Medical Policy Bulletin

Title:
Filgrastim (Neupogen ®) and Related Biosimilars, and Tbo-filgrastim (Granix ®)
Policy #:
MA08.130i

The Company makes decisions on coverage based on the Centers for Medicare and Medicaid Services (CMS) regulations and guidance, benefit plan documents and contracts, and the member's medical history and condition. If CMS does not have a position addressing a service, the Company makes decisions based on Company Policy Bulletins. Benefits may vary based on contract, and individual member benefits must be verified. The Company determines medical necessity only if the benefit exists and no contract exclusions are applicable. Although the Medicare Advantage Policy Bulletin is consistent with Medicare's regulations and guidance, the Company's payment methodology may differ from Medicare.

When services can be administered in various settings, the Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition. This decision is based on the member's current medical condition and any required monitoring or additional services that may coincide with the delivery of this service.

This Policy Bulletin document describes the status of CMS coverage, medical terminology, and/or benefit plan documents and contracts at the time the document was developed. This Policy Bulletin will be reviewed regularly and be updated as Medicare changes their regulations and guidance, scientific and medical literature becomes available, and/or the benefit plan documents and/or contracts are changed.

Policy

Coverage is subject to the terms, conditions, and limitations of the member's Evidence of Coverage.

The Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition.

In the absence of coverage criteria from applicable Medicare statutes, regulations, NCDs, LCDs, CMS manuals, or other Medicare coverage documents, this policy uses internal coverage criteria developed by the Company in consideration of peer-reviewed medical literature, clinical practice guidelines, and/or regulatory status.

MEDICALLY NECESSARY

COMPANY-DESIGNATED PREFERRED PRODUCTS
Although there are many filgrastim products on the market (e.g., filgrastim [Neupogen], filgrastim-aafi [Nivestym], filgrastim-sndz [Zarxio], filgrastim-txid (Nypozi), tbo-filgrastim [Granix], filgrastim-ayow, [Releuko]), there is no reliable evidence of the superiority of any one product of filgrastim compared to other products. The Company has designated the following filgrastim products as its preferred products:

- Filgrastim-aafi (Nivestym)
- Filgrastim-sndz (Zarxio)

These products are less costly and at least as likely to produce equivalent therapeutic results as the nonpreferred products, which include, but are not limited to, filgrastim (Neupogen), tbo-filgrastim (Granix), any other nonpreferred filgrastim biosimilars.

According to the US Food and Drug Administration (FDA), “a biosimilar is a biological product that has no clinically meaningful differences from the existing FDA-approved reference product. All biosimilar products meet the FDA’s rigorous standards for approval for the indications described in the product labeling. Once a biosimilar has been approved by the FDA, the safety and effectiveness of these products have been established, just as they have been

for the reference product." Coverage of a biosimilar product as an alternate to a reference product is not considered a form of step therapy by the Company.

NONPREFERRED PRODUCTS

Use of the nonpreferred filgrastim products, which include, but are not limited to, filgrastim (Neupogen), tbo-filgrastim (Granix), filgrastim-ayow (Releuko) and any other nonpreferred filgrastim biosimilars is considered medically necessary and, therefore, covered only for individuals who are currently receiving or have previously received a nonpreferred product for the specified filgrastim indication.

If the individual has not previously received filgrastim (Neupogen), tbo-filgrastim (Granix), or any other nonpreferred filgrastim biosimilars to treat the specified indication, these nonpreferred products are only eligible for coverage when the individual has contraindication(s) or intolerance(s) to the Company-designated preferred products.

