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

Leukine® (sargramostim;GM-CSF)
Zarxio® (filgrastrim-sndz)
Granix® (tbo-filgrastim)
Udenyca™ (pegfilgrastim-cbqv)
Neulasta Onpro® (peg-filgrastim; G-CSF)

Neupogen® (filgrastim;G-CSF)
Nivestym™ (filgrastim-aafi)
Fulphila™ (pegfilgrastim-jmdb)
Neulasta® (peg-filgrastim; G-CSF)
Ziextenzo (peg-filgrastim; G-CSF)

Preferred Agents
- Leukine and Neupogen

Non-Preferred Agents
- Requires trial of preferred agents in addition to meeting clinical criteria detailed below

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 is submitted with request
- 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 (Neupogen, Neulasta, Fulphila, Udenyca, Granix, Leukine, Zarxio, Nivestym, Ziextenzo)
- Member is receiving chemotherapy for a NON-myeloid cancer (Solid tumor, lymphoma)
  - **Primary prophylaxis**
    - Member meets one of the following:
      - Chemotherapy regimen is given after bone marrow transplant
      - Chemotherapy regimen has >20% risk of febrile neutropenia
      - Chemotherapy regimen has 10%-20% risk of febrile neutropenia AND member has one 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 (creatinine clearance <50)

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- **Secondary Prophylaxis**
  - Member previously experienced febrile neutropenia from same chemotherapy regimen, and reducing or delaying chemotherapy dose may compromise treatment outcome
- **Treatment** (Zarxio, Nivestym, Neupogen, Granix, Leukine):
  - Member meets one of the following criteria:
    - A long acting colony stimulating factor was not received as prophylaxis, and those who previously received Zarxio, Nivestym, Neupogen, or Granix will continue with same agent
    - Prophylactic therapy with a colony stimulating factor was not received, and risk factors for poor outcome resulting from febrile neutropenia are present (For example: Age > 65, sepsis, severe neutropenia (absolute neutrophil count < 100/mcL), current infection, hospitalized at onset of fever, prior episode of febrile neutropenia

- **Severe chronic congenital, cyclic, or idiopathic neutropenia** Zarxio, Nivestym, Neupogen
  - Member has one of the following:
    - Evidence of inadequate bone marrow reserve (recurrent fevers, splenomegaly, mucosal ulcers, abdominal pain)
    - High risk for developing serious bacterial infection (primarily severe neutropenia, indwelling venous catheters, prior serious infections)
    - Current bacterial infection
- **Neutropenia related to Human Immunodeficiency Virus (HIV) or drug therapy; ganciclovir or zidovudine induced** (Zarxio, Nivestym, Neupogen, Leukine)
  - Prescribed by, or in consultation with Infectious Disease Specialist, Hematologist, or Human Immunodeficiency Virus (HIV) Specialist
- **Neupogen, Zarxio, Nivestym**
  - May also be approved for the following indications, if medically necessary:
    - Acute Myeloid Leukemia in members receiving induction or consolidation chemotherapy
    - Mobilization of hematopoietic progenitor cells before autologous stem cell transplant
    - Mobilization of hematopoietic progenitor cells in donor before allogenic stem cell transplant
    - Treatment of acute radiation exposure in members who receive myelosuppressive doses of radiation at
      dose of 2 gray
    - Myelodysplastic Syndrome or aplastic anemia in member with absolute neutrophil count < 500
- **Leukine**
  - May also be approved for the following indications, if medically necessary:
    - Acute Myeloid Leukemia after induction chemotherapy for members age 55 years or older
    - Bone marrow transplant failure or engraftment delay
    - Myeloid reconstitution after allogenic bone marrow transplant

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- Myeloid reconstitution after autologous bone marrow transplant in member with Hodgkin's disease, non- Hodgkin's lymphoma, or acute lymphocytic leukemia
- Before and after autologous peripheral blood stem cell transplantation
- Member acutely exposed to myelosuppressive doses of radiation, administer once daily as subcutaneous injection

