with simultaneous chemotherapy, an unexpected reduced local control was reported.³⁵

Dosing in Radiation-Induced Neutropenia. *Dosing must meet the following:* The dose of is 5 mcg per kg per day SC or 300 mcg SC daily.

Initial Approval/Extended Approval.

- A) *Initial Approval.* Approve for 6 months.
- B) *Extended Approval.* Approve at 6-month intervals.

Duration of Therapy in Radiation-Induced Neutropenia. Therapy may continue as long as the patient is receiving radiation therapy.

Labs/Diagnostics. None required.

Waste Management for All Indications.

Single-use vials and syringes contain 300 and 480 mcg of Neupogen and Nivestym. Single-use prefilled syringes contain 300 or 480 mcg of Zarxio. Dose is sometimes based on a mcg per kg body weight basis with dose adjustment as needed. Use the most efficient formulation that delivers the needed dose.

Conditions Not Recommended for Approval

Filgrastim has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

Coverage is not recommended for circumstances *not* listed in the *Recommended Authorization Criteria*. Criteria will be updated as new published data are available.

SPECIAL CONSIDERATIONS

None.

LIMITATIONS/EXCLUSIONS

Please refer to a product line's certificate of coverage for benefit limitations and exclusions for these services:

PRODUCT LINE	LINK TO CERTIFICATE OF COVERAGE
MEDICARE ADVANTAGE	http://healthfirst.chpw.org/for-members/resource-library/handbooks-and-guides
WASHINGTON APPLE HEALTH	http://chpw.org/our-plans/apple-health/
INTEGRATED MANAGED CARE	http://chpw.org/our-plans/apple-health/

Citations & References

References	
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Other Requirements	
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Revision History

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01/13/2016	New	Kelly Force; Yusuf Rashid, RPh
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01/12/2017	No revisions	Fran McGaugh
01/13/2017	Approval	MMLT
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