Filgrastim Products Clinical Resource

Agents:

- Neupogen® (filgrastim intravenous or subcutaneous injection – Amgen)
- Nivestym™ (filgrastim-aafi intravenous or subcutaneous injection – Hospira/Pfizer)
- Zarxio® (filgrastim-sndz intravenous or subcutaneous injection – Sandoz)
- Releuko (filgrastim-ayow intravenous or subcutaneous injections – Amneal)
- Granix® (tbo-filgrastim subcutaneous injection – Cephalon)

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OVERVIEW

Filgrastim biosimilar products and tbo-filgrastim do not require prior authorization; however, the use of BRAND Neupogen requires an evaluation of medical necessity.

Filgrastim, a leukocyte growth factor, is indicated for the following uses:[1-3]

- **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.
- **Mobilization of hematopoietic progenitor cells,** into the peripheral blood for collection by leukapheresis.
- **Reduce the time to neutrophil recovery and the duration of fever,** following induction or consolidation chemotherapy treatment of adults 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 marrow transplantation.
- **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.

Nivestym, Releuko and Zarxio are products that are biosimilar to Neupogen.[2,3, 21] Neupogen is the only agent indicated to increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome).[1] Granix (tbo-filgrastim subcutaneous injection) is another filgrastim product.[4]

Guidelines

The National Comprehensive Cancer Network (NCCN) addresses the use of filgrastim products in several guidelines.

- **Acute Lymphoblastic Leukemia:** Guidelines (version 3.2021 **–** March 2, 2021) recommend granulocyte colony-stimulating factors (CSF) as supportive care for myelosuppressive blocks of therapy or as directed by treatment protocol.[7]
- **Hematopoietic Growth Factors:** Guidelines (version 4.2021 – May 20, 2021) recommend filgrastim, 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.[5] 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 CSFs in other scenarios in those given myelosuppressive chemotherapy. Filgrastim products are also recommended for mobilization and following hematopoietic cell transplant.
- **Management of Immunotherapy-Related Toxicities:** Guidelines (version 3.2021 – May 14, 2021) recommend granulocyte CSFs as supportive care for neutropenic patients with Grade 1 cytokine release syndrome resulting from chimeric antigen receptor (CAR) T-cell therapy.[20]

- **Myelodysplastic Syndromes (MDS):** Guidelines (version 3.2021 – January 15, 2021) 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] in patients with anemia]).[6]

The American Society of Clinical Oncology clinical practice guidelines for the use of white blood cell growth factors (2015) recommends CSFs to reduce the risk of febrile neutropenia in patients receiving cancer chemotherapy.[6] CSFs may be considered in patients receiving radiation therapy alone if prolonged delays secondary to neutropenia are expected. The guidelines state CSFs should be avoided in patients receiving concomitant chemotherapy and radiation therapy, particularly involving the mediastinum.

Other Uses With Supportive Evidence

Neutropenia occurs in patients with HIV and may be caused by medications or due to the disease process. Studies have demonstrated positive outcomes with the use of filgrastim for the treatment of neutropenia in this patient population.[9-12]

Filgrastim has been used for agranulocytosis caused by non-cytotoxic medications, primarily described in case series, case reports and literature reviews.[13-19]

RECOMMENDED GUIDELINES FOR USE (PRIOR AUTHORIZATION IS NOT REQUIRED)

FDA-Approved Indications

1. **Acute Myeloid Leukemia in a Patient Receiving Chemotherapy.** Use for 6 months if prescribed by or in consultation with an oncologist or hematologist.

   Dosing. Up to 10 mcg/kg per day by intravenous or subcutaneous injection.

2. **Bone Marrow Transplant in a Patient with Cancer Who Received Chemotherapy.** Use for 1 month if prescribed by or in consultation with a hematologist, an oncologist, or a physician who specializes in transplantation.

   Dosing. Up to 30 mcg/kg per day by intravenous or subcutaneous injection.

