filgrastim

Medicare Part B Drug Policy

- Medicare coverage is limited to items and services that are reasonable and necessary for the diagnosis or treatment of an illness or injury (and within the scope of a Medicare benefit category).
- Medicare Benefit Policy Manual - Pub. 100-02, Chapter 15, Section 50, describes national policy regarding Medicare guidelines for coverage of drugs and biologicals.
- Blue Shield of California (BSC) follows Medicare statutes, regulations, National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and policy articles for determining coverage for Part B drug requests when applicable.
- BSC Medicare Part B Drug Policies will be used when coverage criteria are not fully established or there is an absence of any applicable Medicare statutes, regulations, NCDs or LCDs.

Drug Details

USP Category: BLOOD PRODUCTS AND MODIFIERS
Mechanism of Action: Granulocyte colony-stimulating factor (G-CSF)
HCPCS:
J1442:Injection, filgrastim (g-csf), excludes biosimilars, 1 microgram
Q5101:Injection, filgrastim-sndz, biosimilar, (zarxio), 1 microgram
Q5110:Injection, filgrastim-aafi, biosimilar, (nivestym), 1 microgram
Q5125:Injection, filgrastim-ayow, biosimilar, (releuko), 1 microgram
How Supplied:

- 300 mcg and 480 mcg (prefilled syringe)
- 300 mcg and 480 mcg (single use vial)

Condition(s) listed in policy (see coverage criteria for details)

- Acute Exposure to Myelosuppressive Doses of Radiation
- Congenital Agranulocytosis
- Cyclic Neutropenia
- Drug-Induced Neutropenia
- Febrile Neutropenia
- Hematopoietic Stem Cell Transplantation (Bone Marrow Transplantation)
- HIV Patients on Myelosuppressive Therapy
- Idiopathic Neutropenia
- Myelodysplastic Syndromes
- Peripheral Blood Stem Cell Mobilization
- Prevention or Treatment in Cancer Patients Receiving Myelosuppressive Anticancer Agents (J9000 series codes)

Any request for a condition not listed in policy must meet the definition of a medically accepted indication. Section 1861(t)(2)(B) of the Act defines "medically-accepted indication," as any use of a prescription drug or biological product which is approved under the Federal Food, Drug, and Cosmetic Act, or the use of which is supported by one or more citations included (or approved for inclusion) in one or more of the CMS approved compendia.

Special Instructions and Pertinent Information

Provider must submit documentation (such as office chart notes, lab results or other clinical information) to ensure the member has met all medical necessity requirements.

For members enrolled in our Blue Shield Select (PPO) and Blue Shield Medicare (PPO) plans:
Neupogen and Releuko requires step therapy. Step therapy requires you to try other drugs first before a drug can be covered. The BSC preferred step drugs are Zarxio and Nivestym. Both of these drugs will need to be tried for members newly initiating Neupogen or Releuko therapy.

Coverage Criteria

The following condition(s) require Prior Authorization/Preservice:

Acute Exposure to Myelosuppressive Doses of Radiation
Meets medical necessity if all the following are met:

Covered Doses:
Up to 10 mcg/kg subcutaneously per day

Coverage Period:
One dose

ICD-10:
T66.XXXS

Congenital Agranulocytosis
Meets medical necessity if all the following are met:

1. Recurring or persistent neutropenia in association with ONE of the following (a or b):
   a. History of recurring infections (e.g. multiple episodes of infections requiring antibiotics)
   b. 1 hospitalization for an infection within the past year
2. For PPO request for Neupogen and Releuko: Intolerance or contraindication with the preferred filgrastim products (Nivestym and Zarxio) that is not expected with requested filgrastim product

Covered Doses:
Initial: Up to 10 mcg/kg subcutaneously per day
Maintenance: Titrated dosing to maintain response (e.g. Absolute Neutrophil Count between 800/mm^3 – 1400/mm^3)

Coverage Period:
1 year

ICD-10:
D70.0

Cyclic Neutropenia
Meets medical necessity if all the following are met:

