Colony-Stimulating Factors (CSF)/ Myeloid Growth Factors (MGF)

Generic Name: Colony-Stimulating Factors

Therapeutic Class or Brand Name: Colony-Stimulating Factors

Applicable Drugs (if Therapeutic Class): Fulphila™ (pegfilgrastim-jmdb), Fylnetra® (pegfilgrastim-pbbk), Granix® (tbo-filgrastim), Leukine® (sargramostim), Neulasta® /Neulasta Onpro® (pegfilgrastim), Neupogen® (filgrastim), Nivestym™ (filgrastim-aafi), Nyvepria™ (pegfilgrastim-apgf), Releuko® (filgrastim-ayow), Rolvedon™ (eflapegrastim-xnst), Stimufend (pegfilgrastim-fpgk), Udenyca™ (pegfilgrastim-cbqv), Zarxio™ (filgrastim-sndz), Ziextenzo™ (pegfilgrastim-bmex).

Preferred: Granix® (tbo-filgrastim), Udenyca™ (pegfilgrastim-cbqv).

Non-preferred: Fulphila™ (pegfilgrastim-jmdb), Fylnetra® (pegfilgrastim-pbbk), Leukine® (sargramostim), Neulasta® /Neulasta Onpro® (pegfilgrastim), Neupogen® (filgrastim), Nivestym™ (filgrastim-aafi), Nyvepria™ (pegfilgrastim-apgf), Releuko® (filgrastim-ayow), Rolvedon™ (eflapegrastim-xnst), Stimufend (pegfilgrastim-fpgk), Zarxio™ (filgrastim-sndz, Ziextenzo™ (pegfilgrastim-bmex).

Date of Origin: 2/1/2013

Date Last Reviewed / Revised: 12/2/2023

PRIOR AUTHORIZATION CRITERIA

(May be considered medically necessary when criteria I through V are met)

I. Documented diagnosis of one of the following A through H AND must meet criteria listed under applicable diagnosis:

A. Chemotherapy-induced febrile neutropenia (CIN) when myelosuppressive chemotherapy is used for the treatment of a solid tumor or a non-myeloid malignancy (malignancies other than myeloid leukemias) and meets one of the following 1 through 3:

1. Treatment of febrile neutropenia and meets one of the following a or b:

a. Patient is currently receiving a daily prophylactic CSF. Patients taking long-lasting pegfligrastim or eflapegrastim-xnst do not require additional doses of CSF.

b. Patient is not currently receiving a prophylactic CSF with at least 2 of the following risk factors for an infection-associated complication:

i. Sepsis syndrome
ii. Age > 65 years,
iii. Absolute neutrophil count (ANC) < 100/mcL
iv. Neutropenia expected to be > 10 days in duration
v. Pneumonia or other clinically documented infections
vi. Invasive fungal infection
vii. Hospitalization at the time of fever
viii. Prior episode of febrile neutropenia

2. Primary prophylaxis
    a. The chemotherapy regimen has a high risk (20% or greater) for febrile neutropenia (See Appendix Table 1).
    b. Chemotherapy regimen has an intermediate risk (10% to 20%) of febrile neutropenia and documentation that the member is at high risk for developing febrile neutropenia by meeting at least ONE of the following criteria i through x:
        i. Previous chemotherapy or radiation therapy.
        ii. Age > 65 years receiving full chemotherapy dose density
        iii. Persistent neutropenia (ie, ANC < 500 neutrophils/mcL OR < 10,000 neutrophils/mcL and a predicted decline to ≤ 500 neutrophils/mcL over the next 48 hours)
        iv. Bone marrow involvement by tumor
        v. Recent surgery or open wounds
        vi. Renal dysfunction (ie, creatinine clearance < 50 mL/min)
        vii. Liver dysfunction (ie, bilirubin > 2.0 mg/dL)
        viii. HIV infection with low CD4 levels
        ix. Poor performance status (Eastern Cooperative Oncology Group [ECOG] score of 2 to 5).
        x. Chronic immunosuppression post-transplant

1. Secondary prophylaxis
    a. Documentation of febrile neutropenia caused by a prior cycle of the same chemotherapy and a reduction of the chemotherapy dose or a delay in therapy is inappropriate.

