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

Short-acting Filgrastim Agents	Long-acting Pegfilgrastim Agents
Neupogen® (filgrastim)	**Fulphila™(pegfilgrastim-jmdb)**
Leukine® (sargramostim)	**Udenyca® (pegfilgrastim-cbqv)**
Granix® (tbo-filgrastim)	Neulasta® (pegfilgrastim)
Nivestym® (filgrastim-aafi)	Nyvepria® (pegfilgrastim-apgf)
Zarxio® (filgrastim-sndz)	Ziextenzo® (pegfilgrastim-bmez)

Preferred Agents:

- Fulphila, Neupogen Disposable Syringe, Neupogen Vial, and Udenyca

Non-Preferred Agents:

- Require trial and failure, or contraindication with all preferred agents (where indicated), in addition to all other criteria

General Authorization Criteria for ALL Agents and Indications:

- Prescribed by, or in consultation with hematologist or oncologist
- Medical records, labs, and weight or body surface area to support diagnosis and dosing
- Requested agent is dosed and administered within Food and Drug Administration (FDA) labeled recommendations
  - Will not be used concomitantly with radiation and chemotherapy
  - Will be administered at appropriate time after chemotherapy or radiation
- Member does not have any contraindications or hypersensitivity to requested agent
- Will not be used in combination with other myeloid growth factors

Additional Criteria Based on Indication:

Chemotherapy-Induced Febrile Neutropenia for members receiving chemotherapy for a NON-myeloid cancer (solid tumor and lymphoid malignancies):

- **Primary prophylaxis** (Fulphila, Granix, Leukine, Neupogen, Neulasta, Nivestym, Nyvepria, Udenyca, Zarxio, Ziextenzo)
  - Documentation to support member meets one of the following:
    - Chemotherapy regimen has greater than 20% risk of febrile neutropenia (refer to the Appendix)
    - Chemotherapy regimen has 10%-20% risk of febrile neutropenia (refer to the Appendix) AND member has one of the following risk factors for febrile neutropenia:
      - Age greater than 65 years
      - Prior chemotherapy or radiation therapy
      - Persistent neutropenia
      - Bone marrow involvement by tumor

- Recent surgery, open wounds, or active infection
- Liver dysfunction (bilirubin great than 2.0mg/dL)
- Renal dysfunction (creatinine clearance less than 50ml/min)
- Human immunodeficiency virus (HIV) infection

- **Secondary prophylaxis:** (Fulphila, Granix, Leukine, Neupogen, Neulasta, Nivestym, Nyvepria, Udenyca, Zarxio, Ziextenzo)
  - Documentation to support member previously experienced febrile neutropenia from same chemotherapy regimen (for which primary prophylaxis was not received), and reducing or delaying chemotherapy dose may compromise treatment outcome
  - Members with prior use of colony stimulating factor for same chemotherapy regimen who experience febrile neutropenia or neutropenic event should consider chemotherapy dose reduction or change in treatment regimen
- **Treatment:** (Granix, Leukine, Neupogen, Nivestym, Zarxio)
  - Documentation to support member has one of the following:
    - Members who received prophylaxis with short-acting colony stimulating factors should continue therapy
    - Members who did not receive prophylaxis AND have risk factors for infection-associated complication
      - For example: age greater than 65 years, absolute neutrophil count less than 100/microliter, neutropenia expected to be greater than 10 days, pneumonia, invasive fungal infection, hospitalization at the time of fever, and prior episode of febrile neutropenia
    - Members who received prophylaxis with long-acting colony stimulating factors do not require additional therapy with short-acting colony stimulating factors unless there is prolonged neutropenia
- **Bone marrow/stem cell transplant:** (Leukine, Neupogen, Nivestym, Zarxio)
  - Documentation to support member has one of the following:
    - Non-myeloid malignancies and undergoing myeloablative chemotherapy followed by autologous or allogeneic bone marrow transplant (BMT)
    - Used for mobilization of hematopoietic progenitor cells into peripheral blood for collection by leukapheresis
    - Member had peripheral stem cell transplant (PSCT) and received myeloablative chemotherapy
- **Severe chronic congenital, cyclic, or idiopathic neutropenia:** (Neupogen, Neupogen, Zarxio)
  - Documentation to support member experienced infection requiring antibiotic treatment during previous 12 months and one of the following:
    - Chronic neutropenia:

