Medical Policy:

Colony Stimulating Factors: Nivestym™ (filgrastim-aafi)

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.62a	March 21, 2024	2018

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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.

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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:

- 1560 billable units per day

BMT, PBPC, or Radiation:

- 1200 billable units per day

All other indications

- 600 billable units per day

Guideline

I. Initial Approval Criteria

Nivestym is a non-preferred G-CSF product. Preferred agents are Granix and Zarxio.

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

Nivestym *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 Nivestym™ (filgrastim-aafi) is provided in the following conditions:

Bone marrow transplant†

Peripheral Blood Progenitor Cell (PBPC) mobilization and transplant†

Patient with solid tumors or non-myeloid malignancy†

1. Patient is undergoing myelosuppressive chemotherapy with an expected incidence of febrile neutropenia ❖ of greater than 20% §; **OR**
2. Patient is undergoing myelosuppressive chemotherapy with an expected incidence of febrile neutropenia ❖of 10% to 20% § **AND** one or more patient-related risk factors ¥;
3. Patient is undergoing myelosuppressive chemotherapy with an expected incidence of febrile neutropenia ❖ of <10% **AND** two or more patient related risk factors ¥ **

***Use in this setting is based on clinical judgment.*

Note: Dose-dense therapy, in general, requires growth factor support to maintain dose intensity and schedule. In the palliative setting, consideration should be given to dose reduction or change in regimen.

§ Expected incidence of febrile neutropenia percentages for myelosuppressive chemotherapy regimens can be found in the NCCN Hematopoietic Growth Factors Clinical Practice Guideline at NCCN.org

¥ Patient risk factors for febrile neutropenia
• Age >65 years receiving full dose intensity chemotherapy • Prior exposure to chemotherapy or radiation therapy • Persistent neutropenia (ANC ≤ 1000/mm3) • Bone marrow involvement by tumor • Patient has a condition that can potentially increase the risk of serious infection (i.e., HIV/AIDS with low CD4 counts) • Recent surgery and/or open wounds • Poor performance status • Renal dysfunction (creatinine clearance <50 mL/min) • Liver dysfunction (elevated bilirubin >2.0 mg/dL) • Chronic immunosuppression in the post-transplant setting, including organ transplant
❖ Febrile neutropenia is defined as:
• Temperature: 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

Treatment of chemotherapy-induced febrile neutropenia‡

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**

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a. Patient has one or more of the following risk factors for developing infection related complications
    i. Sepsis syndrome
    ii. Age > 65
    iii. Absolute neutrophil count [ANC] < 100/mcL
    iv. Duration of neutropenia expected to be greater than 10 days
    v. Pneumonia or other clinically documented infections
    vi. Invasive fungal infection
    vii. Hospitalization at the time of fever
    viii. 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) ‡

†FDA-labeled indication, ‡ Compendia recommended indication
§ 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

I. Renewal Criteria

Same as initial prior authorization policy criteria

II. Dosage/Administration

Indication	Dose
BMT/PBPC/H-ARS	10 mcg/kg daily for up to 14 days
Congenital Neutropenia	6 mcg/kg twice daily
All other indications	5 mcg/kg daily for up to 14 days

*****Do not administer within 14 days before and 24 hours after administration of cytotoxic chemotherapy

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Applicable Procedure Codes

Code	Description
Q5110	Injection, filgrastim-aafi, biosimilar, (Nivestym), 1 mcg

Applicable NDCs

Code	Description
00069-0291-xx	Nivestym single dose prefilled syringe; 300 mcg/0.5 ml solution
00069-0292-xx	Nivestym single dose prefilled syringe; 480 mcg/0.8 ml solution
00069-0293-xx	Nivestym single use vial; 300 mcg/1 ml solution
00069-0294-xx	Nivestym single use vial; 480 mcg/1.6 ml solution

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
D46.22	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.C	Myelodysplastic syndrome with isolated del(5q), chromosomal abnormality
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

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D70.9	Neutropenia, unspecified
T86.00	Unspecified complication of bone marrow transplant
T86.01	Bone marrow transplant rejection
T86.02	Bone marrow transplant failure
T86.03	Bone marrow transplant infection
T86.09	Other complications of bone marrow transplant
Z41.8	Encounter for other procedures for purposes other than remedying health state
Z51.11	Encounter for antineoplastic chemotherapy
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	3/19/2025	Updated Max units dose Updated risk factors(patient co-morbidities) for febrile neutropenia. Added to criteria: Patient is undergoing myelosuppressive chemotherapy with an expected incidence of febrile neutropenia of <10% AND two or more patient related risk factors ¥ ** Separated from criteria co-morbidities and created chart to reference, as well as defining febrile neutropenia.
EmblemHealth & ConnectiCare	3/21/2024	Annual Review: Updated dosing chart, Initial Criteria: Patient with Non-myeloid malignancy: added: a. Chronic immunosuppression in the post-transplant setting including organ transplant as a co-morbidity
EmblemHealth & ConnectiCare	9/15/2023	Annual Review: Initial Criteria: Treatment of chemotherapy-induced febrile neutropenia‡ After the Statement: Patient has been on prophylactic therapy with filgrastim; Added " or tbo-filgrastim (Note: therapy should not be used concomitantly with pegfilgrastim);"**OR** 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"**
EmblemHealth & ConnectiCare	4/08/2022	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 Nivestym (Medicare members are subject to this step therapy).
EmblemHealth & ConnectiCare	11/20/2019	Granix and Zarxio are the preferred agents for Medicare members (Step protocol not mandated for Medicare members).

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EmblemHealth & ConnectiCare	12/18/2018	Added New NDC Codes 0069-0291-xx, 0069-0292-xx, 0069-0293-xx, 0069-0294-xx

References

1. Nivestym [package insert]. Hospira, Inc., Lake Forest, IL. July, 2018.

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