FILGRASTIM (NEUPOGEN) AND RELATED BIOSIMILARS

Filgrastim (Neupogen) and related biosimilars (e.g., filgrastim-aafi [Nivestym], filgrastim-sndz [Zarxio], filgrastim-txid (Nypozi), filgrastim-ayow [Releuko]) are considered medically necessary and, therefore, covered when used as recommended by the then-current National Comprehensive Cancer Network (NCCN) and American Society of Clinical Oncology (ASCO) guidelines for any of the following indications:

- Prophylaxis of myelosuppressive chemotherapy-induced febrile neutropenia or other dose-limiting neutropenic events in high-risk* (>20% overall risk of febrile neutropenia) individuals with solid tumors and nonmyeloid malignancies receiving treatment in the curative/adjuvant or palliative settings
- Prophylaxis of myelosuppressive chemotherapy-induced febrile neutropenia or other dose-limiting neutropenic events in intermediate-risk* (10% to 20% overall risk of febrile neutropenia) individuals with solid tumors and nonmyeloid malignancies receiving treatment in the curative/adjuvant or palliative settings who have one or more of the following risk factors:
    - Prior chemotherapy or radiation therapy
    - Persistent neutropenia
    - Bone marrow involvement by tumor
    - Recent surgery and/or open wounds
    - Liver dysfunction (bilirubin >2 mg/dL)
    - Renal dysfunction (creatinine clearance <50 mL/min)
    - Age greater than 65 years receiving full chemotherapy dose intensity
    - Poor performance status (Eastern Cooperative Oncology Group [ECOG] Performance Status 3-4)
    - Human immunodeficiency virus (HIV) infection with low CD4 counts (450 cells/mm^3 or less)
    - Chronic immunosuppression in the posttransplant setting, including organ transplant
- Prophylaxis of chemotherapy-induced febrile neutropenia or other dose-limiting neutropenic events in low-risk (<10% overall risk of febrile neutropenia) individuals with solid tumors and nonmyeloid malignancies receiving treatment in the curative/adjuvant or palliative settings who have two or more individual-related risk factors.
- Prophylaxis of chemotherapy-induced febrile neutropenia in individuals with acute myeloid leukemia (AML) who are receiving induction chemotherapy for any of the following:
    - For favorable-risk AML by molecular mutation profile, intermediate-risk AML per European LeukemiaNet (ELN), or poor-risk AML without TP53 mutation or del17p abnormality in combination with cladribine, cytarabine, and mitoxantrone
    - For relapsed or refractory disease in combination with cladribine and cytarabine, with or without mitoxantrone or idarubicin
    - For relapsed or refractory disease in combination with fludarabine and cytarabine, with or without idarubicin, with or without venetoclax

- Prophylaxis of chemotherapy-induced febrile neutropenia in individuals with AML who are receiving consolidation chemotherapy for any of the following:
    - In combination with fludarabine, cytarabine, and idarubicin with or without gemtuzumab ozogamicin (preferred only if given during induction) for patients with poor-risk AML with and without TP53-mutation or del17p abnormality, therapy-related AML other than core-binding fact acute myeloid leukemia (CBF-AML), antecedent myelodysplastic syndromes (MDS)/chronic myelomonocytic leukemia (CMML), or cytogenetic changes consistent with MDS (previously classified as AML-MRC).
- Treatment of chemotherapy-induced febrile neutropenia
    - In individuals who have been receiving prophylactic filgrastim
    - Consider in individuals who have not received prophylactic granulocyte colony-stimulating factors but who have risk factors for an infection-associated complication

- For hematopoietic cell transplantation for any of the following:
    - Additional therapy for an insufficient collection of stem cells in combination with plerixafor following treatment with filgrastim alone or filgrastim and disease-specific chemotherapy
    - Treatment for hematopoietic cell mobilization for allogeneic donors as a single agent
    - Treatment for hematopoietic cell mobilization for autologous donors
        - In combination with plerixafor
        - In combination with cyclophosphamide with or without plerixafor
        - As a single agent
        - In combination with disease-specific chemotherapy with or without plerixafor
        - In combination with motixafortide in individuals with multiple myeloma