        - Documented absolute neutrophil count (ANC) less than 500 neutrophils/microliter on three occasions during a 6-month period
    - Cyclic neutropenia:
        - Documented five consecutive days of absolute neutrophil count (ANC) less than 500 neutrophils/microliter per cycle

- **Neutropenia related to Human Immunodeficiency Virus (HIV):** (Leukine, Neupogen, Nivestym, Zarxio)
    - Documentation to support a diagnosis of advanced Human Immunodeficiency Virus infection
    - In addition to Hematology or Oncology specialty, the following prescriber specialties are also accepted for this indication:
        - Infectious Disease Specialist
        - Human Immunodeficiency Virus (HIV) Specialist
- **Acute Myeloid Leukemia (AML) Induction or Consolidation Therapy:** (Leukine, Neupogen, Nivestym, Zarxio)
    - Documentation to support diagnosis of acute myeloid leukemia (AML) and member completed either induction or consolidation chemotherapy
- **Hematopoietic Syndrome of Acute Radiation Syndrome:** (Granix, Fulphila, Leukine, Neulasta, Neupogen, Nivestym, Nyvepria, Udenyca, Zarxio, Ziextenzo)
    - Documentation to support member has been acutely exposed to myelosuppressive doses of radiation

Initial Approval:

- **Chemotherapy-induced neutropenia:** (primary or secondary prophylaxis)
    - Approve per cycle of chemotherapy:
        - Up to a 14-day supply for Granix, Leukine, Neupogen, Nivestym, and Zarxio
        - One 6 mg dose of long-acting colony stimulating factors no less than every 14 days
        - Include refills if number of cycles is provided
- **Treatment of neutropenia:** (bone marrow transplant, chronic congenital, cyclic, idiopathic neutropenia, Human Immunodeficiency Virus)
    - Approve 3 months
- **All other indications**
    - Approve up to 6 months or less

Renewal Approval:

- **Chemotherapy-induced neutropenia:** (primary or secondary prophylaxis)
    - Recent absolute neutrophil count showing response to therapy

- Approve per cycle of chemotherapy:
  - Up to a 14-day supply for Granix, Leukine, Neupogen, Nivestym, and Zarxio
  - One 6 mg dose of long-acting colony stimulating factors no less than every 14 days
  - Include refills if number of cycles is provided, or up to 12 months

- **All other indications**
  - Recent absolute neutrophil count showing response to therapy
  - Approve up to 6 months

Additional Information

Febrile neutropenia: a single temperature greater than or equal to 38.3 degrees Celsius orally or greater than 38 degrees Celsius over an hour, with an absolute neutrophil count of less than 500 neutrophils/microliter or an absolute neutrophil count of less than 1000 neutrophils/microliter with a predicted decline to less than or equal to 500 neutrophils/microliter over the next 48 hours

Neutropenia: absolute neutrophil count of less than 1500 neutrophils/microliter

Severe neutropenia: absolute neutrophil count of less than 500 neutrophils/microliter

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

Dosing Table:

Medication	Dosing	Available Dosage forms

Neupogen
Zarxio
Nivestym
	• Febrile Neutropenia or acute myeloid leukemia: 5 mcg/kg/day (Not given 24 hours before chemotherapy and 24 hours after)
	• Bone marrow transplant: 10 mcg/kg/day (given 24 hrs. after bone marrow transplant and given for at least 24 hours)
	• Peripheral Blood Progenitor Cell: 10 mcg/kg/day; at least 4 days before and up to 7 days
	• Severe Chronic Neutropenia:
	  ○ Idiopathic:1.2 mcg/kg/day
	  ○ Cyclic: 2.1 mcg/kg/day
		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

