Aetna Better Health®

Pharmacy Prior Authorization
Colony Stimulating Factor (CSF)/Myeloid Growth Factor (MGF) – Clinical Guideline

Zarxio® (filgrastrim-sndz)
Granix® (tbo-filgrastim)
Neulasta® (peg-filgrastim; G-CSF)
Neulasa Onpro® (peg-filgrastim; G-CSF)
Neupogen® (filgrastim; G-CSF)
Leukine® (sargramostim; GM-CSF)

Preferred Agent: Zarxio is the preferred G-CSF. Requests for non-preferred agents require trial of Zarxio in addition to meeting the clinical criteria detailed below.

General Authorization Criteria for ALL Agents and Indications:

- Prescribed by, or in consultation with, a hematologist or oncologist
- Medical records, including labs and weight or BSA, to support diagnosis and dosing is submitted with request
- Requested agent is dosed and administered within FDA labeled recommendations
  - Will not be used concomitantly with radiation
  - Will be administered at the appropriate time after chemotherapy
- Patient does not have any contraindications to the requested agent
  - Leukine- patients with excessive leukemic blasts (≥ 10%) in the bone marrow or peripheral blood)
  - Neupogen/Zarxio- E-Coli hypersensitivity
- Will not be used in combination with other myeloid growth factors

Additional Criteria Based on Indication:

- **Chemotherapy-Induced Febrile Neutropenia: (Neupogen, Neulasta, Granix, and Zarxio)**
  - Patient is receiving chemotherapy for a NON-myeloid cancer (i.e., solid tumor, lymphoma)
    - For PRIMARY prophylaxis:
      - Patient meets ONE of the following:
        - Chemotherapy regimen is given after bone marrow transplant; OR
        - Chemotherapy regimen has >20% risk of febrile neutropenia; OR
        - Chemotherapy regimen has 10%-20% risk of febrile neutropenia AND patient has ANY of the following risk factors for febrile neutropenia:
          - age > 65 years
          - prior chemotherapy or radiation therapy
          - persistent neutropenia
          - bone marrow involvement by tumor
          - Recent surgery and or open wounds
          - Liver dysfunction (bilirubin > 2.0)
          - Renal dysfunction (CRCL <50)
          - HIV
    - For SECONDARY prophylaxis: Patient previously experienced febrile neutropenia from the same chemotherapy regimen and reducing or delaying chemotherapy dose may compromise treatment outcome
    - For TREATMENT of febrile neutropenia in patients who did NOT receive CSF's prophylaxis: Patient has risk factors for poor outcomes resulting from febrile neutropenia (e.g., age > 65, sepsis, severe neutropenia (ANC< 100/mcL), current infection, hospitalized at onset of fever, prior episode of febrile neutropenia)
- **Severe chronic congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia: (Zarxio, Neupogen)**
  - Patient has ONE of the following:

  - Evidence of inadequate bone marrow reserve (e.g., recurrent fevers, splenomegaly, mucosal ulcers, abdominal pain)
  - High risk for developing serious bacterial infection (e.g., primarily severe neutropenia, indwelling venous catheters, prior serious infections)
  - Current bacterial infection
- **Neutropenia related to HIV: (Zarxio, Neupogen)**
  - Patient is taking antiretroviral therapy regimen that does NOT contain zidovudine
  - Patient is NOT taking sulfamethaxazole/trimethoprim. NOTE: Patients who require pneumocystis prophylaxis should be switched to atovaquone or dapsone (unless contraindicated)
  - Patient has ONE of the following:
    - Evidence of inadequate bone marrow reserve (e.g., recurrent fevers, splenomegaly, mucosal ulcers, abdominal pain)
    - High risk for developing serious bacterial infection (e.g., primarily severe neutropenia, indwelling venous catheters, prior serious infections)
    - Patient has a documented bacterial infection

- **Neupogen and Zarxio may also be approved if medically necessary for the following indications:**
  - Acute Myeloid Leukemia in patients receiving induction or consolidation chemotherapy
  - Mobilization of hematopoietic progenitor cells before autologous stem cell transplant
  - Mobilization of hematopoietic progenitor cells in the donor before allogenic stem cell transplant
  - Treatment of acute radiation exposure in patients who receive myelosuppressive doses of radiation at a dose of 2 gray (Gy)
  - Myelodysplastic Syndrome (MDS) or aplastic anemia in a patient with an ANC <500