- Therapeutic use in acute lymphoblastic leukemia (ALL) in adult individuals with relapsed/refractory (R/R) Philadelphia chromosome–negative B-ALL, T-ALL, and Philadelphia chromosome– positive B-ALL if refractory to tyrosine kinase inhibitors (TKIs) as a component of:
    - FLAG: induction/consolidation (fludarabine, cytarabine, granulocyte colony-stimulating factor)
    - FLAG-IDA: induction/consolidation (fludarabine, cytarabine, granulocyte colony-stimulating factor; with idarubicin)
- Acute lymphoblastic leukemia (ALL) or acute myeloid leukemia (AML) in pediatric individuals who have relapsed disease and have serious/life-threatening neutropenic infection
- Prophylaxis of chemotherapy-induced febrile neutropenia in individuals with Wilms tumor (nephroblastoma), when administered with Regimen M and Regimen I for courses of either:
    - Cyclophosphamide and etoposide
    - Cyclophosphamide, doxorubicin, and vincristine
- Diffuse aggressive lymphoma in individuals age 65 years and older treated with curative chemotherapy regimen cyclophosphamide, doxorubicin, vincristine, prednisone, and rituximab (R-CHOP)

- In pediatric individuals where dose-intense chemotherapy is administered for an indication that is known to have a survival benefit (e.g., Ewing sarcoma)
- Dose-dense therapy (standard doses given more frequently) for the adjuvant treatment of high-risk breast cancer or for the use of high-dose intensity methotrexate, vinblastine, doxorubicin, and cisplatin (HD-M-VAC) in urothelial cancer

- Secondary prophylaxis in individuals who have experienced a neutropenic event from a prior cycle of chemotherapy (for which primary prophylaxis was not received), in which a reduced dose or treatment delay may compromise disease-free or overall survival or treatment outcome
- Therapeutic use in individuals with cancer who have fever and neutropenia and are at high risk for infection-associated complications or who have prognostic factors that are predictive of poor clinical outcomes. High-risk features include the following factors:
    - Expected prolonged (>10 days) and profound ($<0.1 \times 10^9$/L) neutropenia
    - Age greater than 65 years
    - Pneumonia
    - Hypotension and multiorgan dysfunction (sepsis syndrome)
    - Invasive fungal infection
    - Hospitalization at the time of fever development
    - Other clinically documented infections
    - Prior episode of febrile neutropenia
- Prophylaxis of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia, in individuals with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation (BMT)
- Mobilize autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis
- Prophylaxis of sequelae of severe neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic individuals with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia
- Prophylaxis of neutropenia in individuals undergoing hematopoietic cell transplant for any of the following indications:
    - Mobilization of hematopoietic progenitor cells in combination with plerixafor in the autologous setting for individuals with non-Hodgkin lymphoma or multiple myeloma
    - Mobilization of donor hematopoietic progenitor cells or for granulocyte transfusion in the allogeneic setting
    - As supportive care in the posttransplant setting
- Mobilization of hematopoietic progenitor cells in hematopoietic cell transplant in the autologous setting for any of the following:
    - As a single agent
    - Following combination chemotherapy
    - In combination with sargramostim
    - In combination with plerixafor for individuals with non-Hodgkin lymphoma or multiple myeloma
- Hematopoietic cell transplant for mobilization of donor hematopoietic progenitor cells or for granulocyte transfusion in the allogeneic setting
- Supportive care for hematopoietic cell transplant in the posttransplant setting
- Treatment of chemotherapy-induced febrile neutropenia for one of the following conditions:
    - In individuals who have been receiving prophylactic tbo-filgrastim
    - In individuals who have not received prophylactic granulocyte colony-stimulating factors but who have risk factors for an infection-associated complication
- Treatment for individuals with radiation-induced myelosuppression following a radiological or nuclear incident (hematopoietic acute radiation syndrome [H-ARS]):
- Management of chimeric antigen receptor (CAR) T-cell–related toxicities as additional supportive care for neutropenic individuals

