Medical Policy:

Colony Stimulating Factors: Neupogen®, Granix®, Releuko® And Zarxio® (Filgrastim) Subcutaneous/Intravenous

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.95	March 21, 2024	

The treating physician or primary care provider must submit to EmblemHealth, or ConnectiCare, as applicable (hereinafter jointly referred to as "EmblemHealth"), the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care.

EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary.

If there is a discrepancy between this guideline and a member's benefits program, the benefits program will govern. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test or procedure over another. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and web site links are accurate at time of publication.

EmblemHealth may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. EmblemHealth Services Company, LLC, has adopted this policy in providing management, administrative and other services to EmblemHealth Plan, Inc., EmblemHealth Insurance Company, EmblemHealth Services Company, LLC, and Health Insurance Plan of Greater New York (HIP) related to health benefit plans offered by these entities. ConnectiCare, an EmblemHealth company, has also adopted this policy. All of the aforementioned entities are affiliated companies under common control of EmblemHealth Inc.

Length of Authorization

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

Dosing Limits [Medical Benefit]

Max Units (per dose and over time):

Severe Chronic Neutropenia:

- 1380 billable units per day

BMT or PBPC or Radiation:

- 1200 billable units per day

All other indications:

- 600 billable units per day

Guideline

I. Initial Approval Criteria

Neupogen and Releuko are non-preferred G-CSF product. **Preferred agents are Granix and Zarxio**.

Granix and Zarxio are the preferred agents for Commercial, Medicaid, and Medicare members.

Neupogen *may be considered medically necessary if:*

- The patient has a contraindication or severe intolerance to Granix **AND** 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

Releuko *may be considered medically necessary if:*

- The patient has a contraindication or severe intolerance to Granix **AND** Zarxio†;

† Commercial, Medicaid, AND Medicare members are subject to this step therapy

Coverage for Neupogen®, Granix®, Zarxio® or Releuko® (filgrastim) is provided in the following conditions:

Bone marrow transplant (BMT) †

Peripheral Blood Progenitor Cell (PBPC) mobilization and transplant † (Excludes Releuko)

Prophylactic use in patients with non-myeloid malignancy †

1. Patient is undergoing myelosuppressive chemotherapy with an expected incidence of febrile neutropenia of 20% or greater **§**; **OR**
2. 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:
   a. Elderly patients (age 65 or older) receiving full dose intensity chemotherapy
   b. History of recurrent febrile neutropenia from chemotherapy
   c. Extensive prior exposure to chemotherapy
   d. Previous exposure of pelvis, or other areas of large amounts of bone marrow, to radiation
   e. Pre-existing neutropenia (ANC ≤ 1000/mm^3) or bone marrow involvement with tumor
   f. Patient has a condition that can potentially increase the risk of serious infection (i.e. HIV/AIDS)
   g. Infection/open wounds
   h. Recent surgery
   i. Poor performance status
   j. Poor renal function (creatinine clearance <50)
   k. Liver dysfunction (elevated bilirubin >2.0)
   l. Chronic immunosuppression in the post-transplant setting including organ transplant

Treatment of chemotherapy-induced febrile neutropenia ‡

Used for the treatment of chemotherapy induced febrile neutropenia; **AND**

1. Patient has been on prophylactic therapy with filgrastim or tbo-filgrastim *(Note: therapy should not be used concomitantly with pegfilgrastim);* **OR**
2. Patient has not received prophylactic therapy with a granulocyte colony stimulating factor; **AND**
   a. Patient has one or more of the following risk factors for developing infection-related complications:
      ii. Sepsis Syndrome
      iii. Age >65
      iv. Absolute neutrophil count [ANC] <100/mcL

v. Duration of neutropenia expected to be greater than 10 days
vi. Pneumonia or other clinically documented infections
vii. Invasive fungal infection
viii. Hospitalization at the time of fever
ix. Prior episode of febrile neutropenia

Patient who experienced a neutropenic complication from a prior cycle of the same chemotherapy ‡

Acute Myeloid Leukemia (AML) patient following induction or consolidation chemotherapy †

Bone Marrow Transplantation (BMT) failure or Engraftment Delay ‡

Severe chronic neutropenia †

1. Patient must have an absolute neutrophil count (ANC) < 500/mm^3; **AND**
2. Patient must have a diagnosis of one of the following:
   A. Congenital neutropenia; **OR**
   B. Cyclic neutropenia; **OR**
   C. Idiopathic neutropenia

Myelodysplastic Syndrome ‡

1. Endogenous serum erythropoietin level of ≤500 mUnits/mL; **AND**
2. Patient has lower risk disease (i.e., defined as IPSS-R [Very Low, Low, Intermediate]); **AND**
3. Used for treatment of symptomatic anemia with no del(5q) mutation; **AND**
4. Patient is receiving concurrent therapy with Erythropoiesis Stimulating Agents (ESAs)

Patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Subsyndrome of Acute Radiation Syndrome) † (Neupogen Only)

† FDA-labeled indication(s); **‡** Compendia recommended indication(s)
§ Expected incidence of febrile neutropenia percentages for myelosuppressive chemotherapy regimens can be found in the NCCN Myeloid Growth Factors Clinical Practice Guideline at NCCN.org.