- **Leukine may also be approved if medically necessary for the following indications:**
  - Acute Myeloid Leukemia after induction chemotherapy for patients age 55 years or older
  - Bone marrow transplant failure or engraftment delay
  - Myeloid reconstitution after allogenic bone marrow transplant
  - Myeloid reconstitution after autologous bone marrow transplant in patients with Hodgkin's disease, non-Hodgkin's lymphoma, or acute lymphocytic leukemia
  - Before and after autologous peripheral blood stem cell transplantation

Initial Approval:

- Chemotherapy-induced neutropenia (primary or secondary prophylaxis):
  - Approve per cycle of chemotherapy:
    - Up to a 14 day supply for Neupogen, Zarxio, Granix, and Leukine
    - one (1) 6 mg dose of Neulasta
    - Include refills if number of cycles is provided
  - Treatment of neutropenia (e.g., congenital, cyclic, or idiopathic, HIV, or after chemo + BMT):
    - Approve for 3 months
- For other indications
  - Up to 6 months or less

Renewal:

- Chemotherapy-induced neutropenia (primary or secondary prophylaxis):

- Recent ANC showing a response to therapy
- Approve per cycle of chemotherapy:
  - Up to a 14 day supply for Neupogen, Zarxio, Granix and Leukine
  - one (1) 6 mg dose of Neulasta
  - Include refills if number of cycles is provided

- All other indications:
  - Recent ANC, CBC, and/or platelet counts
  - Approve up to 1 year or less, depending on the indication

Additional Information:

Note: Neutropenia is defined as an absolute neutrophil count (ANC) of < 500 neutrophils/mcL or an ANC of < 1000 neutrophils/mcL and a predicted decline to < than or equal to 500 neutrophils/mcL over the next 48 hours.

Determining the risk of febrile neutropenia:
A patient's risk for developing neutropenic fever may be assessed prior to the use of colony stimulating factors. This may be achieved by evaluating the degree of myelosuppression of the patient's chemotherapy regimen in addition to the presence of other patient-related risk factors. Both Infectious Diseases Society of America (IDSA) and National Comprehensive Cancer Network (NCCN) recommend that colony stimulating factors be considered when the risk of febrile neutropenia is >20%.

Dosing Table:

Medication	Dosing	Available Dosage forms
Neupogen Zarxio	• Febrile Neutropenia (FN) or AML: 5 mcg/kg/day (Not given 24 hours before chemotherapy and 24 hours after) • BMT: 10 mcg/kg/day (given 24 hrs after BMT and given for at least 24 hours) • PBPC: 10 mcg/kg/day; at least 4 days before and up to 7 days • Severe Chronic Neutropenia: o Idiopathic neutropenia:1.2 mcg/kg/day o Cyclic neutropenia: 2.1 mcg/kg/day o Congenital neutropenia: 6 mcg/kg/day divided 2 times per day • Radiation exposure: 10mg/kg (give immediately after exposure and GY > 2)	Vials: • 300 mcg/mL, single-dose vial • 480 mcg/1.6 mL, single-dose vial Prefilled Syringe • 300 mcg/0.5 mL per syringe • 480 mcg/0.8 mL per syringe
Neulasta	• Febrile Neutropenia- 5mcg/kg/day Not given 24 hours before chemotherapy and 24 hours after chemotherapy Given once per chemotherapy cycle	• 6 mg/0.6 mL, single-dose prefilled syringe • 6 mg/0.6 mL, single-dose prefilled syringe co-packaged with the On-body Injector (Neulasta Onpro kit).
Leukine	• AML:250 mcg/m^2/day SQ or IV on day 11 or 4 days following the completion of induction chemotherapy • PBPC: 250mcg/m^2/day SQ or IV over 24 hours	• 500 mcg/mL vial • 250 mcg powder for injection
Granix	• FN 5mcg/kg/day SQ injection	• 300 mcg/0.5 mL, single-use

	Not given 24 hours before chemotherapy and 24 hours after chemotherapy	prefilled syringe • 480 mcg/0.8 mL, single-use prefilled syringe

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