

Colony Stimulating Factors

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[Terms and Conditions](#)

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- | Related Medicare Advantage Policy Guidelines |
|---|
| <ul style="list-style-type: none"> Self-Administered Drug(s) (SAD) Stem Cell Transplantation (Formerly 110.8.1) (NCD 110.23) |
| Related Medicare Advantage Reimbursement Policies |
| <ul style="list-style-type: none"> Medically Unlikely Edits Policy, Professional National Drug Code (NDC) Requirement Policy, Professional and Facility Procedure to Modifier Policy, Professional |
| Related Medicare Advantage Coverage Summary |
| <ul style="list-style-type: none"> Medications/Drugs (Outpatient/Part B) |

Policy Summary

[See Purpose](#)

Overview

White blood cell growth factors, also known as granulocyte colony stimulating factors (G-CSF), are administered to enhance recovery of blood related functions in neutropenia (low white blood count) including febrile neutropenia (FN). G-CSFs regulate the production of neutrophils in the bone marrow. Neutrophils are essential in the body's fight against infections.

Filgrastim/Neupogen® is a human granulocyte colony stimulating factor (G-CSF), produced by recombinant DNA technology. Pegfilgrastim/Neulasta® is a pegylated form of filgrastim. Pegylated means that polyethylene glycol, a dispensing agent, has been added to the drug. Filgrastim is a synthetic human granulocyte colony-stimulating factor (G-CSF). Pegfilgrastim is produced by recombinant DNA technology using E. coli bacteria.

Filgrastim/Neupogen® and Pegfilgrastim/Neulasta® are CSFs that act on hematopoietic cells by binding to specific cell surface receptors thereby stimulating proliferation, differentiation, commitment, and end cell functional activation.

- Filgrastim-aafi/Nivestym™ is biosimilar to Neupogen® (filgrastim)
- Filgrastim-sndz/Zarxio® is biosimilar to Neupogen® (filgrastim)
- Pegfilgrastim-bmez /Ziextenzo™ is biosimilar to Neulasta® (pegfilgrastim)
- Pegfilgrastim-cbqv /Udenyca™ is biosimilar to Neulasta® (pegfilgrastim)
- Pegfilgrastim-jmdb/Fulphila™ is biosimilar to Neulasta® (pegfilgrastim)

Tbo-filgrastim/Granix® is a non-glycosylated recombinant methionyl human granulocyte colony-stimulating growth factor (G-CSF) manufactured by recombinant DNA technology using the bacterium E. coli

Sargramostim/Leukine® is a synthetic granulocyte-macrophage colony-stimulating factor (GM-CSF) produced by recombinant DNA technology in S. cerevisiae yeast. Granulocyte Macrophage Colony Stimulating Factor (GM-CSF) is a-hematopoietic growth factor which stimulates proliferation and differentiation of hematopoietic progenitor cells.

Indications

Filgrastim (Neupogen[®]), filgrastim-sndz (Zarxio[®]), and filgrastim-aafi (Nivestym[™]) are approved for the following uses:

- Patients with Cancer Receiving Myelosuppressive Chemotherapy: Decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever.
- Patients with Acute Myeloid Leukemia Receiving Induction or Consolidation Chemotherapy: Reduce the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML).
- Patients Undergoing Autologous Peripheral Blood Progenitor Cell Collection and Therapy: Mobilize autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis [See also the Medicare Advantage Policy Guideline titled [Stem Cell Transplantation \(Formerly 110.8.1\) \(NCD 110.23\)](#)].
- Patients with Cancer Undergoing Bone Marrow Transplantation: 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.
- Patients with Severe Chronic Neutropenia: 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.
- Patients Acutely Exposed to Myelosuppressive Doses of Radiation (Hematopoietic Syndrome of Acute Radiation Syndrome): To increase survival in patients acutely exposed to myelosuppressive doses of radiation.

Pegfilgrastim (Neulasta[®]), pegfilgrastim-bmez (Ziextenzo[™]), pegfilgrastim-cbqv (Udenyca[™]), and Pegfilgrastim-jmdb (Fulphila[™]) are approved for the following use:

- Patients with Cancer Receiving Myelosuppressive Chemotherapy: To decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.
- Patients with Hematopoietic Subsyndrome of Acute Radiation Syndrome: To increase survival in patients acutely exposed to myelosuppressive doses of radiation.

Pegfilgrastim (Neulasta[®]), pegfilgrastim-bmez (Ziextenzo[™]), pegfilgrastim-cbqv (Udenyca[™]), and Pegfilgrastim-jmdb (Fulphila[™]) are not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation.

