Medical Policy

Colony Stimulating Factors – Short Acting [Granix® (tbo-filgrastim), Neupogen® (filgrastim), Nivestym™ (filgrastim-aafi), Zarxio® (filgrastim-sndz), Releuko (filgrastim-ayow)]	
MEDICAL POLICY NUMBER	MED_Clin_Ops_047a
ORIGINAL EFFECTIVE DATE	7/1/2021
CURRENT VERSION NUMBER	2
CURRENT VERSION EFFECTIVE DATE	1/1/2022
APPLICABLE PRODUCT AND MARKET	Individual Family Plan: ALL Small Group: ALL

***IMPORTANT INFORMATION – PLEASE READ BEFORE USING THIS POLICY**: These services may or may not be covered by all Bright Health Plans. Please refer to the member's plan document for specific coverage information.*

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Before using this policy, please check the member benefit plan document and any federal or state mandates, if applicable. Bright Health policies and practices are compliant with all federal and state requirements, including mental health parity laws.

PURPOSE

To promote consistency between reviewers in clinical coverage decision-making by providing the criteria that generally determine the medical necessity of Short Acting Colony Stimulating Factors therapy.

POLICY/CRITERA

Prior Authorization and Medical Review is required.

Coverage will be provided for 6 months and may be renewed.

Neupogen, Nivestym, Granix, and Releuko are Non-Preferred products.

The Preferred product is Zarxio.

Neupogen, Nivestym, Granix, and Releuko may be considered medically necessary if:

- The patient has a contraindication or severe intolerance to Zarxio; **OR**
- The dose required necessitates use of a vial and cannot be met with the fixed-dose 300 mcg or 480 mcg prefilled syringes

Coverage for Granix® (tbo-filgrastim), Neupogen® (filgrastim), Nivestym™ (filgrastim-aafi), Releuko (filgrastim-ayow) or Zarxio® (filgrastim-sndz) is provided in the following conditions:

1. **Bone marrow transplant (BMT)**
2. **Peripheral Blood Progenitor Cell (PBPC) mobilization and transplant**
3. **Prophylactic use in patients with non-myeloid malignancy**
    - **a.** Patient is undergoing myelosuppressive chemotherapy with an expected incidence of febrile neutropenia of 20% or greater §; OR
    - **b.** Patient is undergoing myelosuppressive chemotherapy with an expected incidence of febrile neutropenia of 10% or greater§ AND one or more of the following co-morbidities:
        - i. Elderly patients (age 65 or older) receiving full dose intensity chemotherapy
        - ii. History of recurrent febrile neutropenia from chemotherapy
        - iii. Extensive prior exposure to chemotherapy
        - iv. Previous exposure of pelvis, or other areas of large amounts of bone marrow, to radiation
        - v. Pre-existing neutropenia (ANC ≤ 1000/mm3) or bone marrow involvement with tumor
        - vi. Patient has a condition that can potentially increase the risk of serious infection (i.e., HIV/AIDS)
        - vii. Infection/open wounds
        - viii. Recent surgery
        - ix. Poor performance status
        - x. Poor renal function (creatinine clearance <50)
        - xi. Liver dysfunction (elevated bilirubin >2.0)
        - xii. Chronic immunosuppression in the post-transplant setting including organ transplant
4. **Acute Myeloid Leukemia (AML) patient following induction or consolidation chemotherapy**
5. **Severe chronic neutropenia**
    - **a.** Patient must have an absolute neutrophil count (ANC) < 500/mm3; **AND**
    - **b.** Patient must have a diagnosis of one of the following:
        - **i.** Congenital neutropenia; OR
        - **ii.** Cyclic neutropenia; OR
        - **iii.** Idiopathic neutropenia

6. **Patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Subsyndrome of Acute Radiation Syndrome)**

*Febrile neutropenia is defined as:

- a single temperature ≥38.3 °C orally or ≥38.0 °C over 1 hour; AND – neutropenia: <500 neutrophils/mcL or <1,000 neutrophils/mcL and a predicted decline to ≤500
- neutrophils/mcL over the next 48 hours

LIMITATIONS/EXCLUSIONS

1. Any indication other than those listed above due to insufficient evidence of therapeutic value.
2. Patients with a history of serious allergic reactions to human granulocyte colony-stimulating factors such as filgrastim products or pegfilgrastim products