1. Recurring or persistent neutropenia in association with EITHER of the following (a or b):
   a. History of recurring infections (e.g. multiple episodes of infections requiring antibiotics)

b. 1 hospitalization for an infection within the past year

2. For PPO request for Neupogen and Releuko: Intolerance or contraindication with the preferred filgrastim products (Nivestym and Zarxio) that is not expected with requested filgrastim product

Covered Doses:
Initial: Up to 10 mcg/kg subcutaneously per day
Maintenance: Titrated dosing to maintain response (e.g. Absolute Neutrophil Count between 800/mm^3 – 1400/mm^3)

Coverage Period:
1 year

ICD-10:
D70.4

Drug-Induced Neutropenia
Meets medical necessity if all the following are met:
1. Neutropenia is caused by an identified drug
2. ONE of the following (a or b):
   a. Initial Absolute Neutrophil Count (ANC) ≤800/mm^3
   b. ANC ≤ 1000/mm^3 with expected neutropenia of > 5 days
3. For PPO request for Neupogen and Releuko: Intolerance or contraindication with the preferred filgrastim products (Nivestym and Zarxio) that is not expected with requested filgrastim product

Covered Doses:
Initial: Up to 10mcg/kg subcutaneously per day
Maintenance: Titrated dosing to maintain response (e.g. Absolute Neutrophil Count between 800/mm^3 – 1400/mm^3)

Coverage Period:
Up to the length of therapy that the drug causing neutropenia is prescribed or up to one year (whichever is less)

ICD-10:
D70.2

Febrile Neutropenia
Meets medical necessity if all the following are met:
1. ONE of the following (a or b):
   a. Initial absolute neutrophil count (ANC) ≤800/mm^3
   b. ANC ≤ 1000/mm^3 with expected neutropenia of > 5 days
2. Patient has not received pegfilgrastim for neutropenia prophylaxis in the past 14 days
3. For PPO request for Neupogen and Releuko: Intolerance or contraindication with the preferred filgrastim products (Nivestym and Zarxio) that is not expected with requested filgrastim product

Covered Doses:
Initial: Up to 10 mcg/kg subcutaneously per day
Maintenance: Titrated dosing to maintain response (e.g. Absolute Neutrophil Count between 800/mm^3 – 1400/mm^3)

Coverage Period:
Up to 2 months

ICD-10:
D70.9, R50.81

Hematopoietic Stem Cell Transplantation (Bone Marrow Transplantation)
Meets medical necessity if all the following are met:
1. For PPO request for Neupogen and Releuko: Intolerance or contraindication with preferred filgrastim products (Nivestym and Zarxio) that is not expected with requested filgrastim product

Covered Doses:
Up to 10 mcg/kg subcutaneously per day

Coverage Period:
6 months

ICD-10:
Z94.81

HIV Patients on Myelosuppressive Therapy
Meets medical necessity if all the following are met:
1. ONE of the following:
   a. Initial absolute neutrophil count (ANC) ≤800/mm^3
   b. ANC ≤ 1000/mm^3 with expected neutropenia of > 5 days
2. For PPO request for Neupogen and Releuko: Intolerance or contraindication with the preferred filgrastim products (Nivestym and Zarxio) that is not expected with requested filgrastim product

Covered Doses:
Initial: Up to 10 mcg/kg subcutaneously per day
Maintenance: Titrated dosing to maintain response (e.g., Absolute Neutrophil Count between 800/mm^3 – 1400/mm^3)

Coverage Period:
Up to the length of therapy that the drug causing neutropenia is prescribed or up to one year (whichever is less)

ICD-10:
B20, D70.2

Idiopathic Neutropenia
Meets medical necessity if all the following are met:
1. Recurring or persistent neutropenia in association with EITHER of the following (a or b):

a. a history of recurring infections (*e.g.,* multiple episodes of infections requiring antibiotics)

b. 1 hospitalization for an infection within the past year

2. For PPO request for Neupogen and Releuko: Intolerance or contraindication with the preferred filgrastim products (Nivestym and Zarxio) that is not expected with requested filgrastim product