II. Renewal Criteria

Same as initial prior authorization policy criteria.

Limitations/Exclusions

Neupogen is not considered medically necessary for indications other than those listed above due to insufficient evidence of therapeutic value.

Applicable Procedure Codes

Code	Description
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
Q5125	Injection, filgrastim-ayow, biosimilar, (Releuko), 1 mcg; 1 billable unit = 1 mcg

Applicable NDCs

Code	Description
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
63459-0918-xx	Granix 300 mcg single-dose vial
63459-0920-xx	Granix 480 mcg single-dose vial
61314-0318-xx	Zarxio 300 mcg prefilled syringe
61314-0326-xx	Zarxio 480 mcg prefilled syringe
70121-1568-xx	Releuko 300mcg prefilled syringe
70121-1569-xx	Releuko 300mcg vial
70121-1570-xx	Releuko 480mcg prefilled syring
70121-1571-xx	Releuko 480mcg vial

ICD-10 Diagnoses

Code	Description
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
D46.4	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 than 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

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	3/21/2024	Annual Review: Removed J3590, Added Q5125, added NDC's: 63459-0918-xx and 63459-0920-xx
EmblemHealth & ConnectiCare	9/14/2023	Annual Review: Initial Criteria: **Myelodysplastic Syndrome Added:** Patient has lower risk disease (i.e., defined as IPSS-R [Very Low, Low, Intermediate]); **AND** Used for treatment of symptomatic anemia with no del(5q) mutation; **AND" Treatment of chemotherapy-induced febrile neutropenia ‡** After Statement: Patient has been on prophylactic therapy with filgrastim Added "or tbo-filgrastim *(Note: therapy should not be used concomitantly with pegfilgrastim"*
EmblemHealth & ConnectiCare	5/12/2022	Added Releuko to affected agents (2Q2022 P&T approved)
EmblemHealth & ConnectiCare	4/07/2022	Transferred policy to new template
EmblemHealth & ConnectiCare	1/1/2021	Extended coverage duration from 4 to 6 months.
EmblemHealth & ConnectiCare	11/2/2020	Effective 01/01/2021, Member must fail trial of Granix AND Zarxio, prior to using Neupogen (Medicare members are subject to this step therapy).
EmblemHealth & ConnectiCare	11/20/2019	Added Granix and Zarxio to the policy title Added clarifying language: Granix and Zarxio are the preferred agents for Medicare members (Step protocol not mandated for Medicare members).

EmblemHealth & ConnectiCare	1/1/2019	Annual review

References

1. Neupogen [package insert]. Thousand Oaks, CA; Amgen Inc; June 2016. Accessed March 2018.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) filgrastim. National Comprehensive Cancer Network, 2018. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc." To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed March 2018.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Myeloid Growth Factors. Version 1.2018. National Comprehensive Cancer Network, 2017. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc." To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed March 2018.
4. Smith TJ, Bohlke K, Lyman GH, Carson KR, Crawford J, Cross SJ, Goldberg JM, Khatcheressian JL, Leighl NB, Perkins CL, Somlo G, Wade JL, Wozniak AJ, Armitage JO. Recommendations for the use of WBC growth factors: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol. 2015 Jul 13. pii: JCO.2015.62.3488. [Epub ahead of print]
5. Wisconsin Physicians Service Insurance Corporation. Local Coverage Determination (LCD): Human Granulocyte/Macrophage Colony Stimulating Factors (L34699). Centers for Medicare & Medicaid Services, Inc. Updated on 1/23/2018 with effective date 02/1/2018. Accessed March 2018.
6. First Coast Service Options, Inc. Local Coverage Determination (LCD): G-CSF (Neupogen®, Granix™, Zarxio™) (L34002). Centers for Medicare & Medicaid Services, Inc. Updated on 6/10/2016 with effective date 7/5/2016. Accessed March 2018.
7. National Government Services, Inc. Local Coverage Article: Filgrastim, Pegfilgrastim, Tbo-filgrastim, Filgrastim-sndz (e.g., Neupogen®, Neulasta™, Granix™, Zarxio™) - Related to LCD L33394 (A52408). Centers for Medicare & Medicaid Services, Inc. Updated on 9/23/2016 with effective date 10/1/2016. Accessed March 2018.
8. Palmetto GBA. Local Coverage Determination: White Cell Colony Stimulating Factors (L37176). Centers for Medicare & Medicaid Services, Inc. Updated on 12/7/2017 with effective date 2/26/2018. Accessed March 2018.
9. Releuko® subcutaneous or intravenous injection [prescribing information]. Bridgewater, NJ: Amneal; February 2022.