DEFINITIONS

1. NEUPOGEN (filgrastim) injection, for subcutaneous or intravenous use. Initial U.S. Approval: 1991
    a. Single-dose vials containing 300 mcg/mL of filgrastim. Dispensing packs of 10 vials
    b. Single-dose vials containing 480 mcg/1.6 mL (300 mcg/mL) of filgrastim. Dispensing
    c. packs of 10 vials
    d. Single-dose, prefilled syringe with 27 gauge, ½ inch needle with an UltraSafe Needle Guard, containing 300 mcg/0.5 mL of filgrastim.
    e. Single-dose, prefilled syringe with 27 gauge, ½ inch needle with an UltraSafe Needle Guard, containing 480 mcg/0.8 mL of filgrastim.
2. GRANIX (tbo-filgrastim) injection, for subcutaneous use. Initial U.S. Approval: 2012
    a. Prefilled Syringes (w & w/o UltraSafe Passive Needle Guard)
    b. GRANIX 300 mcg/0.5 mL: Each prefilled syringe contains 300 mcg of tbo-filgrastim in 0.5 mL
    c. GRANIX 480 mcg/0.8 mL: Each prefilled syringe contains 480 mcg of tbo-filgrastim in 0.8 mL
    d. GRANIX 300 mcg/1 mL: Each vial contains 300 mcg of tbo-filgrastim in 1 mL solution.
    e. GRANIX 480 mcg/1.6 mL: Each vial contains 480 mcg of tbo-filgrastim in 1.6 mL solution.
3. ZARXIO (filgrastim-sndz) injection, for subcutaneous or intravenous use. Initial U.S. Approval: 2015
    a. ZARXIO (filgrastim-sndz) is biosimilar* to NEUPOGEN (filgrastim).
    b. Injection: Single-dose, preservative-free, prefilled syringes with an UltraSafe Passive Needle Guard, containing 300 mcg/0.5 mL of a clear, colorless to slightly yellowish filgrastim-sndz solution.
    c. Injection: Single-dose, preservative-free, prefilled syringes with an UltraSafe Passive Needle Guard, containing 480 mcg/0.8 mL of a clear, colorless to slightly yellowish filgrastim-sndz solution.

4. NIVESTYM™ (filgrastim-aafi) injection, for subcutaneous or intravenous useInitial U.S. Approval: 2018
    a. NIVESTYM (filgrastim-aafi) is biosimilar to NEUPOGEN (filgrastim).
    b. Injection: Single-dose vials containing 300 mcg/mL of a sterile, clear, colorless, preservative-free filgrastim-aafi solution. Dispensing packs of 10 vials
    c. Injection: Single-dose vials containing 480 mcg/1.6 mL (300 mcg/mL) of a sterile, clear, colorless, preservative-free filgrastim-aafi solution. Dispensing packs of 10 vials
    d. Injection: Single-dose prefilled syringe with BD UltraSafe Plus™ Passive Needle Guard, containing 300 mcg/0.5 mL of a sterile, clear, colorless, preservative-free filgrastim-aafi
    e. Injection: Single-dose, prefilled syringe with BD UltraSafe Plus™ Passive Needle Guard,
    f. containing 480 mcg/0.8 mL of a sterile, clear, colorless, preservative-free filgrastim-aafi

CODING

Applicable NDC Codes	
55513-0530-xx	Neupogen 300 mcg vial
55513-0924-xx	Neupogen 300 mcg SingleJect
55513-0546-xx	Neupogen 480 mcg vial
55513-0209-xx	Neupogen 480 mcg SingleJect
63459-0910-xx	Granix 300 mcg prefilled syringe
63459-0912-xx	Granix 480 mcg prefilled syringe
61314-0318-xx	Zarxio 300 mcg prefilled syringe
61314-0326-xx	Zarxio 480 mcg prefilled syringe
70121-1568-xx	Releuko 300 mcg/0.5 mL Single-dose prefilled syringe
70121-1569-xx	Releuko 300 mcg/mL Single-dose vials
70121-1571-xx	Releuko 480 mcg/1.6 mL (300 mcg/mL) Single-dose vials
70121-1570-xx	Releuko 480 mcg/0.8 mL Single-dose prefilled syringe