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Neulasta Fulphila Udenyca Ziextenzo	• Febrile Neutropenia: 6mg subcutaneously once per chemotherapy cycle • Not given 14 days before chemotherapy to 24 hours after	• 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	• Acute myeloid leukemia: 250 mcg/m^2/day intravenous on day 11- or 4-days following completion of induction chemotherapy
	• Mobilization of peripheral blood progenitor cells: 250 mcg/ m^2/day administered intravenously over 24 hours or subcutaneous injection once daily.
	• Myeloid reconstitution after autologous or allogeneic bone marrow transplant: 250 mcg/m^2/day administered intravenously over a 2-hour period
	• BMT failure or engraftment delayed: 250 mcg/m^2/day for 14 days as a 2-hour intravenous infusion
	• Patients acutely exposed to myelosuppressive doses of radiation, administer once daily as subcutaneous injection:
	  ○ Adults and pediatric patients weighing >40 kg: 7 mcg/kg once daily
	  ○ Pediatric patients 15 kg to 40 kg: 10mcg/kg once daily
	  ○ Pediatric patients less than 15 kg: 12mcg/kg once daily
	• Post Peripheral Blood Progenitor Cell Transplantation: 250mcg/m^2/day SQ once or IV over 24 hours
		• 500 mcg/mL vial
		• 250 mcg powder for injection

Granix	• Febrile Neutropenia 5mcg/kg/day subcutaneous injection • Not given 24 hours before chemotherapy to 24 hours after	• 300 mcg/0.5 mL, single-use prefilled syringe • 480 mcg/0.8 mL, single-use prefilled syringe

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Table 1: Selected Chemotherapy Regimens with an Incidence of Febrile Neutropenia of 20% or Higher

Cancer Histology	Regimen
Acute Lymphoblastic Leukemia (ALL)	Select ALL regimens as directed by treatment protocol (see NCCN guidelines)
Bladder Cancer	Dose dense MVAC (methotrexate, vinblastine, doxorubicin, cisplatin)
	CBDCa/Pac (carboplatin, paclitaxel)
Bone Cancer	VAI (vincristine, doxorubicin or dactinomycin, ifosfamide)
	VDC-IE (vincristine, doxorubicin or dactinomycin, and cyclophosphamide alternating with ifosfamide and etoposide)
	VIDE (vincristine, ifosfamide, doxorubicin or dactinomycin, etoposide)
	Cisplatin/doxorubicin
	VDC (cyclophosphamide, vincristine, doxorubicin or dactinomycin
Breast Cancer	Docetaxel + trastuzumab
	Dose-dense AC (doxorubicin, cyclophosphamide) + paclitaxel (or dose dense paclitaxel)
	TAC (docetaxel, doxorubicin, cyclophosphamide)
	AT (doxorubicin, docetaxel)
	Doc (docetaxel)
	TC (docetaxel, cyclophosphamide)
	TCH (docetaxel, carboplatin, trastuzumab)

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Colorectal Cancer	FOLFOXIRI (Fluorouracil, leucovorin, oxaliplatin, irinotecan)
Esophageal and Gastric Cancers	Docetaxel/cisplatin/fluorouracil
Head and Neck Squamous Cell Carcinoma	TPF (docetaxel, cisplatin, 5-fluorouracil)
Hodgkin Lymphoma	Brentuximab vedotin + AVD (doxorubicin, vinblastine, dacarbazine)
	Escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone)
Kidney Cancer	Doxorubicin/gemcitabine
Melanoma	Dacarbazine-based combination with IL-2, interferon alpha (dacarbazine, cisplatin, vinblastine, IL-2, interferon alpha)
Multiple myeloma	DT-PACE (dexamethasone/ thalidomide / cisplatin / doxorubicin / cyclophoaphamide / etoposide) + bortezomib (VTD-PACE)
	DT-PACE (dexamethasone / thalidomide / cisplatin / doxorubicin / cyclophoaphamide/etoposide)
Non-Hodgkin's Lymphoma	Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)
	ICE (ifosfamide, carboplatin, etoposide)
	Dose-dense CHOP-14 (cyclophosphamide, doxorubicin, vincristine, prednisone) + rituximab
	MINE (mesna, ifosfamide, novantrone, etoposide)
	DHAP (dexamethasone, cisplatin, cytarabine)