Tbo-filgrastim (Granix[®]) is approved for the following uses:

- Patients with Cancer Receiving Myelosuppressive Chemotherapy: To reduce the duration of severe neutropenia in patients with nonmyeloid malignancies receiving myelosuppressive anticancer drugs associated with a clinically significant incidence of febrile neutropenia.

Sargramostim (Leukine[®]) is approved for the following uses:

- Acute Myeloid Leukemia Following Induction Chemotherapy: To shorten time to neutrophil recovery and to reduce the incidence of severe and life-threatening infections and infections resulting in death following induction chemotherapy in adult patients 55 years and older with acute myeloid leukemia (AML).
- Autologous Peripheral Blood Progenitor Cell Mobilization and Collection: For the mobilization of hematopoietic progenitor cells into peripheral blood for collection by leukapheresis and autologous transplantation in adult patients [See also the Medicare Advantage Policy Guideline titled [Stem Cell Transplantation \(Formerly 110.8.1\) \(NCD 110.23\)](#)].
- Autologous Peripheral Blood Progenitor Cell and Bone Marrow Transplantation: For the acceleration of myeloid reconstitution following autologous bone marrow or peripheral blood progenitor cell transplantation.
- Allogeneic Bone Marrow Transplantation: For the acceleration of myeloid reconstitution following allogeneic bone marrow transplantation from HLA-matched related donors.
- Allogeneic or Autologous Bone Marrow Transplantation - Treatment of Delayed Neutrophil Recovery or Graft Failure
 - For treatment of delayed neutrophil recovery or graft failure after autologous or allogeneic bone marrow transplantation.
- Acute Exposure to Myelosuppressive Doses of Radiation: To increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome).

For off-label indications, see related Local Coverage Determinations (LCDs).

Limitations

Colony stimulating factors are *not covered* when:

- Self-administered
- Administered by a caregiver

Dosing Information

Dose and frequency should be in accordance with the FDA label or recognized compendia (for off-label uses). When services are performed in excess of established parameters, they may be subject to review for medical necessity.

Documentation Requirements

The patient's medical record must document the medical necessity of services performed for each date of service submitted on a claim, and documentation must be available upon request.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this guideline does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

Coding Clarifications: For ICD-10 diagnosis codes, see related Local Coverage Determinations.

| HCPCS Code | Description |
|------------|--|
| C9058 | Injection, pegfilgrastim-bmez, biosimilar, (Ziextenzo) 0.5 mg (Effective 11/15/2019 - 06/30/2020, See Q5120) |
| J1442 | Injection, filgrastim (G-CSF), excludes biosimilars, 1 mcg |
| J1447 | Injection, tbo-filgrastim, 1 microgram |
| J2505 | Injection, pegfilgrastim, 6 mg |
| J2820 | Injection, sargramostim (GM-CSF), 50 mcg |
| Q5101 | Injection, filgrastim-sndz, biosimilar, (Zarxio) 1 microgram |
| Q5108 | Injection, pegfilgrastim-jmdb, biosimilar, (Fulphila), 0.5 mg |
| Q5110 | Injection, filgrastim-aafi, biosimilar, (Nivestym), 1 mcg |
| Q5111 | Injection, pegfilgrastim-cbqv, biosimilar, (Udenyca), 0.5 mg (Effective 01/01/2019) |
| Q5120 | Injection, pegfilgrastim-bmez, biosimilar, (Ziextenzo), 0.5 mg (Effective 11/15/2019) |

Definitions

Biosimilar: The biological product is approved based on data demonstrating that it is highly similar to an FDA-approved biological product, known as a reference product, and that there are no clinically meaningful differences between the biosimilar product and the reference product.

Off-Label Drug Use: An off-label/unlabeled use of a drug is defined as a use for a non-FDA approved indication, that is, one that is not listed on the drug's official label/prescribing information. An indication is defined as a diagnosis, illness, injury, syndrome, condition, or other clinical parameter for which a drug may be given. Off-label use is further defined as giving the drug in a way that deviates significantly from the labeled prescribing information for a particular indication. This includes but is not necessarily limited to, dosage, route of administration, duration and frequency of administration, and population to whom the drug would be administered. Drugs used for indications other than those in the approved labeling may be covered if it is

determined that the use is medically accepted, taking into consideration the major drug compendia, authoritative medical literatures and/or accepted standards of medical practice. Determinations as to whether medication is reasonable and necessary for an individual patient are made on appeal on the same basis as all other such determinations (i.e., with support from the peer-reviewed literature, with the advice of medical consultants, with reference to accepted standards of medical practice, and in consideration of the medical circumstance of the individual case).