B. Acute myeloid leukemia (AML)
    1. Documentation that the patient is receiving induction or consolidation chemotherapy.
    2. For requests for Leukine: Age ≥ 55 years old

C. Acute radiation syndrome (ARS)- related neutropenia
    1. Medication is prescribed by or in consultation with a radiologist, hematologist, or oncologist.

D. Stem cell mobilization and transplantation
    1. Documentation of use in one of the following settings a through c:
        a. Priming collection and mobilization of peripheral-blood stem cells for harvest prior to transplantation.
        b. Acceleration of neutrophil recovery following stem cell transplantation.

c. Neutropenia in conjunction with high-dose chemotherapy with autologous stem cell support.

2. The medication is prescribed by or in consultation with an oncologist, hematologist, or physician who specializes in transplantation.

E. Bone marrow transplant (BMT)

1. Documentation of use in one of the following settings a or b:

a. Non-myeloid malignancy undergoing myeloablative chemotherapy followed by autologous or allogenic BMT.

b. After BMT with graft failure or delayed engraftment.

2. The medication is prescribed by or in consultation with an oncologist, hematologist, or physician who specializes in transplantation.

F. Severe chronic neutropenia (congenital, idiopathic, or cyclic)

1. Documentation of an ANC < 500 cells/mcL on three separate occasions during a 6-month period for congenital or idiopathic neutropenia OR five consecutive days of ANC < 500 cells/mcL per cycle for cyclic neutropenia.

2. Documentation of multiple clinically significant episodes of fevers, infections, or oropharyngeal ulcers requiring treatment with antibiotics within the past 12 months.

G. Human immunodeficiency virus (HIV)-related neutropenia

1. Documentation of ANC < 750/mcL.

2. Documentation of fever and other localizing symptoms of infection.

3. Medication is prescribed by or in consultation with a hematologist, oncologist, or infectious disease, or HIV specialist.

H. Myelodysplastic syndrome (MDS)-related neutropenia

1. Documentation of symptomatic anemia and serum erythropoietin level ≤ 500 mUnits/mL.

2. Documentation of prior failure with an erythropoiesis stimulating agent (ESA) as monotherapy.

3. Documentation that the CSF will be used with an ESA.

a. Documentation of adequate iron stores or use of oral or intravenous iron (IV) supplementation (See Appendix Table 2).

II. Documented laboratory values and weight or BSA to support diagnosis and dosing.

III. Treatment must be prescribed by a hematologist or oncologist unless otherwise listed in criteria above A through H.

IV. Request is for a medication with the appropriate FDA labeling and dosage, or its use is supported by current clinical practice guidelines.

V. Refer to the plan document for the list of preferred products. If the requested agent is not listed as a preferred product, must have a documented failure, intolerance, or contraindication to a preferred product(s).

Exclusion Criteria

- Primary prophylaxis of cytopenia in patients who are scheduled for, but not receiving, myelosuppressive chemotherapy.
- Primary prophylaxis in previously untreated adult patients receiving chemotherapy regimens with a low probability (< 10%) of causing fever during anticipated periods of neutropenia.
- Treatment of chronic marrow failure (low white blood cell counts) due to prior chemotherapy treatment.
- Treatment of neutropenias other than those causes listed above under Prior Authorization Criteria (ie, infection prophylaxis of uncomplicated febrile neutropenia or afebrile neutropenia, drug-induced neutropenias other than listed in criteria, etc).
- Use of Fulphila, Fylnetra, Neulasta/Neulasta Onpro, Nyvepria, Rolvedon, Stimufend, Udenyca and Ziextenzo for mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation.
- Concurrent use of another colony-stimulating factor.

Other Criteria

- Febrile neutropenia is defined as:
  - A single temperature ≥ 38.3˚C OR ≥ 38.3˚C for over 1 hour AND
  - Neutrophil count < 500 neutrophils/mcL OR < 1,000 neutrophils/mcL and a predicted decline to ≤ 500 neutrophils/mcL over the next 48 hours.
- Non-myeloid malignancies are cancers that are not classified as myelodysplastic syndromes (MDSs), myeloproliferative neoplasms (MPNs), myelodysplastic/myeloproliferative neoplasms (MDS/MPN) or myeloid malignancies associated with eosinophilia and abnormalities of growth factor receptors derived from platelets or fibroblasts.

