MEDICAL MUTUAL®

Drug Policy

Policy:	**201424**	**Initial Effective Date: 10/30/2014**
Code(s):	**HCPCS J1442, J1447, J2505, J2820, J3590 and Q5101**	**Annual Review Date: 07/19/2018**
SUBJECT:	**Colony Stimulating Factors** - **Neupogen® (Filgrastim)** - **Granix™ (tbo-filgrastim)** - **Neulasta® (Pegfilgrastim)** - **Leukine® (Sargramostim)** - **Zarxio™ (filgrastim-sndz)** - **Fulphila™ (pegfilgrastim-jmdb)**	**Last Revised Date: 07/19/2018**

Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.

Definition: Colony stimulating factors (e.g., Fulphilia, Neupogen, Granix, Neulasta, Leukine, Zarxio) are recombinant cytokine proteins that act on hematopoietic cells by binding to specific cell surface receptors, thereby stimulating proliferation, differentiation, commitment and end cell functional activation. These glycoproteins stimulate bone marrow proliferation, reduce the maturation time of neutrophils, increase peripheral neutrophil count and prevent infection.

Policy Statement
This policy involves the use of Fulphilia, Granix, Leukine, Neulasta, Neupogen and Zarxio. Prior authorization is recommended for pharmacy and medical benefit coverage of Colony Stimulating Factors. Coverage is recommended for those who meet the conditions of coverage in the **Criteria, Dosing, Initial/Extended Approval, Duration of Therapy, and Labs/Diagnostics** for the diagnosis provided. The requirement that the patient meet the Criteria for coverage of the requested medication applies to the initial authorization only. **Waste Management** applies for all covered conditions administered by a healthcare professional. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria and Waste Management section.

*The site of care medical necessity criteria applies to initial therapy and reauthorizations under the medical benefit.

I. Granix:

FDA-Approved Indications

1. <u>Cancer Patients Receiving Myelosuppressive Chemotherapy who are Adults</u>.

Criteria. *<u>The patient must meet the following criteria (A, B, and C)</u>:*
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, <u>or</u> 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 factor (e.g., Granix, Neulasta® [pegfilgrastim injection], Neupogen® [filgrastim injection], Zarxio™ [filgrastim-sndz injection], 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 physician (e.g., sepsis syndrome; age > 65 years; severe neutropenia [absolute neutrophil count < 100 cells/mm^3]); neutropenia expected to be > 10 days in duration; invasive fungal infection; other clinically documented infections; prior episode of febrile neutropenia).

C) Site of care medical necessity is met*.

Dosing in Adults with Cancer Receiving Myelosuppressive Chemotherapy. *Dosing must meet the following:* The dose is 5 mcg per kg per day by SC injection.

According to the NCCN guidelines for myeloid growth factors (version 1.2017), the SC route is preferred. Granix is started the next day or up to 3 to 4 days after completion of chemotherapy and continued through post-nadir ANC recovery to normal levels.

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 Adults with Cancer Receiving Myelosuppressive Chemotherapy. Therapy may be continued as long as the patient is receiving myelosuppressive chemotherapy.

Labs/Diagnostics. None required.

Waste Management for All Indications.

Single use, preservative free syringes are in strengths of 300 mcg/0.5 mL and 480 mcg/0.5 mL. The dose is based on a mcg per kg body weight basis. Use the most efficient formulation that delivers the needed dose.

II. Leukine:

FDA-APPROVED INDICATIONS

1. Acute Myelogenous Leukemia (AML).

Criteria. *Patient must meet the following criteria*: Leukine is prescribed by, or in consultation with, an oncologist or hematologist and Site of care medical necessity is met*.

Leukine is indicated for use following induction chemotherapy in older patients with AML to shorten time to neutrophil recovery and to reduce the incidence of severe and life-threatening infections and infections resulting in death. In the professional opinion of specialist physicians reviewing the data, we have adopted these criteria.

Dosing in AML: *Dosing must meet the following*: The dose is 250 mcg/m^2 per day given IV over a 4-hour period. The dose should start after the completion of induction chemotherapy. Additional doses of induction chemotherapy may be needed. Consolidation chemotherapy may follow with Leukine being given after completion of chemotherapy.

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 AML. Therapy may be continued as long as the patient is on chemotherapy.

Labs/Diagnostics. None required.