Covered Doses:
Initial: Up to 10 mcg/kg subcutaneously per day
Maintenance: Titrated dosing to maintain response (e.g. Absolute Neutrophil Count between 800/mm^3 – 1400/mm^3)

Coverage Period:
1 year

ICD-10:
D70.9

Myelodysplastic Syndromes
Meets medical necessity if all the following are met:

1. ONE of the following (a or b):
   a. Initial absolute neutrophil (ANC) ≤800/mm3 or ANC ≤ 1000/mm3 with expected neutropenia of > 5 days

   b. Being used in combination with an erythropoiesis-stimulating agent [ESA] (e.g., Procrit or Aranesp) to improve symptoms of anemia AND BOTH of the following:
      i. Hgb < 10 gm/dL

      ii. EPO level ≤ 500 mU/mL

2. For PPO request for Neupogen and Releuko: Intolerance or contraindication with the preferred filgrastim products (Nivestym and Zarxio) that is not expected with requested filgrastim product

Covered Doses:
Up to 10 mcg/kg subcutaneously per day

Coverage Period:
yearly

ICD-10:
D46.0, D46.1, D46.4, D46.9, D46.Z

Peripheral Blood Stem Cell Mobilization
Meets medical necessity if all the following are met:

1. For PPO request for Neupogen and Releuko: Intolerance or contraindication with the preferred filgrastim products (Nivestym and Zarxio) that is not expected with requested filgrastim product

Covered Doses:

Up to 12 mcg/kg subcutaneously per day

Coverage Period:
Up to 3 months
Reauthorization requires continued response to therapy

ICD-10:
Z48.290, Z52.001, Z52.011, Z52.091

Prevention or Treatment in Cancer Patients Receiving Myelosuppressive Anticancer Agents (J9000 series codes)

Meets medical necessity if all the following are met:

1. Drug is not being used concurrently with long-acting or short-acting granulocyte colony stimulating factors (e.g. filgrastim or pegfilgrastim drugs)
2. For PPO request for Neupogen and Releuko: Intolerance or contraindication with the preferred filgrastim products (Nivestym and Zarxio) that is not expected with requested filgrastim product

Covered Doses:
Up to 10 mcg/kg subcutaneously per day

Coverage Period:
Up to the length of the chemotherapy treatment

ICD-10:
C00.0-C91.91, C92.00, C92.01, C92.02, C92.2x-C92.6x, C92.A0, C92.A1, C92.A2, C93.00, C93.02, C94.00, C94.02, C94.20, C94.22, D00.00-D49.9, D70.1

Additional Information

Summary of Evidence

The contents of this policy were created after examining the following resources:

1. The prescribing information for Neupogen, Nivestym, Releuko, and Zarxio
2. CMS approved compendium in accordance with the accepted compendia ratings listed:
   a. Micromedex DrugDex - Class I, Class IIa, of Class IIb
   b. American Hospital Formulary Service-Drug Information (AHFS-DI) - supportive narrative text
   c. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium - Category 1 or 2A
   d. Lexi-Drugs – "Use: Off-Label" and rated as "Evidence Level A" (cancer indications only)
   e. Clinical Pharmacology - supportive narrative text (cancer indications only)
3. Noridian Healthcare Solutions Medicare: Drugs, Biologics and Injections
4. NCCN Guideline: Hematopoietic Growth Factors
5. NCCN Guideline: Acute Myeloid Leukemia; Hematopoietic Stem Cell Transplantation
6. NCCN Guideline: Myelodysplastic Syndromes

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Neupogen, Nivestym, Releuko, and Zarxio are covered in addition to the following:

- Drug-induced neutropenia
- Febrile neutropenia
- HIV patients on myelosuppressive therapy
- Myelodysplastic syndromes
- Peripheral blood stem cell mobilization