Primary Prophylaxis: Refers to administration of CSF during the first cycle of chemotherapy.

Secondary Prophylaxis: Refers to administration of CSF during subsequent cycles of chemotherapy.

Severe Neutropenia: Generally defined as an absolute neutrophil count of less than 500 cells per ml.

References

CMS Local Coverage Determinations (LCDs) and Articles

| LCD | Article | Contractor | Medicare Part A | Medicare Part B |
|---|--|-------------|--|--|
| L34002 (G-CSF Neupogen®, Granix™, Zarxio™, Nivestym™) | A57789 Billing and Coding: G-CSF Filgrastim | First Coast | FL, PR, VI | FL, PR, VI |
| | A54942 G-CSF (Neupogen®, Granix™, Zarxio™) clarification related to HCPCS code Q5101 | | | |
| | A55942 G-CSF (Neupogen®, Granix™, Zarxio™) revision to the Part A and Part B LCD | | | |
| L33747 Pegfilgrastim (Neulasta®) | A57725 Billing and Coding: Pegfilgrastim | First Coast | FL, PR, VI | FL, PR, VI |
| | A56145 Pegfilgrastim (Neulasta®) revision to the Part A and B LCD | | | |
| | A58054 Pegfilgrastim - revision to the Part A and Part B billing and coding article | | | |
| | A58314 Pegfilgrastim - revision to the Part A and Part B billing and coding article | | | |
| L33394 Drugs and Biologicals, Coverage of, for Label and Off-Label Uses | A52408 Filgrastim, Pegfilgrastim, Tbo-filgrastim, Filgrastim-sndz (e.g., Neupogen®, Neulasta™, Granix™, Zarxio™) - Related to LCD L33394 | NGS | CT, IL, MA, ME, MN, NH, NY, RI, VT, WI | CT, IL, MA, ME, MN, NH, NY, RI, VT, WI |
| L37176 White Cell Colony Stimulating Factors | A56748 Billing and Coding: White Cell Colony Stimulating Factors | Palmetto | AL, GA, NC, SC, TN, VA, WV | AL, GA, NC, SC, TN, VA, WV |
| | A54682 Neulasta® (pegfilgrastim) Delivery Kit (On-Body Injector) | | | |
| N/A | A55447 Pegfilgrastim (Neulasta) J2505 | Noridian | AK, AZ, ID, MT, ND, OR, SD, UT, WA WY | AK, AZ, ID, MT, ND, OR, SD, UT, WA WY |

| LCD | Article | Contractor | Medicare Part A | Medicare Part B |
|---|---|-------------|--|---------------------------------------|
| N/A | A52889 Pegfilgrastim (Neulasta) J2505 | Noridian | AS, CA, GU, HI, MP, NV | AS, CA, GU, HI, MP, NV |
| N/A | A54848 Drug Administration Coding | CGS | KY, OH | KY, OH |
| N/A | A52991 Chemotherapy Administration | Noridian | AK, AZ, ID, MT, ND, OR, SD, UT, WA WY | AK, AZ, ID, MT, ND, OR, SD, UT, WA WY |
| N/A | A52953 Chemotherapy Administration | Noridian | AS, CA, GU, HI, MP, NV | AS, CA, GU, HI, MP, NV |
| L34093 Chemotherapy and Biologicals Retired 06/07/2020 | A56829 Billing and Coding: Neulasta® (pegfilgrastim) - J2505,Q5108,Q5111 Retired 06/07/2020 | CGS | KY, OH | KY, OH |
| N/A | A54837 (2016 HCPCS local coverage determination changes Part B) Retired 12/06/2019 | First Coast | | FL, PR, VI |
| N/A | A55350 (2017 ICD-10-CM Coding Changes Part B) Retired 12/06/2019 | First Coast | | FL, PR, VI |
| N/A | A54836 (2016 HCPCS local coverage determination changes) Retired 09/03/2019 | First Coast | FL, PR, VI | |
| N/A | A55348 (2017 ICD-10-CM Coding Changes Part A) Retired 09/03/2019 | First Coast | FL, PR, VI | |
| N/A | A54826 (Neulasta® (pegfilgrastim) Delivery Kit (On-Body Injector)) Retired 08/07/2019 | CGS | KY, OH | KY, OH |
| L34699 (Human Granulocyte/Macrophage Colony Stimulating Factors) Retired 03/18/2019 | N/A | WPS | AK, AL, AR, AZ, CA, CO, CT, DE, FL, GA, HI, IA, ID, IL, IN, KS, KY, LA, MA, MD, ME, MI, MO, MS, MT, NC, ND, NE, NH, NJ, NM, NV, OH, OK, OR, PA, RI, SC, SD, TN, TX, UT, VA, VT, WA, WI, WV, WY | IA, IN, KS, MI, MO, NE |