Initial Approval:

- **Chemotherapy-induced neutropenia (primary or secondary prophylaxis)**
  - Approve per cycle of chemotherapy:
    - Up to a 14-day supply for Neupogen, Zarxio, Nivestym, Granix, Leukine
    - One 6 mg dose of Neulasta, Fulphila, Udenyca, Ziextenzo no less than every 14 days
    - Include refills if number of cycles is provided
- **Treatment of neutropenia**
  - Congenital, cyclic, or idiopathic, Human Immunodeficiency Virus, or after chemo + bone marrow transplant
  - 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 Neupogen, Zarxio, Nivestym, Granix, Leukine
    - One 6 mg dose of Neulasta, Fulphila, Udenyca, Ziextenzo, 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, complete blood count, and/or platelet counts
  - Approve up to 1 year

Additional Information

Neutropenia is defined as absolute neutrophil count of < 500 neutrophils/mcL, or absolute neutrophil count of < 1000 neutrophils/mcL, and predicted decline to < than or equal to 500 neutrophils/mcL over next 48 hours

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.

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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
	  ○ Congenital: 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 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 syringeco-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	• 500 mcg/mL vial • 250 mcg powder for injection

	• 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	

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

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

Cancer Histology	Treatment Setting	Regimen
Acute Lymphoblastic Leukemia (ALL)	Induction	ALL induction regimens (see NCCN guidelines)
Bladder Cancer	Neoadjuvant, adjuvant, metastatic	MVAC (methotrexate, vinblastine, doxorubicin, cisplatin)
	Prior adjuvant allowed	CBDCa/Pac (carboplatin, paclitaxel)
Breast Cancer	Metastatic or relapsed	Docetaxel + trastuzumab
	Adjuvant	Dose-dense AC followed by T (doxorubicin, cyclophosphamide, paclitaxel)
	Adjuvant	TAC (docetaxel, doxorubicin, cyclophosphamide)
	Metastatic (1st line)	AT (doxorubicin, docetaxel)
	Metastatic (2nd line)	Doc (docetaxel)
Esophageal and Gastric Cancers		Docetaxel/cisplatin/fluorouracil

Hodgkin Lymphoma		BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone)
Kidney Cancer		Doxorubicin/gemcitabine
Non-Hodgkin's Lymphoma	Diffuse large B-cell lymphoma {DLBCL], peripheral T-cell lymphomas (PTCL], 2nd line	ICE (ifosfamide, carboplatin, etoposide)
		RICE (rituximab, ifosfamide, carboplatin, etoposide)
		CHOP-14 (cyclophosphamide, doxorubicin, vincristine, prednisone) + rituximab
	DLBCL, 2nd line, refractory	MINE (mesna, ifosfamide, novantrone, etoposide)
	PTCL, DLBCL, 2nd line	DHAP (dexamethasone, cisplatin, cytarabine)
	DLBCL, PTCL, 2nd line, recurrent	ESHAP (etoposide, methylprednisolone, cisplatin, cytarabine (Ara-C))
		HyperCVAD + rituximab (cyclophosphamide, vincristine, doxorubicin, dexamethasone + rituximab)
	Relapsed	VAPEC-B (vincristine, doxorubicin, prednisolone, etoposide, cyclophosphamide, bleomycin)
Melanoma	Advanced, metastatic, or recurrent	Dacarbazine-based combination (dacarbazine, cisplatin, vinblastine)
	Advanced, metastatic, or recurrent	Dacarbazine-based combination with IL-2, interferon alpha (dacarbazine, cisplatin, vinblastine, IL-2, interferon alpha)
Ovarian Cancer		Topotecan
		Paclitaxel
		Docetaxel
Pancreatic Cancer	Advanced or metastatic	FOLFIRINOX (leucovorin calcium, fluorouracil, irinotecan hydrochloride, and oxaliplatin)
Soft Tissue Sarcoma		MAID (mesna, doxorubicin, ifosfammide, dacarbazine)