- Treatment of individuals with lower risk[†,††] myelodysplastic syndromes (MDS) associated with symptomatic anemia with no del(5q), with or without other cytogenetic abnormalities with serum erythropoietin ≤500 mU/mL for any of the following:
    - With ring sideroblasts <15% (or ring sideroblasts <5% with an SF3B1 mutation) in combination with an erythropoiesis-stimulating agent (ESA) following no response (despite adequate iron stores) to either an ESA alone or luspatercept-aamt (REBLOZYL)
    - With ring sideroblasts ≥15% (or ring sideroblasts ≥5% with an SF3B1 mutation), in combination with an erythropoiesis-stimulating agent (ESA) following no response to luspatercept-aamt (REBLOZYL)

TBO-FILGRASTIM (GRANIX)

Tbo-filgrastim (Granix) is considered medically necessary and, therefore, covered for any of the following indications:

- May be used as a substitute for filgrastim
- Prophylaxis of severe neutropenia in adult and pediatric individuals 1 month and older with nonmyeloid malignancies receiving myelosuppressive anticancer therapy associated with a clinically significant incidence of febrile neutropenia
- Prophylaxis of chemotherapy-induced febrile neutropenia or other dose-limiting neutropenic events in high-risk (>20% overall risk of febrile neutropenia[‡]) individuals with solid tumors and nonmyeloid malignancies receiving treatment in the curative/adjuvant or palliative settings
- Prophylaxis of chemotherapy-induced febrile neutropenia or other dose-limiting neutropenic events in intermediate-risk (10% to 20% overall risk of febrile neutropenia[‡]) individuals with solid tumors and nonmyeloid malignancies receiving treatment in the curative/adjuvant or palliative settings who have one or more risk factors
- Prophylaxis of chemotherapy-induced febrile neutropenia or other dose-limiting neutropenic events in low-risk (<10% overall risk of febrile neutropenia) individuals with solid tumors and nonmyeloid malignancies receiving treatment in the curative/adjuvant or palliative settings who have two or more individual-related risk factors.
- Treatment for individuals with radiation-induced myelosuppression following a radiological/nuclear incident (hematopoietic acute radiation syndrome [H-ARS])
- Treatment of chemotherapy-induced febrile neutropenia for one of the following conditions:
    - In individuals who have been receiving prophylactic tbo-filgrastim
    - In individuals who have not received prophylactic granulocyte colony-stimulating factors but who have risk factors for an infection-associated complication
- Treatment of individuals with lower risk[†,††] myelodysplastic syndromes (MDS) associated with symptomatic anemia with no del(5q), with or without other cytogenetic abnormalities with serum erythropoietin ≤500 mU/mL and any of the following:
    - In combination with an erythropoiesis-stimulating agent (ESA) following no response (despite adequate iron stores) to or relapse after either an ESA alone or luspatercept-aamt (REBLOZYL) in individuals with ring sideroblasts <15% (or ring sideroblasts <5% with an SF3B1 mutation)
    - In combination with an erythropoiesis-stimulating agent (ESA) following no response to or relapse after luspatercept-aamt (REBLOZYL) in individuals with ring sideroblasts ≥15% (or ring sideroblasts ≥5% with an SF3B1 mutation)

[*] *See Attachment A for examples of disease settings and chemotherapy regimens with a high (>20%) or intermediate (10%–20%) risk for febrile neutropenia (Note: These are not all-inclusive lists).*

[†,††] *Lower risk defined as IPSS-R (Very Low, Low, Intermediate), IPSS (Low/Intermediate-1), WPSS (Very Low, Low, Intermediate).*

NOT MEDICALLY NECESSARY

For individuals receiving their first course of filgrastim, use of filgrastim (Neupogen), filgrastim-aafi (Nivestym), or any other nonpreferred filgrastim biosimilars, is considered not medically necessary and, therefore, not covered since they are more costly than the preferred products that are at least as likely to produce equivalent therapeutic results for that individual's condition.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for filgrastim (Neupogen) and related biosimilars (e.g., filgrastim-aafi [Nivestym], filgrastim-sndz [Zarxio], filgrastim-txid (Nypozi), filgrastim-ayow, [Releuko]) and tbo-filgrastim [Granix])

are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage

for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office,

hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider.