CMS Benefit Policy Manual

[Chapter 15: § 50 Drugs and Biologicals](#)

CMS Claims Processing Manual

[Chapter 17: § 10 Payment Rules for Drugs and Biologicals](#)

CMS Transmittal(s)

[Transmittal 10166, Change Request 11814, Dated 06/05/2020 \(July 2020 Update of the Hospital Outpatient Prospective Payment System \(OPPS\)\)](#)

[Transmittal 10196, Change Request 11769, Dated 06/23/2020 \(Quarterly Healthcare Common Procedure Coding System \(HCPCS\) Drug/Biological Code Changes - July 2020 Update\)](#)

MLN Matters

[Article MM11814, July 2020 Update of the Hospital Outpatient Prospective Payment System \(OPPS\)](#)

[Article MM11769, Quarterly Healthcare Common Procedure Coding System \(HCPCS\) Drug/Biological Code Changes - July 2020 Update](#)

UnitedHealthcare Commercial Policies

[Maximum Dosage and Frequency](#)

[White Blood Cell Colony Stimulating Factors](#)

Other(s)

[National Comprehensive Cancer Network \(NCCN\) Drugs & Biologics Compendium®](#)

Guideline History/Revision Information

Revisions to this summary document do not in any way modify the requirement that services be provided and documented in accordance with the Medicare guidelines in effect on the date of service in question.

| Date | Summary of Changes |
|------------|--|
| 04/01/2021 | Template Update <ul style="list-style-type: none">Reformatted policy; transferred content to new template |
| 12/09/2020 | Related Policies <ul style="list-style-type: none">Added reference link to the:<ul style="list-style-type: none">Medicare Advantage Reimbursement policy titled <i>National Drug Code (NDC) Requirement Policy, Professional and Facility</i>Medicare Advantage Coverage Summary titled <i>Medications/Drugs (Outpatient/Part B)</i> Policy Summary <p><i>Overview</i></p> <ul style="list-style-type: none">Added language to indicate:<ul style="list-style-type: none">White blood cell growth factors, also known as granulocyte colony stimulating factors (G-CSF), are administered to enhance recovery of blood related functions in neutropenia (low white blood count) including febrile neutropenia (FN)Pegfilgrastim-bmez /Ziextenzo™ is biosimilar to Neulasta® (pegfilgrastim)Pegfilgrastim-cbqv /Udenyca™ is biosimilar to Neulasta® (pegfilgrastim)Removed language indicating colony stimulating factors (CSF) are hematopoietic growth factors, which act on progenitor cells capable of forming either single differentiated (lineage-specific) cell types, such as the neutrophilic granulocyte, or forming several differentiated cell types (i.e., non-lineage-specific)Replaced language indicating “granulocyte macrophage colony stimulating factor (GM-CSF) is an antineutropenic, hematopoietic growth factor, which <i>supports survival, clonal expansion,</i> and differentiation of hematopoietic progenitor cells” with “granulocyte macrophage colony stimulating factor (GM-CSF) is a hematopoietic growth factor which <i>stimulates proliferation</i> and differentiation of hematopoietic progenitor cells” <p><i>Indications</i></p> <ul style="list-style-type: none">Added language to indicate:<ul style="list-style-type: none">Pegfilgrastim-bmez (Ziextenzo™) and pegfilgrastim-cbqv (Udenyca™) are approved for the following uses: |