Applicable Procedure Code	
J1442	Injection, filgrastim (g-csf), excludes biosimilars, 1microgram (1 mcg=1 billable unit)
J1447	Injection, tbo-filgrastim, (Granix), 1 microgram (1 microgram=1 billable unit)
Q5101	Injection, filgrastim-sndz, biosimiliar, (Zarxio), 1 microgram: 1 billable unit=1 microgram
Q5110	Injection, filgrastim-aafi, biosimilar, (Nivestym), 1 mcg
J3590	Unclassified biologic when used for RELEUKO (filgrastim-ayow soln)

Applicable ICD-10 Codes	
C92.00	Myeloid leukemia not having achieved remission
C92.02	Myeloid leukemia in relapse
C92.50	Acute myelomonocytic leukemia not having achieved remission

C92.52	Acute myelomonocytic leukemia in relapse
C92.60	Acute myeloid leukemia with 11q23-abnormality not having achieved remission
C92.62	Acute myeloid leukemia with 11q23-abnormality in relapse
C92.A0	Acute myeloid leukemia with multilineage dysplasia not having achieved remission
C92.A2	Acute myeloid leukemia with multilineage dysplasia in relapse
C93.00	Acute monoblastic/monocytic leukemia not having achieved remission
C93.02	Acute monoblastic/monocytic leukemia in relapse
C93.10	Chronic myelomonocytic leukemia, not having achieved remission
C94.00	Acute erythroid leukemia not having achieved remission
C94.02	Acute erythroid leukemia in relapse
C94.20	Acute megakaryoblastic leukemia not having achieved remission
C94.22	Acute megakaryoblastic leukemia in relapse
D46.0	Refractory anemia without ring sideroblasts, so stated
D46.1	Refractory anemia with ring sideroblasts
D46.20	Refractory anemia with excess of blasts, unspecified
D46.21	Refractory anemia with excess of blasts 1
D46.22	Refractory anemia with excess of blasts 2
D46.4	Refractory anemia, unspecified
D46.9	Myelodysplastic syndrome, unspecified
D46.A	Refractory cytopenia with multilineage dysplasia
D46.B	Refractory cytopenia with multilineage dysplasia and ring sideroblasts
D46.Z	Other myelodysplastic syndrome
D70.0	Congenital agranulocytosis
D70.1	Agranulocytosis secondary to cancer chemotherapy
D70.2	Other drug-induced agranulocytosis
D70.4	Cyclic neutropenia
D70.9	Neutropenia, unspecified
T45.1X5A	Adverse effect of antineoplastic and immunosuppressive drugs initial encounter
T45.1X5D	Adverse effect of antineoplastic and immunosuppressive drugs subsequent encounter
T45.1X5S	Adverse effect of antineoplastic and immunosuppressive drugs sequela
T66.XXXA	Radiation sickness, unspecified, initial encounter
Z41.8	Encounter for other procedures for purposes other then remedying health state
Z48.290	Encounter for aftercare following bone marrow transplant
Z51.11	Encounter for antineoplastic chemotherapy
Z51.12	Encounter for antineoplastic immunotherapy
Z51.89	Encounter for other specified aftercare
Z52.001	Unspecified donor, stem cells

Z52.011	Autologous donor, stem cells
Z52.091	Other blood donor, stem cells
Z94.81	Bone marrow transplant status
Z94.84	Stem cells transplant status

EVIDENCE BASED REFERENCES

1. Neupogen [package insert]. Thousand Oaks, CA; Amgen Inc; June 2018. Accessed May 2021.
2. Nivestym [package insert]. Lake Forest, IL; Hospira Inc; July 2018. Accessed May 2021.
3. Zarxio [package insert]. Princeton, NJ; Sandoz Inc; August 2019. Accessed May 2021.
4. Granix [package insert]. North Wales, PA; Teva Pharmaceuticals USA, Inc.; November2019. Accessed May 2021.
5. Product Information: RELEUKO(R) subcutaneous, intravenous injection, filgrastim-ayow subcutaneous, intravenous injection. Amneal Biosciences LLC (per FDA), Bridgewater, NJ, 2022.

POLICY HISTORY

Revision History	Month Day, Year	Updates
Original Effective Date	JULY 1, 2021	
Revision	5/24/2022	Addition of Releuko as a non-preferred filgrastim product.
P&T Committee Endorsement	MAY 24, 2021	

DISCLAIMER

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