2. Peripheral Blood Progenitor Cell (PBPC) Collection in Patients with Cancer (Adults and Children) or Patients with Cancer (Adults and Children) who have Received Therapy with PBPC (Autologous):

Criteria. *Patient must meet the following criteria*: Leukine is prescribed by, or in consultation with, an oncologist, a hematologist, or a physician that specializes in transplantation and Site of care medical necessity is met*.

Leukine is indicated for the mobilization of hematopoietic progenitor cells into peripheral blood for collection by leukapheresis. Mobilization allows for the collection of increased number of progenitor cells capable of engraftment as compared with collection without mobilization. Following myeloabalative chemotherapy, the transplantation of an increased number of progenitor cells can result to more rapid engraftment, which may decrease the need for

supportive care. In the professional opinion of specialist physicians reviewing the data, we have adopted these criteria.

Dosing in Patients with Cancer Undergoing Mobilization of PBPC: *Dosing must meet the following (A OR B)*:
A) 250 to 500 mcg/m^2 per day administered IV over 24 hours or SC once daily; OR
B) 7.5 mcg/kg SC once daily.

Dosing in Patients with Cancer Post PBPC Transplantation (Autologous): *Dosing must meet the following (A OR B)*:
A) 250 mcg/m^2 per day administered IV over 24 hours or SC once daily; OR
B) 7.5 mcg/kg once daily SC.

Dosing should continue at the same dose through the period of PBPC collection. Leukine has been used as a single agent, as well as with Neupogen® (filgrastim injection); Leukine was administered as 7.5 mcg/kg SC in the evening while Neupogen was administered in the morning. The optimal schedule for PBPC collection has not been established. Collection of PBPC is usually begun by Day 5 and performed daily until protocol specified targets were achieved. Exceptions may be made based upon transplant-center protocols.

Initial Approval/Extended Approval.

Patients with Cancer Undergoing Mobilization of PBPC:
A) *Initial Approval*. Initial approval is for 5 to 7 days. Exceptions may be made based upon transplant center protocols.
B) *Extended Approval*. Not applicable.

Patients with Cancer Post PBPC Transplantation (Autologous):
A) *Initial Approval*. Initial approval is for 14 days or until the absolute neutrophil count (ANC) is > 1,500 cells/mm^3 for 3 consecutive days. Exceptions may be made based upon transplant center protocols.
B) *Extended Approval*. Approve for an additional 14 days if ANC is not at a sustainable level (> 1,500 cells/m^3 for 3 consecutive days). Exceptions may be made based upon transplant center protocols.

Duration of Therapy in PBPC:

Patients with Cancer Undergoing Mobilization of PBPC: 5 days. Exceptions may be made based upon transplant center protocols.

Patients with Cancer post PBPC Transplantation (Autologous): 14 days. Approve for another 14 days if the ANC is not at a sustainable level according to the prescribing physician. Most patients have a response after 28 days.

Labs/Diagnostics. None required.

3. Bone Marrow Transplantation (BMT). For the FDA-approved indication in autologous BMT; allogeneic BMT from a Human Leukocyte Antigen (HLA)-Matched Related Donors; and for BMT failure or engraftment delay in patients who have undergone allogeneic or autologous BMT, forward to the Medical Director for review. Coverage criteria are not addressed in this document but will be considered on a case-by-case basis.

Other Uses with Supportive Evidence

4. Patients with Cancer Receiving Myelosuppressive Chemotherapy.

Criteria. *The patient must meet the following criteria (A, B and C)*:

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 factor (Neupogen® [filgrastim injection], Zarxio™ [filgrastim-sndz injection], Neulasta® [pegfilgrastim injection], Granix™ [tbo-filgrastim injection], Leukine) 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 physician (e.g., neutropenia expected to be > 10 days in duration; severe neutropenia [ANC < 100 cells/mm^3], age greater than 65 years; prior episode of febrile neutropenia; invasive fungal infection, and other clinically documented infections).

C) Site of care medical necessity is met*.

The National Comprehensive Cancer Network (NCCN) guidelines for myeloid growth factors (version **1.2017**), recommends use of CSFs in various scenarios in patients with cancer receiving myelosuppressive chemotherapy. It is notable that Leukine has been removed from the list of prophylactic options based on limited use.

Dosing in Patients with Cancer Receiving Myelosuppressive Chemotherapy. *Dosing must meet the following*: The dose is 250 mcg/m^2 per day by SC injection.