Quantity / Days Supply Restrictions

- The quantity is limited to a maximum of a 30-day supply per fill.

Approval Length

- **Authorization:** 6 months.
- **Re-Authorization:** An updated letter of medical necessity or progress notes showing current medical necessity criteria are met and that the medication is effective including:
    - Recent ANC, complete blood count, and/or platelet counts showing a response to therapy.

APPENDIX

Table 1. Disease Settings and Chemotherapy Regimens with a High Risk For Febrile Neutropenia (> 20%)*

DIAGNOSIS	CHEMOTHERAPY REGIMEN
Acute lymphoblastic leukemia (ALL)	• Recommended for myelosuppressive blocks of therapy or as directed by treatment protocol • FLAG-IDA (Fludarabine/Cytarabine/Granulocyte Colony-Stimulating Factor/Idarubicin) • For patients ≥ 65 years or adults with substantial comorbidities, NCCN recommends growth factors for all regimens
Bladder cancer	• Dose-dense MVAC (methotrexate, vinblastine, doxorubicin, cisplatin)
Bone cancer	• VAIA (vincristine, doxorubicin, dactinomycin, ifosfamide) • VDC-IE (vincristine, doxorubicin or dactinomycin and cyclophosphamide alternating with ifosfamide and etoposide) • cisplatin/doxorubicin • VDC (vincristine, doxorubicin or dactinomycin and cyclophosphamide) • VIDE (vincristine, ifosfamide, doxorubicin or dactinomycin, etoposide)
Breast cancer	• Dose-dense AC followed by dose-dense paclitaxel (doxorubicin, cyclophosphamide, paclitaxel) • TAC (docetaxel, doxorubicin, cyclophosphamide) • TC (docetaxel, cyclophosphamide) • TCH (docetaxel, carboplatin, trastuzumab)
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 alfa (dacarbazine, cisplatin, vinblastine, IL-2, interferon alfa)
Multiple myeloma	• DT-PACE (dexamethasone/thalidomide/cisplatin/doxorubicin/ cyclophosphamide/etoposide ± bortezomib (VTD-PACE)
Non-Hodgkin's lymphomas	• CHP (cyclophosphamide, doxorubicin, prednisone) + brentuximab vedotin

	• Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) • ICE (ifosfamide, carboplatin, etoposide) • Dose-dense CHOP-14 (cyclophosphamide, doxorubicin, vincristine, prednisone) • MINE (mesna, ifosfamide, mitoxantrone, etoposide) • DHAP (dexamethasone, cisplatin, cytarabine) • ESHAP (etoposide, methylprednisolone, cisplatin, cytarabine) • HyperCVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone) • Pola-R-CHP (polatuzumab vedotin-piiq, rituximab, cyclophosphamide, doxorubicin, prednisone)
Ovarian cancer	• Topotecan • DocetaxeL
Small cell lung Cancer	• Topotecan
Soft tissue sarcoma	• MAID (mesna, doxorubicin, ifosfamide, dacarbazine) • Doxorubicin • Ifosfamide/doxorubicin
Testicular cancer	• VeIP (vinblastine, ifosfamide, cisplatin) • VIP (etoposide, ifosfamide, cisplatin) • TIP (paclitaxel, ifosfamide, cisplatin)

*This list is not comprehensive. Additional regimens may be considered for coverage if listed in the current NCCN guidelines.

Table 2. Evaluation of Iron Deficiency

TYPE	FERRITIN (ng/mL)		TRANSFERRIN SATURATION	TYPE OF IRON SUPPLEMENTATION
Absolute Iron Deficiency	< 30	**AND**	< 20%	Oral or IV
Functional Iron Deficiency	30 to 500	**AND**	20 to 50%	IV
Possible Functional Iron Deficiency	> 500 to 800	**AND**	< 50%	No iron supplementation needed or IV iron for select patients
No Iron Deficiency	> 800	**OR**	≥ 50%	No iron supplementation needed

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