		Doxorubicin
		Ifosfamide/doxorubicin
Small Cell Lung Cancer	Recurrent	Top (topotecan)
		CAV (cyclophosphamide, doxorubicin, vincristine)
Testicular cancer	Relapsed	VelP (vinblastine, ifosfamide, cisplatin)
		VIP (etoposide, ifosfamide, cisplatin)
		BEP (bleomycin, etoposide, cisplatin)
		TIP (paclitaxel, ifosfamide, cisplatin)

Source: Smith, et al., 2006; NCCN, 2016.

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

Cancer Histology	Treatment Setting	Regimen
Occult primary - adenocarcinoma		Gemcitabine/docetaxel
Breast cancer		Docetaxel every 21 days
	Adjuvant	CMF classic (cyclophosphamide, methotrexate, fluorouracil)
	Adjuvant	CA (doxorubicin, cyclophosphamide) (60 mg/m2) (hospitalized)
	Adjuvant (taxane portion only)	AC (doxorubicin, cyclophosphamide) + sequential docetaxel
	Adjuvant	AC + sequential docetaxel + trastuzumab
	Metastatic (1st line)	A (doxorubicin) (75)
	Metastatic (1st line)	AC (doxorubicin, cyclophosphamide)
	Metastatic (2nd line)	CapDoc (capecitabine, docetaxel)
		FEC (fluorouracil, epirubicin, cyclophosphamide) + sequential docetaxel
	Metastatic or relapsed	Paclitaxel every 21 days
		TC (docetaxel, cyclophosphamide)

Cervical Cancer		FOLFOX (fluorouracil, leucovorin, oxaliplatin)
Colorectal	Advanced	FL (fluorouracil, leucovorin)
	Advanced (one prior chemo allowed)	CPT-11 (irinotecan) (350 mg/m2 q 3 wk)
Esophageal and Gastric Cancers		Irinotecan/cisplatin
		Epirubicin/cisplatin/5-fluorouracil
		Epirubicin/cisplatin/capecitabine
Head and Neck	Induction	Cis/Doc/5-FU (cisplatin, docetaxel, 5-fluorouracil)
Multiple myeloma		DT-PACE dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophoaphamide/etoposide
		DT-PACE + bortezomib (VTD-PACE)
Non-Hodgkin's lymphomas	AIDS-related NHL, Burkitt lymphoma, recurrent, other NHL subtypes	EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)
	AIDS-related NHL, DLBCL, recurrent	EPOCH-IT chemotherapy
	DLBCL, PTCL, 2nd line	GDP (gemcitabine, dexamethasone, cisplatin)
	DLBCL, 2nd line, Burkitt lymphoma, other NHL subtypes	GDP (gemcitabine, dexamethasone, cisplatin) + rituximab
		FMR (fludarabine, mitoxantrone, rituximab)
		CHOP + rituximab (cyclophosphamide, doxorubicin, vincristine, prednisone, rituximab) including regimens with pegylated liposomal doxorubicin or mitoxantrone substituted for doxorubicin
Non-Small Cell Lung Cancer	Advanced/metastatic	Cisplatin/paclitaxel

	Adjuvant, advanced/metastatic	Cisplatin/vinorelbine
	Adjuvant, advanced/metastatic	Cisplatin/docetaxel
	Adjuvant, advanced/metastatic	Cisplatin/etoposide
	Adjuvant, advanced/metastatic	Carboplatin/paclitaxel
	Advanced/metastatic	Docetaxel
Ovarian Cancer		Carboplatin/docetaxel
Pancreatic Cancer		FOLFIRINOX
Prostate Cancer		Cabazitaxel
Small Cell Lung Cancer		Etoposide/carboplatin
Testicular Cancer		Etoposide/carboplatin
Uterine Sarcoma	Advanced or metastatic	Docetaxel

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