According to the NCCN guidelines for myeloid growth factors (version **1.2017**), Leukine therapy starts the next day up to 3 to 4 days after the completion of chemotherapy and is treated through post-nadir recovery.[3] Because the duration of neutropenia often increases with each cycle of chemotherapy, longer periods of Leukine therapy may be required for later chemotherapy cycles than for early cycles.

Initial Approval/Extended Approval.

A) *Initial Approval*. Approve for up to 6 months.

B) *Extended Approval*. Approve at 6-month intervals if the patient continues to receive myelosuppressive chemotherapy.

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

Labs/Diagnostics. None required.

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

Criteria. *The patient must meet the following criteria*: Leukine is prescribed by, or in consultation with, an oncologist or hematologist and Site of care medical necessity is met*.

Leukine is recommended in NCCN guidelines for MDS (version 1.2016) for use in selected patients (e.g., those with recurrent or resistant infections in neutropenic patients, combination use with Epogen®/Procrit® [epoetin alfa injection]).[5] This criterion is recommended based on the professional opinion of specialized and other physicians.

Dosing in MDS in Adults. *Dosing must meet ONE of the following (A, B OR C)*:

A) Leukine 15 to 500 mcg/m^2 once daily by IV infusion over 1 to 12 hours; OR

B) Leukine 30 to 500 mcg/m^2 given by continuous IV infusion over 24 hours; OR

C) Leukine 125 to 250 mcg/m^2 SC once daily.

Initial Approval/Extended Approval.

A) *Initial Approval*. Approve at 3-month intervals.

B) *Extended Approval*. Approve at 3-month intervals.

Duration of Therapy in MDS in Adults. Therapy is usually intermittent.

Labs/Diagnostics. None required.

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

Criteria. *The patient must meet the following criteria*: Leukine is prescribed by, or in consultation with, a physician with expertise in treating acute radiation syndrome and Site of care medical necessity is met*.

The Strategic National Stockpile Radiation Working Group published recommendations for the medical management of acute radiation syndrome in 2004. In any adult with a whole body or significant partial body exposure greater than 3 Grays, therapy with a CSF should be started as soon as biodosimetry results indicate that exposure has occurred or when clinical signs and symptoms indicate a level 3 or 4 degree of hematotoxicity. People at the extremes of age (children < 12 years of age and adults > 60 years of age) may be more susceptible to irradiation and therefore a lower threshold exposure dose (2 Grays) for initiation of CSF therapy is appropriate, as well as in patients who have major trauma injuries or burns. The Radiation Injury Treatment Network updated guidelines in September 2010 for the treatment of acute radiation syndrome (injury). CSF therapy is recommended in a variety of clinical scenarios in patients who have experienced radiation injury (syndrome) based on factors such as the radiation dose.

Dosing in Radiation Syndrome (Hematopoietic Syndrome of Acute Radiation Syndrome): *Dosing must meet the following*: 250 mcg/m^2 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 Radiation Syndrome (Hematopoietic Syndrome of Acute Radiation Syndrome). Usually only one course of Leukine is needed until the ANC is adequate.

Labs/Diagnostics. None required.

Waste Management for All Indications.
Vials contain 250 mcg or 500 mcg. Use the lowest amount of Leukine possible to achieve the dose required.

III. Neulasta and Fulphilia:

FDA-APPROVED INDICATIONS

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

Criteria for Neulasta and Fulphilia. *The patient must meet the following criteria (A, B and C):*

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, or iii):

i. The patient is receiving myelosuppressive anti-cancer medications that are associated with a high risk of febrile neutropenia (i.e., 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 function; 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 factor (Leukine® [sargramostim injection], Neulasta, Neupogen® [filgrastim injection], Zarxio™ [filgrastim-sndz injection] and Granix® [tbo-filgrastim injection]) and a reduced dose or frequency of chemotherapy may compromise treatment outcome; AND

C) Site of care medical necessity is met.*

Neulasta and Fulphilia are indicated 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. The National Comprehensive Cancer Network (NCCN) guidelines for myeloid growth factors (version 1.2017), recommends use of CSF in various scenarios in patients with cancer receiving myelosuppressive chemotherapy.[2] Data are also available in children. In the professional opinion of specialist physicians reviewing the data, we have adopted these criteria.

Dosing in Patients with Cancer Receiving Myelosuppressive Chemotherapy: *Dosing must meet ONE of the following (A, B OR C)*:

A) In adults, the dose is a single SC injection of 6 mg administered once per chemotherapy cycle; OR

B) In children, a single 100 mcg per kg dose is given SC once per chemotherapy cycle; maximum dose is 6 mg.