	ESHAP (etoposide, methylprednisolone, cisplatin, cytarabine (Ara-C))
	HyperCVAD + rituximab (cyclophosphamide, vincristine, doxorubicin, dexamethasone + rituximab)
	VAPEC-B (vincristine, doxorubicin, prednisolone, etoposide, cyclophosphamide, bleomycin)
Ovarian Cancer	Topotecan
	Docetaxel
Pancreatic Cancer	FOLFIRINOX (fluorouracil, leucovorin, irinotecan, oxaliplatin)
Soft Tissue Sarcoma	MAID (mesna, doxorubicin, ifosfammide, dacarbazine)
	Doxorubicin
	Ifosfamide/doxorubicin
Small Cell Lung Cancer	Top (topotecan)
	CAV (cyclophosphamide, doxorubicin, vincristine)
Testicular cancer	VelP (vinblastine, ifosfamide, cisplatin)
	VIP (etoposide, ifosfamide, cisplatin)
	TIP (paclitaxel, ifosfamide, cisplatin)

Source: Smith et al, 2006; NCCN Hematopoietic Growth Factors, 2020

Table 2: Selected Chemotherapy Regimens with an Incidence of Febrile Neutropenia of 10% to 19%

Cancer Histology	Regimen

Occult primary - adenocarcinoma	Gemcitabine/docetaxel
Breast Cancer	Docetaxel
	CMF classic (cyclophosphamide, methotrexate, fluorouracil)
	CA (doxorubicin, cyclophosphamide) (60 mg/m^2) (hospitalized)
	AC (doxorubicin, cyclophosphamide) + sequential docetaxel (taxane portion only)
	AC + sequential docetaxel + trastuzumab
	A (doxorubicin) (75 mg/m^2)
	AC (doxorubicin, cyclophosphamide)
	CapDoc (capecitabine, docetaxel)
	Paclitaxel every 21 days
Cervical Cancer	Irinotecan
	Cisplatin/topotecan
	Paclitaxel/cisplatin
	Topotecan
Colorectal	FL (fluorouracil, leucovorin)
	CPT-11 (irinotecan) (350 mg/m^2 q 3 wk)
	FOLFOX (fluorouracil, leucovorin, oxaliplatin)
Esophageal and Gastric Cancers	Irinotecan/cisplatin

	Epirubicin/cisplatin/5-fluorouracil
	Epirubicin/cisplatin/capecitabine
Non-Hodgkin's lymphomas	EPOCH-IT chemotherapy
	GDP (gemcitabine, dexamethasone, cisplatin/carboplatin)
	GDP (gemcitabine, dexamethasone, cisplatin/carboplatin) + rituximab
	FMR (fludarabine, mitoxantrone, rituximab)
	CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) including regiments with pegylated liposomal doxorubicin
	CHOP + rituximab (cyclophosphamide, doxorubicin, vincristine, prednisone, rituximab) including regimens with pegylated liposomal doxorubicin
	CHP (cyclophosphamide, doxorubicin, prednisone) + brentuximab vedotin
	Bendamustine
Non-Small Cell Lung Cancer	Cisplatin/paclitaxel
	Cisplatin/vinorelbine
	Cisplatin/docetaxel
	Cisplatin/etoposide
	Carboplatin/paclitaxel
	Docetaxel
Ovarian Cancer	Carboplatin/docetaxel
Prostate Cancer	Cabazitaxel
Small Cell Lung Cancer	Etoposide/carboplatin
Testicular Cancer	BEP (bleomycin, etoposide, cisplatin)

	Etoposide/cisplatin
Uterine Sarcoma	Docetaxel

Source: Smith et al, 2006; NCCN Hematopoietic Growth Factors, 2020