All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Guidelines

There is no Medicare coverage determination addressing filgrastim (Neupogen) and related biosimilars and tbo-pegfilgrastim (Granix); therefore, the Company policy is applicable.

DRUG ADMINISTRATION

Filgrastim (Neupogen) and related biosimilars and tbo-pegfilgrastim (Granix) are available as a single-dose prefilled syringe for manual use only and a single-dose vial.

BENEFIT APPLICATION

Subject to the applicable Evidence of Coverage, filgrastim (Neupogen) and related biosimilars and tbo-pegfilgrastim (Granix) are covered under the medical benefits of the Company’s Medicare Advantage products when the medical necessity criteria listed in this medical policy are met.

For Medicare Advantage members, certain drugs are available through either the member's medical benefit (Part B benefit) or pharmacy benefit (Part D benefit), depending on how the drug is prescribed, dispensed, or administered. This medical policy only addresses instances when filgrastim (Neupogen) and related biosimilars and tbo-pegfilgrastim (Granix) are covered under a member's medical benefit (Part B benefit). It does not address instances when filgrastim (Neupogen) and related biosimilars and tbo-pegfilgrastim (Granix) are covered under a member’s pharmacy benefit (Part D benefit).

However, biosimilars that are identified in this policy as not medically necessary are not eligible for coverage or reimbursement by the Company.

US FOOD AND DRUG ADMINISTRATION (FDA) STATUS

Filgrastim (Neupogen) was approved by the FDA on February 20, 1991, to decrease the incidence of infection, as manifested by febrile neutropenia, in individuals with nonmyeloid malignancies receiving myelosuppressive

anticancer drugs associated with a clinically significant incidence of febrile neutropenia. Supplemental approvals for filgrastim (Neupogen) have since been issued by the FDA. The FDA has also issued subsequent approvals for biosimilar products.

Tbo-pegfilgrastim (Granix) was approved by the FDA on August 29, 2012, to decrease the incidence of infection, as manifested by febrile neutropenia, in individuals with nonmyeloid malignancies receiving myelosuppressive anticancer drugs associated with a clinically significant incidence of febrile neutropenia.

PEDIATRIC USE

The safety and effectiveness of filgrastim (Neupogen) and related biosimilars have been established in pediatric individuals with severe chronic neutropenia (SCN).

The safety and effectiveness of tbo-pegfilgrastim (Granix) are established in pediatric individuals 1 month old and less than 17 years of age.

The safety and effectiveness of tbo-pegfilgrastim (Granix) have not been established in pediatric individuals less than 1 month of age.

IPSS-R Cytogenetic risk groups†,††

Cytogenetic Prognostic Subgroups	**Cytogenetic Abnormalities**
Very good	-Y, del(11q)
Good	Normal, del(5q), del(12p), del(20q), double including del(5q)
Intermediate	del(7q), +8, +19, i(17q), any other single or double independent clones
Poor	-7, inv(3)/t(3q)/del(3q), double including -7/del(7q), Complex: 3 abnormalities
Very poor	Complex: >3 abnormalities

IPSS-R Prognostic Score Values†

Prognostic variable	**0**	**0.5**	**1**	**1.5**	**2**	**3**	**4**
Cytogenetics	Very Good		Good		Intermediate	Poor	Very Poor
BM Blast %	≤2		>2%–<5%		5%–10%	>10%	
Hemoglobin	≥10		8–<10	<8			
Platelets	≥100	50–<100	<50				
ANC	≥0.8	<0.8					

IPSS-R Prognostic Risk Categories/Scores††

RISK CATEGORY	RISK SCORE
Very Low	≤1.5
Low	>1.5–3
Intermediate	>3–4.5
High	>4.5–6
Very High	>6

†Greenberg PL, Tuechler H, Schanz J, et al. Revised international prognostic scoring system (IPSS-R) for myelodysplastic syndrome. *Blood.* 2012;120(12):2454-2465.

††Schanz J, Tüchler H, Solé F, et al. New comprehensive cytogenetic scoring system for primary myelodysplastic syndromes (MDS) and oligoblastic acute myeloid leukemia after MDS derived from an international database merge. *J Clin Oncol.* 2012;30(8):820-829.