C) For pediatric patients < 45 kg give a single SC dose once per chemotherapy cycle as follows: 4 mg (0.4 mL) is recommended in patients 31 to 44 kg; 2.5 mg (0.25 mL) is recommended for patients 21 to 30 kg; 1.5 mg (0.15 mL) is recommended for patients 10 to 20 kg; and 0.1 mg/kg (0.01 mL/kg) is recommended for patients < 10 kg. Of note, the Neulasta prefilled syringe is not designed to allow for direct administration of doses < 0.6 mL (6 mg). The syringe does not bear graduation marks, which are needed to accurately measure doses of Neulasta < 0.6 mL

(6 mg) for direct administration to patients. Thus, the direct administration to patients requiring dosing of < 0.6 mL (6 mg) is not recommended due to the potential for errors.

According to the NCCN guidelines for myeloid growth factors (version 1.2017), pegfilgrastim should be administered the day after chemotherapy but pegfilgrastim can also be administered up to 3 to 4 days after chemotherapy. For patients who cannot return to the clinic for next-day administration, alternative options exist. Evidence is available to support use for chemotherapy regimens given once every 3 weeks. Phase II data demonstrate efficacy for chemotherapy regimens given every 2 weeks. In sufficient data support use for cytotoxic chemotherapy regimens given once every week; therefore, pegfilgrastim should not be used.

Initial Approval/Extended Approval.

A) *Initial Approval*. Approval is for up to 6 months at one dose per each chemotherapy cycle. Multiple doses in the same cycle are not recommended.

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

Duration of Therapy in Patients with Cancer Receiving Myelosuppressive Chemotherapy. Therapy may continue as long as the patient is receiving myelosuppressive chemotherapy with one dose per cycle.

Labs/Diagnostics. None required.

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

Criteria for Neulasta. *The patient must meet the following criteria*: Neulasta is prescribed by, or in consultation with, a physician with expertise in treating acute radiation syndrome and Site of care medical necessity is met.*

Neulasta is indicated to increase survival in patients acutely exposed to myelosuppresive doses or radiation (hematopoietic subsyndrome of acute radiation syndrome). The recommended dose of Neulasta is two doses, 6 mg each, given SC 1 week apart. Dosing in pediatric patients < 45 kg is cited in the Neulasta prescribing information. Give the first Neulasta dose as soon as possible after suspected or confirmed exposure to radiation levels > 2 gray. Administer the second dose 1 week after the first dose.

Dosing in Radiation Syndrome (Hematopoietic Syndrome of Acute Radiation Syndrome): *Dosing must meet ONE of the following (A OR B)*:

A) Two doses, 6 mg each, given SC 1 week apart;OR

B) For pediatric patients < 45 kg give two doses SC 1 week apart as follows: 4 mg (0.4 mL) for patients 31 to 44 kg; 2.5 mg (0.25 mL) for patients 21 to 30 kg; 1.5 mg (0.15 mL) for patients 10 to 20 kg; and 0.1 mg/kg (0.01 mL/kg) is recommended for pediatric patients < 10 kg. Of note, the Neulasta prefilled syringe is not designed to allow for direct administration of doses < 0.6 mL (6 mg). The syringe does not bear graduation marks, which are needed to

accurately measure doses of Neulasta < 0.6 mL (6 mg) for direct administration to patients. Thus, the direct administration to patients requiring dosing of < 0.6 mL (6 mg) is not recommended due to the potential for errors.

Initial Approval/Extended Approval.
A) *Initial Approval*. Initial approval is for 1 month.
B) *Extended Approval*. Not applicable.

Duration of Therapy in Radiation Syndrome (Hematopoietic Syndrome of Acute Radiation Syndrome). Two doses of Neulasta are given 1 week apart until the ANC is adequate.

Labs/Diagnostics. None required.

Other Uses with Supportive Evidence

3. Patients with Cancer Following Peripheral Blood Progenitor Cell (PBPC) Transplantation.

Criteria for Neulasta. *The patient must meet the following criteria*: Neulasta is prescribed by, or in consultation with, an oncologist, a hematologist, or a physician that specializes in transplantation and Site of care medical necessity is met.*

Neulasta has been studied in patients with cancer undergoing high dose chemotherapy, followed by infusion of stem cell transplantation, which was usually autologous. Results have been similar to that noted with use of daily Neupogen. Neulasta was usually administered on Day 1 and sometimes up to Day 5 after stem cell transplantation. The NCCN guidelines for myeloid growth factors (version 1.2017) note that Neulasta has been utilized for post autologous hematopoetic cell transplantation.