| Date | Summary of Changes |
|------|--|
| | <ul style="list-style-type: none"> ▪ Patients with cancer receiving myelosuppressive chemotherapy; to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia ▪ Patients with hematopoietic subsyndrome of acute radiation syndrome; to increase survival in patients acutely exposed to myelosuppressive doses of radiation ○ Pegfilgrastim (Neulasta®), pegfilgrastim-bmez (Ziextenzo™), pegfilgrastim-cbqv (Udenyca™), and pegfilgrastim-jmdb (Fulphila™) are not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation ● Removed language indicating pegfilgrastim, pegfilgrastim-jmdb and pegfilgrastim-cbqv (Udenyca™) are covered for the following uses: <ul style="list-style-type: none"> ▪ To decrease the incidence of infection, as manifested by febrile neutropenia in patients with non-myeloid malignancies receiving myelosuppressive cancer drugs ▪ Prophylaxis of chemotherapy-induced febrile neutropenia or other neutropenic events compromising treatment in high-risk patients (greater than 20% risk of febrile neutropenia) with solid tumors and non-myeloid malignancies receiving <ul style="list-style-type: none"> - Curative or adjuvant chemotherapy treatment - Chemotherapy to prolong survival and improve quality of life - Chemotherapy to manage symptoms and improve quality of life ▪ Harvesting of peripheral blood stem cells, prior to autologous stem-cell transplantation ▪ To increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Sub-syndrome of Acute Radiation Syndrome) (Effective 11/13/2015 based on FDA approval) ▪ Supportive care in the post-transplant setting ● Updated list of approved uses for sargramostim (Leukine®): <ul style="list-style-type: none"> ○ Replaced “allogeneic bone marrow transplantation: for the acceleration of myeloid reconstitution following allogeneic bone marrow transplantation” with “allogeneic bone marrow transplantation: for the acceleration of myeloid reconstitution following allogeneic bone marrow transplantation <i>from HLA-matched related donors</i>” <p>Documentation Requirements</p> <ul style="list-style-type: none"> ● Revised list of items to be documented in the medical record; removed language indicating “the medical record should indicate the patient is on a 14 day dose dense chemotherapy cycle” <p>Applicable Codes</p> <ul style="list-style-type: none"> ● Added HCPCS codes C9058 and Q5120 <p>Supporting Information</p> <ul style="list-style-type: none"> ● Updated <i>References</i> section to reflect the most current information ● Archived previous policy version MPG214.05 |

Purpose

The Medicare Advantage Policy Guideline documents are generally used to support UnitedHealthcare Medicare Advantage claims processing activities and facilitate providers’ submission of accurate claims for the specified services. The document can be used as a guide to help determine applicable:

- Medicare coding or billing requirements, and/or
- Medical necessity coverage guidelines; including documentation requirements.

UnitedHealthcare follows Medicare guidelines such as NCDs, LCDs, LCAs, and other Medicare manuals for the purposes of determining coverage. It is expected providers retain or have access to appropriate documentation when requested to support coverage. Please utilize the links in the [References](#) section below to view the Medicare source materials used to develop this resource document. This document is not a replacement for the Medicare source materials that outline Medicare coverage requirements. Where there is a conflict between this document and Medicare source materials, the Medicare source materials will apply.

Terms and Conditions

The Medicare Advantage Policy Guidelines are applicable to UnitedHealthcare Medicare Advantage Plans offered by UnitedHealthcare and its affiliates.

These Policy Guidelines are provided for informational purposes, and do not constitute medical advice. Treating physicians and healthcare providers are solely responsible for determining what care to provide to their patients. Members should always consult their physician before making any decisions about medical care.

Benefit coverage for health services is determined by the member specific benefit plan document* and applicable laws that may require coverage for a specific service. The member specific benefit plan document identifies which services are covered, which are excluded, and which are subject to limitations. In the event of a conflict, the member specific benefit plan document supersedes the Medicare Advantage Policy Guidelines.

Medicare Advantage Policy Guidelines are developed as needed, are regularly reviewed and updated, and are subject to change. They represent a portion of the resources used to support UnitedHealthcare coverage decision making. UnitedHealthcare may modify these Policy Guidelines at any time by publishing a new version of the policy on this website. Medicare source materials used to develop these guidelines include, but are not limited to, CMS National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), Medicare Benefit Policy Manual, Medicare Claims Processing Manual, Medicare Program Integrity Manual, Medicare Managed Care Manual, etc. The information presented in the Medicare Advantage Policy Guidelines is believed to be accurate and current as of the date of publication and is provided on an "AS IS" basis. Where there is a conflict between this document and Medicare source materials, the Medicare source materials will apply.

You are responsible for submission of accurate claims. Medicare Advantage Policy Guidelines are intended to ensure that coverage decisions are made accurately based on the code or codes that correctly describe the health care services provided. UnitedHealthcare Medicare Advantage Policy Guidelines use Current Procedural Terminology (CPT®), Centers for Medicare and Medicaid Services (CMS), or other coding guidelines. References to CPT® or other sources are for definitional purposes only and do not imply any right to reimbursement or guarantee claims payment.

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*For more information on a specific member's benefit coverage, please call the customer service number on the back of the member ID card or refer to the [Administrative Guide](#).