THE EASTERN COOPERATIVE ONCOLOGY GROUP (ECOG) PERFORMANCE STATUS

The Eastern Cooperative Oncology Group (ECOG), established in 1955, was one of the first groups to coordinate multicenter cancer clinical trials. The National Cancer Institute (NCI) is the primary funding source, and ECOG has evolved from a small consortium of institutions in the eastern United States to one of the largest clinical cancer research organizations in the country. As part of their work in the treatment of cancer, ECOG has developed the ECOG Performance Status (EPS), originally published in 1982 in the *American Journal of Clinical Oncology.* The use of the scales and the criteria in the EPS allows clinicians and researchers to determine an individual's disease progression in terms of how the activities of daily living (ADL) are affected.

ECOG Performance Status	
Grade	ECOG
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature (eg, light house work, office work)
2	Ambulatory and capable of all self care but unable to carry out any work activities. Up and about more than 50 percent of waking hours
3	Capable of only limited self care, confined to bed or chair more than 50 percent of waking hours
4	Completely disabled. Cannot carry on any self care: Totally confined to bed or chair
5	Dead

Oken MM, Creech RH, Tormey DC, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. *Am J Clin Oncol.*1982;5(6):649-655.

Description

Certain intensive cytotoxic chemotherapy regimens are known to cause severe, prolonged febrile neutropenia that may increase the risk of infections and hospitalization. The risk of febrile neutropenia is related to the treatment regimen and delivered dose intensity. The National Comprehensive Cancer Network (NCCN) defines febrile neutropenia as a single temperature of 38.3°C or greater orally, or 38.0°C over 1 hour; neutropenia as less than 500 neutrophils/µL or less than 1000 neutrophils/µL and a predicted decline to 500 neutrophils/µL or less over the next 48 hours.

Granulocyte colony-stimulating factor (G-CSF) has been shown to reduce the duration and severity of neutropenia, as well as the risk of febrile neutropenia, thereby enabling the delivery of the current dose of chemotherapy or even dose-intensive (increased dose) or dose-dense (increased frequency) regimens when indicated. Without the use of G-CSFs in some chemotherapy regimens, the need to reduce the chemotherapeutic dose may cause a poor prognosis for the individual.

Filgrastim (Neupogen), filgrastim-aafi (Nivestym), filgrastim-sndz (Zarxio), filgrastim-txid (Nypozi), tbo-pegfilgrastim (Granix) are G-CSFs that affect the proliferation and differentiation of neutrophils within the bone marrow.

Filgrastim (Neupogen) was approved by the US Food and Drug Administration (FDA) in 1991 to decrease the incidence of infection, as manifested by febrile neutropenia, in individuals with nonmyeloid malignancies receiving myelosuppressive anticancer drugs associated with a clinically significant incidence of febrile neutropenia. Subsequent indications were FDA-approved for the following:

- To reduce the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML).
- To reduce the duration of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation (BMT).
- Mobilize autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.
- To reduce the incidence and duration of sequelae of severe neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia.
- Increase survival in patients acutely exposed to myelosuppressive doses of radiation (hematopoietic syndrome of acute radiation syndrome).

Since 2015, the FDA has approved several biosimilar products. These are highly similar to the reference biologic, filgrastim (Neupogen), and have the same indications; there are no clinically meaningful differences between the biosimilars and the reference product.

Tbo-pegfilgrastim (Granix) was approved by the FDA in 2014 to decrease the incidence of infection, as manifested by febrile neutropenia, in individuals with nonmyeloid malignancies receiving myelosuppressive anticancer drugs associated with a clinically significant incidence of febrile neutropenia.

OFF-LABEL INDICATIONS

There may be additional indications contained in the Policy section of this document due to the evaluation of criteria highlighted in the Company's off-label policy, and/or review of clinical guidelines issued by leading professional organizations and government entities.