Dosing in Patients with Cancer Following PBPC Transplantation. *Dosing must meet ONE of the following (A OR B):*
A) The dose in adults is 6 mg SC on Day +1 or up to Day +5 after PBPC transplantation; OR
B) The dose in children is 100 mcg per kg or 200 mcg per kg SC one time.

Initial Approval/Extended Approval.
A) *Initial Approval*. Initial approval is for one dose.
B) *Extended Approval*. Not applicable.

Duration of Therapy in Patients with Cancer Following PBPC Transplantation. Usually only one dose of Neulasta is needed until the absolute neutrophil count (ANC) is adequate.

Labs/Diagnostics. None required.

Waste Management for All Indications.
Pegfilgrastim is available as a 6 mg syringe. This dose should be sufficient in most situations.

IV. Neupogen and Zarxio:

FDA-Approved Indications

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

Criteria. *The patient must meet the following criteria (A, B and C):*

A) The Neupogen or Zarxio 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 factor (e.g., Granix™ [tbo-filgrastim injection], Leukine® [sargramostim injection], Neulasta® [pegfilgrastim injection], Neupogen, Zarxio) 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 physician (e.g., sepsis syndrome; age > 65 years; severe neutropenia [absolute neutrophil count {ANC} < 100 cells/mm^3]; neutropenia expected to be > 10 days in duration; invasive fungal infection; other clinically documented infections); AND

C) Site of care medical necessity is met.*

Neupogen or Zarxio 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. The National Comprehensive Cancer Network (NCCN) guidelines for myeloid growth factors (version 1.2017) 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. 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. 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 Neupogen or Zarxio 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. 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 Neupogen or Zarxio if the ANC increases beyond 10,000 cells/mm^3. Neupogen or Zarxio 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 Neupogen or Zarxio. To ensure a sustained therapeutic response, these agents are given daily for up to 2 weeks or until the ANC reaches 10,000 cells/mm^3 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. Neupogen or Zarxio is started the next day to 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.

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.

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

Criteria. *The patient must meet the following criteria:* Neupogen or Zarxio is prescribed by, or in consultation with, an oncologist or hematologist and Site of care medical necessity is met.*

Neupogen or Zarxio is indicated to reduce the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of adults with AML. 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 recovery 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 Neupogen or Zarxio 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. 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 Neupogen or Zarxio if the ANC increases beyond 10,000 cells/mm^3. Neupogen or Zarxio 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 Neupogen or Zarxio. To ensure a sustained therapeutic response, these agents are given daily for up to 2 weeks or until the ANC reaches 10,000 cells/mm^3 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. Neupogen or Zarxio 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:* Neupogen or Zarxio is prescribed by, or in consultation with, a hematologist, an oncologist, or a physician that specializes in transplantation and Site of care medical necessity is met.*

Neupogen or Zarxio is 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. 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. Alternative dosing will be assessed individually on a case-by-case basis.

The recommended dose of Neupogen or Zarxio 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 Neupogen or Zarxio 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/mm^3 for 3 consecutive days, reduce the dose to 5 mcg/kg/day; 2) then, if the ANC remains > 1,000 cells/mm^3 for 3 or more consecutive days, discontinue Neupogen or Zarxio; and 3) then, if ANC decreases to < 1,000 cells/mm^3 resume at 5 mcg/kg/day. If the ANC decreases to < 1,000 cells/mm^3, 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 Neupogen or Zarxio 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.

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

Criteria. *Patient must meet the following criteria:* Neupogen or Zarxio is prescribed by, or in consultation with, an oncologist, a hematologist, or a physician that specializes in transplantation and Site of care medical necessity is met.*

Neupogen or Zarxio is indicated for the mobilization of hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis. 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 Neupogen or Zarxio are utilized includes patients with cancer or healthy donors undergoing mobilization of PBPC, as well as patients with cancer post autologous PBPC transplantation. 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. Alternate dosing will be assessed individually on a case-by-case basis.