3. **Cancer in a Patient Receiving Myelosuppressive Chemotherapy.** Use for 6 months if the patient meets the following (A and B):

   A) Patient meets ONE of the following conditions (i, ii, iii, or iv):

   i. Patient is receiving myelosuppressive anti-cancer medications that are associated with a high risk of febrile neutropenia (the risk is at least 20% based on the chemotherapy regimen); OR

   ii. 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 at least one risk factor for febrile neutropenia according to the prescriber; OR

   Note: Examples of risk factors include age ≥ 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.

iii. Patient has had a neutropenic complication from prior chemotherapy and did not receive prophylaxis with a colony stimulating factor and a reduced dose or frequency of chemotherapy may compromise treatment outcome; OR

Note: Examples of colony-stimulating factors include filgrastim products, pegfilgrastim products, and sargramostim products (e.g., Leukine®).

iv. 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 prescriber; AND

Note: Examples of risk factors include 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; or other clinically documented infections.

B) The medication is prescribed by or in consultation with an oncologist or hematologist.

Dosing. Up to 10 mcg/kg per day by intravenous or subcutaneous injection for up to 14 days per month.

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4. Peripheral Blood Progenitor Cell Collection and Therapy. Use for 1 month if prescribed by or in consultation with an oncologist, a hematologist, or a physician who specializes in transplantation.

Dosing. Up to 32 mcg/kg per day by intravenous or subcutaneous injection.

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5. Radiation Syndrome (Hematopoietic Syndrome of Acute Radiation Syndrome). Use for 1 month if prescribed by or in consultation with a physician who has expertise in treating acute radiation syndrome.

Dosing. Up to 10 mcg/kg per day as a subcutaneous injection.

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6. Severe Chronic Neutropenia (e.g., Congenital Neutropenia, Cyclic Neutropenia, Idiopathic Neutropenia). Use for 6 months if prescribed by or in consultation with a hematologist.

Dosing. Up to 12 mcg/kg per day by subcutaneous injection.

Other Uses with Supportive Evidence

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7. Acute Lymphoblastic Leukemia. Use for 1 month if prescribed by or in consultation with an oncologist or a hematologist.

Dosing. Up to 10 mcg/kg per day as a subcutaneous injection.

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8. Cytokine Release Syndrome Associated with Chimeric Antigen Receptor (CAR) T-Cell Therapy. Use for 1 month if prescribed for a patient who has neutropenia.
Note: Examples of CAR T-cell therapy include Kymriah™ (tisagenlecleucel intravenous infusion) and Yescarta™ (axicabtagene ciloleucel intravenous infusion).

Dosing. Up to 10 mcg/kg per day by intravenous or subcutaneous injection.

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9. Drug-Induced (Non-Chemotherapy) Agranulocytosis or Neutropenia. Use for 1 month.

Dosing. Up to 10 mcg/kg per day as a subcutaneous injection.

10. **Myelodysplastic Syndromes.** Use for 3 months if prescribed by or in consultation with an oncologist or hematologist.

    Dosing. Up to 5 mcg/kg per day as a subcutaneous or intravenous injection.

11. **Neutropenia Associated with Human Immunodeficiency Virus (HIV) or Acquired Immunodeficiency Syndrome (AIDS).** Use for 4 months if the agent is prescribed by or in consultation with a physician that specializes in infectious diseases, a hematologist, or a physician who specializes in the management of HIV/AIDS.

    Dosing. Up to 10 mcg/kg per day as a subcutaneous injection.

12. **Radiation-Induced Neutropenia.** Use for 6 months if the patient meets the following criteria (A and B):

    A) Patient is not currently receiving chemotherapy; AND

    B) The medication is prescribed by or in consultation with an oncologist, radiologist, or radiation oncologist.

    Dosing. Up to 5 mcg/kg per day as a subcutaneous injection.

CONDITIONS NOT RECOMMENDED FOR USE

Use of filgrastim products is not recommended in the following situations:

1. Use is not recommended for circumstances not listed in package labeling, NCCN, or supporting literature as cited above. This resource will be updated as new published data are available.

REFERENCES

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