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Coding

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

CPT Procedure Code Number(s)

N/A

ICD - 10 Procedure Code Number(s)

N/A

ICD - 10 Diagnosis Code Number(s)

Report the most appropriate diagnosis code in support of medically necessary criteria as listed in the policy.

HCPCS Level II Code Number(s)

J1442 Injection, filgrastim (G-CSF), excludes biosimilars, 1 mcg
J1447 Injection, tbo-filgrastim, 1 mcg
Q5101 Injection, filgrastim-sndz, biosimilar, (Zarxio), 1 mcg
Q5110 Injection, filgrastim-aafi, biosimilar, (Nivestym), 1 mcg
Q5125 Injection, filgrastim-ayow, biosimilar, (Releuko), 1 mcg
Q5148 Injection, filgrastim-txid (nypozi), biosimilar, 1 microgram

Revenue Code Number(s)

N/A

Policy History

Revisions From MA08.130i:

09/16/2025	This version of the policy will become effective 09/16/2025. This policy has been updated to communicate the coverage criteria in alignment with recommendations from the US Food and Drug Administration (FDA), National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO), and Company-recognized drug compendia. The following indication was revised, per NCCN: • Prophylaxis of chemotherapy-induced febrile neutropenia in individuals with acute myeloid leukemia (AML) who are receiving consolidation chemotherapy • Treatment of individuals with lower risk[†,††] MDS associated with symptomatic anemia with no del(5q), with or without other cytogenetic abnormalities with serum erythropoietin ≤500 mU/mL and any of the following: The following updates were made to the examples of chemotherapy regimens in Attachment A, per NCCN: BrECADD was added to Hodgkin's lymphoma, sacituzumab govitecan-hziy (Enhertu) was added to Breast Cancer and Carboplatin/docetaxel was moved from the intermediate risk category and added to high risk (>20%) for Ovarian Cancer. The following HCPCS code has been deleted from this policy: • C9173 Injection, filgrastim-txid (nypozi), biosimilar, 1 microgram All of the ICD-10 CM codes have been removed from this policy, since they are informational. Report the most appropriate diagnosis code in support of medically necessary criteria as listed in the policy.

Revisions From MA08.130h:

06/13/2025	This version of the policy will become effective 06/13/2025. The following HCPCS code has been added to this policy: • Q5148 Injection, filgrastim-txid (nypozi), biosimilar, 1 microgram The following NOC code has been removed from this policy: • J3590 Unclassified biologics

Revisions From MA08.130g:

03/28/2025	This version of the policy will become effective 03/28/2025. The following HCPCS code has been added to this policy:

	• C9173 Injection, filgrastim-txid (nypozi), biosimilar, 1 microgram The following HCPCS code has been removed from this policy: • C9399 Unclassified drugs or biologics

Revisions From MA08.130f:

12/16/2024	This version of the policy will become effective 12/16/2024. This policy has been updated to communicate the coverage criteria in alignment with recommendations from US Food and Drug Administration (FDA), National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO), and Company-recognized Drug Compendia. The following criteria have been **added,** per NCCN: • Therapeutic use in acute lymphoblastic leukemia (ALL) The following indications were **revised**, per NCCN: • Prophylaxis of chemotherapy-induced febrile neutropenia in individuals with acute myeloid leukemia (AML) who are receiving consolidation chemotherapy • Hematopoietic cell transplantation in combination with motixafortide in individuals with multiple myeloma • Treatment of myelodysplastic syndromes (MDS) The following biosimilar drug has been **added** to the policy in accordance with the FDA (06/28/2024): • filgrastim-txid (Nypozi) The following ICD-10 codes were **added** to the policy as medically necessary: • C64.1 Malignant neoplasm of right kidney, except renal pelvis • C64.2 Malignant neoplasm of left kidney, except renal pelvis • C91.00 Acute lymphoblastic leukemia not having achieved remission • C94.6 Myelodysplastic disease, not elsewhere classified • D46.9 Myelodysplastic syndrome, unspecified The following ICD-10 codes were **removed** from the policy: • T66.XXXA Radiation sickness, unspecified, initial encounter • T66.XXXD Radiation sickness, unspecified, subsequent encounter • T66.XXXS Radiation sickness, unspecified, sequela The following HCPCS codes have been **added** to this policy as medically necessary: • C9399 Unclassified drugs or biologics • J3590 Unclassified biologics