The recommended dosage of Neupogen or Zarxio for the mobilization of autologous PBPC is 10 mcg/kg/day as a SC injection. Neupogen or Zarxio is given for at least 4 days before the first leukapheresis procedure and continued until the last leukapheresis. The optimal duration of Neupogen or Zarxio administration and leukapheresis schedule have not been established, but Neupogen or Zarxio 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. Neupogen or Zarxio is discontinued if the white blood cell count increases to > 100,000 cells/mm^3. Other sources indicate 5 days of Neupogen or Zarxio 10 mcg per kg per day is adequate but some patients may require a longer duration of therapy (see duration of therapy section). Twice daily dosing may be utilized in certain circumstances.

B) Patients Undergoing Mobilization of PBPC Who Are Poor Mobilizers: 12.5 to 50 mcg per kg per day IV or SC. Dosing can be once daily or twice daily. 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 Neupogen or Zarxio or use other regimens that add Leukine to Neupogen or Zarxio, add Mozobil® (plerixafor injection), or mobilization with chemotherapy plus Neupogen or Zarxio.

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. Dosing can be once daily or twice daily. Alternative dosing will be assessed individually on a case-by-case basis.

In clinical trials of Neupogen for mobilization of hematopoietic progenitor cells, Neupogen was given to patients at doses of 5 to 24 mcg/kg/day after reinfusion of the collected cells until a sustainable ANC ≥ 500 cells/mm^3 was reached. Another recommendation for supportive care in patients post autologous stem cell or cord blood transplant, is to give Neupogen 5 mcg/kg/day beginning ≥ 5 days post transplant until recovery of ANC (e.g., > 1,500 cells/mm^3 for 2 consecutive days).

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 Neupogen or Zarxio 10 mcg per kg per day are used. For patients with cancer, 5 to 7 days of Neupogen or Zarxio 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/mm^3 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 Neupogen or Zarxio. 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 Neupogen for 4 consecutive days (in patients weighing < 35 kg) or 5 consecutive days in unrelated donors (allogeneic transplantation). 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 Neupogen or Zarxio. Approve for another 14 days if ANC is not at a sustainable level. Most patients have a response after 28 days of Neupogen or Zarxio. Alternative durations will be assessed individually on a case-by-case basis.

Labs/Diagnostics. None required.

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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*: Neupogen or Zarxio is prescribed by, or in consultation with, a hematologist and Site of care medical necessity is met.*

Neupogen or Zarxio 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. 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. 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. 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 Neupogen 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 Neupogen ≥ 100 mcg/kg/day. Many different doses have been used long-term. ANC should not be used as the sole indication of efficacy. Some data show that patients with idiopathic and cyclic neutropenia generally respond to low-dose daily, alternative day, or thrice-per-week Neupogen (1 to 3 mcg per kg per day SC). 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.

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

Criteria. *The patient must meet the following criteria:* Neupogen is prescribed by, or in consultation with, a physician with expertise in treating acute radiation syndrome and Site of care medical necessity is met.*

Neupogen is indicated to increase survival in patients acutely exposed to myelosuppressive dose of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome). 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/mm^3 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 in animals and data supporting the use of Neupogen for other approved indications. Other sources also cite filgrastim being used for this scenario.[9-10]

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. Neupogen or Zarxio 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/mm^3 for three consecutive CBCs. Administration of Neupogen or Zarxio is not delayed if a CBC is not readily available. Administration of Neupogen or Zarxio is continued until the ANC remains > 1,000 cells/mm^3 for three consecutive CBCs or exceeds 10,000 cells/mm^3 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*: Neupogen or Zarxio 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 and Site of care medical necessity is met.*

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

Dosing for Neutropenia in Adults with HIV or AIDS. *Dosing must meet the following:* Neupogen or Zarxio 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.

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

Criteria. *Patient must meet the following criteria*: Neupogen or Zarxio is prescribed by, or in consultation with, an oncologist or hematologist and Site of care medical necessity is met.*

The NCCN guidelines on MDS (version 2.2017) recommend Neupogen for use in certain patients with MDS (e.g., neutropenic patients with recurrent or resistant infections, combination use with Epogen®/Procrit® [epoetin alfa injection] or Aranesp® [darbepoetin alfa injection]). 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. Other data are available.

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

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.

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9. Aplastic Anemia (Adults and Children).

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

Neupogen has been utilized in the treatment of aplastic anemia, usually in combination with immunosuppressive therapy or with erythropoietin-stimulating products. In one multicenter, randomized, controlled study, patients with anemia associated with aplastic anemia (n = 131) were treated with G-CSF alone or with Epogen/Procrit. The response rates at 12 weeks in 110 evaluable patients were between 12.9% and 36.8%. Guidelines for aplastic anemia published by the British Committee for Standards in Haematology in 2009 state that a short course of G-CSF may be considered for severe systemic infections that are not responding to IV antibiotics and anti-fungal medications, but should be discontinued after 1 week if no increase in neutrophil count is noted.

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

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.

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

Criteria. Approve Neupogen or Zarxio and Site of care medical necessity is met.*

Neupogen has been used for agranulocytosis caused by non-cytotoxic medications, primarily described in case series, case reports and literature reviews.

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.

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11. Acute Lymphocytic Leukemia (ALL).

Criteria. *The patient must meet the following criteria:* Neupogen or Zarxio is prescribed by, or in consultation with, an oncologist or hematologist and Site of care medical necessity is met.*

Data notes some benefits in patients with ALL in selected scenarios. This criterion is recommended based on the professional opinion of specialized and other physicians.

Dosing in ALL: *Dosing must meet the following:* Neupogen or Zarxio dose is in the range of 5 to 10 mcg per kg per day SC.

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, B, and C).*
A) Neupogen or Zarxio is prescribed by, or in consultation with, an oncologist, radiologist, or radiation oncologist; AND
B) The patient is not concurrently receiving chemotherapy; AND
C) Site of care medical necessity is met.*

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. However, the Neupogen and Zarxio prescribing information notes that the safety and efficacy of Neupogen and Zarxio have not been evaluated in patients receiving concurrent radiation therapy. Simultaneous use of Neupogen or Zarxio 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. The NCCN guidelines for myeloid growth factors (version 1.2017) state the prophylactic use of CSFs in patients given concurrent chemotherapy and radiation is not recommended. In one trial that administered radiotherapy with simultaneous chemotherapy, an unexpected reduced local control was reported.

Dosing in Radiation-Induced Neutropenia. *Dosing must meet the following*: The dose of Neupogen or Zarxio 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 requir

Waste Management for All Indications.
Single-use vials and syringes contain 300 and 480 mcg of Neupogen. 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
Colony Stimulating Factors have 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.)

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

2. **Concomitant use of Colony Stimulating Factors**: Colony Stimulating Factors are not recommended as combination therapy.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

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- The NCCN Acute Lymphoblastic Leukemia Clinical Practice Guidelines in Oncology (Version 2.2014). © 2014 National Comprehensive Cancer Network, Inc. Available at http://www.nccn.org. Accessed on June 10, 2015.
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MEDICAL MUTUAL®

Drug Policy

FOR MEDICAL BENEFIT COVERAGE REQUESTS:

***MMO Site of Care Medical Necessity Criteria:**

Medications in this policy will be administered in a place of service that identifies the location to be a non-hospital facility based location (i.e., home infusion provider, provider's office, free-standing ambulatory infusion center) unless *at least one* of the following are met[†]:

1. Age less than 21 years; or
2. Clinically unstable based upon documented medical history (e.g., patient is hemodynamically unstable); or
3. History of a severe adverse event from previous administration of the prescribed medication; or
4. Requested medication is being administered as follows:
   - part of a chemotherapy regimen (e.g., anti-neoplastic agent, colony stimulating factor, erythropoiesis-stimulating agent, anti-emetic) for treatment of cancer; or
   - administered with dialysis; or
5. Physical or cognitive impairment and caregiver is not available to assist with safe administration of prescribed medication in the home; or
6. Experiencing adverse events that are not managed by premedication or resources available at a non-hospital facility based location.

No initial doses are allowed in a hospital based outpatient facility without other above criteria being met.

[†]This criterion does not apply to Medicare or Medicare Advantage members.

Prior approval is required for HCPCS Codes J1442, J1447, J2505, J2820, J3590[†] and Q5101.

[†]**When *unclassified biologics* (J3590) is determined to be Fulphilia**

HCPCS Code(s):	
J1442	Injection, filgrastim (g-csf), excludes biosimilars, 1 microgram
J1447	Injection, tbo-filgrastim, 1 microgram
J2505	Injection, pegfilgrastim, 6 mg
J2820	Injection, sargramostim (GM-CSF), 50 mcg
J3590	Unclassified biologics
Q5101	Injection, filgrastim-sndz, biosimilar, (zarxio), 1 microgram