Revisions From MA08.130e:

01/01/2024	This version of the policy will become effective 01/01/2024. This policy has been updated to communicate the coverage criteria in alignment with recommendations from US Food and Drug Administration (FDA), National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO), and Company-recognized Drug Compendia and also to communicate changes in prefered agents. The Company has designated the following filgrastim products as its preferred products: • filgrastim-aafi (Nivestym) • filgrastim-sndz (Zarxio)

	The following codes were added to the policy: C91.02 Acute lymphoblastic leukemia, in relapse C92.00 Acute myeloblastic leukemia, not having achieved remission C92.02 Acute myeloblastic leukemia, in relapse 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 C93.30 Juvenile myelomonocytic leukemia, not having achieved remission C93.32 Juvenile myelomonocytic leukemia, in relapse

Revisions From MA08.130c:

10/01/2022	This policy has been identified for the HCPCS code update, effective 10/01/2022. The following HCPCS codes have been **added** to this policy: Q5125 Injection, filgrastim-ayow, biosimilar, (releuko), 1 microgram The following HCPCS codes have been **removed** from this policy: C9096 Injection, filgrastim-ayow, biosimilar, (releuko), 1 microgram J3590 Unclassified biologics

Revisions From MA08.130b:

07/01/2022	This policy has been identified for the HCPCS code update, effective 07/01/2022. The following HCPCS codes have been **added** to this policy: C9096 Injection, filgrastim-ayow, biosimilar, (releuko), 1 microgram J3590 Unclassified biologics

Revisions From MA08.130a:

11/22/2021	This version of the policy will become effective 11/22/2021. This policy has been updated to communicate the coverage criteria in alignment with recommendations from US Food and Drug Administration (FDA), National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO), and Company-recognized Drug Compendia. The indication of prophylaxis of chemotherapy-induced febrile neutropenia in individuals with Wilms Tumor (Nephroblastoma) has been **added** as Medically Necessary. • Acute lymphoblastic leukemia in pediatric individuals who have relapsed disease and have serious/life-threatening neutropenic infection The following indications were **removed**, per ASCO: • The prophylaxis of chemotherapy-induced febrile neutropenia for nonmyelosuppressive chemotherapy • Intermittent use in individuals with myelodysplastic syndromes (MDS) who have severe neutropenia and recurrent infection The following indications were **revised**, per ASCO or NCCN: • Therapeutic use in individuals with cancer who have fever and neutropenia and are at high risk for infection-associated complications or who have prognostic factors that are

	predictive of poor clinical outcomes. • After autologous or allogeneic hematopoietic stem-cell transplant to reduce the duration of severe neutropenia • Chemotherapy regimen was revised, per NCCN Guidelines for Hematopoietic growth factors: ○ Non-Hodgkin Lymphomas: CHP (cyclophosphamide, doxorubicin, prednisone) + brentuximab vedotin was moved from intermediate risk to high risk. The following code was added to the policy: **C91.02 Acute lymphoblastic leukemia, in relapse**

Revisions From MA08.130:

04/01/2021	This policy has been identified for the HCPCS code update, effective 04/01/2021. The following HCPCS codes **termed** from this policy: C9399 Unclassified drugs or biologics J3590 Unclassified biologics The following HCPCS codes have been **added** to this policy: J1447 Injection, tbo-filgrastim, 1 mcg This policy has been developed to communicate the Company's preferred product designation for tbo-filgrastim (Granix)**,** filgrastim-sndz (Zarxio). All other filgrastim products are considered non-preferred products. Additionally, this policy has been developed to communicate the coverage criteria in alignment with recommendations from US Food and Drug Administration (FDA), National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO), and Company-recognized Drug Compendia.

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