Explanation of Rationale:

- Support for FDA-approved indications can be found in the manufacturer's prescribing information.
- Support for using biosimilars as step requirement is found in Noridian Health Care Solutions and supported by the FDA. Noridian will accept a biosimilar drug on the same criteria as the drug to which it is a biosimilar unless an article is published to the contrary. Per the FDA, a biosimilar is highly similar to and has no clinically meaningful difference from an existing FDA approved biologic reference drug.
- Support for using biosimilars in oncology can be found in The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) via the footnote on the reference product (an FDA-approved biosimilar is an appropriate substitute) and in the NCCN Drugs & Biologics Compendium® by the notation that a biosimilar agent may be an appropriate substitute for the reference product.
- NCCN Clinical Practice Guidelines in Oncology for the use of hematopoietic growth factors support use of filgrastim: 1) as prophylaxis of chemotherapy-induced febrile neutropenia or other dose-limiting neutropenic events in patients at risk of febrile neutropenia with solid tumors and non-myeloid malignancies who are receiving treatment in the curative/adjuvant or palliative settings; 2) as treatment of chemotherapy-induced febrile neutropenia: in patients who have been receiving prophylactic filgrastim or in patients who have not received prophylactic granulocyte colony-stimulating factors but who have risk factors for an infection-associated complication; and 3) for treatment for patients with radiation-induced myelosuppression following a radiologic/nuclear incident (hematopoietic acute radiation syndrome [H-ARS])
- NCCN Clinical Practice Guidelines in Oncology for acute myeloid leukemia (AML) support use of filgrastim for patients with AML receiving chemotherapy.
- NCCN Clinical Practice Guidelines in Oncology for myelodysplastic syndromes (MDS) support use of filgrastim for use in MDS patients with neutropenia with recurrent or resistant infections, and for treatment of lower risk MDS associated with symptomatic anemia, in combination with an erythropoiesis-stimulating agent.
- NCCN Clinical Practice Guidelines in Oncology for hematopoietic stem cell transplantation support use of filgrastim for hematopoietic cell mobilization.
- Support for using filgrastim for HIV patients on myelosuppressive therapy is found in DrugDex and AHFS compendia. The compendia support use of filgrastim to reverse or correct or minimize neutropenia caused by HIV-associated neutropenia and/or drug-induced neutropenia.

- Support for using filgrastim for febrile neutropenia is found in DrugDex compendium. DrugDex compendium supports use of filgrastim to reduce hospitalization and time to neutrophil recovery in patients with febrile neutropenia.
- Support for using filgrastim for drug-induced neutropenia is found in DrugDex and AHFS compendia. The compendia support use of filgrastim: to help reverse leukopenia/neutropenia in post-solid organ transplant patients; in patients with nonmalignant conditions who developed neutropenia while receiving various myelosuppressive drugs; and for management of drug-associated agranulocytosis

References

1. CMS Benefit Policy Manual. Chapter 15; § 50 Drugs and Biologicals
2. Medicare Coverage Database. Available at https://www.cms.gov/Medicare-Coverage-Database/search.aspx
3. Social Security Act (Title XVIII) Standard References, Sections: 1862(a)(1)(A) Medically Reasonable & Necessary; 1862(a)(1)(D) Investigational or Experimental; 1833(e) Incomplete Claim; 1861(t) (1) Drugs and Biologicals
4. AHFS®. Available by subscription at http://www.lexi.com
5. DrugDex®. Available by subscription at http://www.micromedexsolutions.com/home/dispatch
6. National Comprehensive Cancer Network. Hematopoietic Growth Factors, v3.2024. Available at http://www.nccn.org.
7. National Comprehensive Cancer Network. Acute Myeloid Leukemia, v3.2024. Available at http://www.nccn.org.
8. National Comprehensive Cancer Network. Hematopoietic Stem Cell Transplantation, v1.2024. Available at http://www.nccn.org.
9. National Comprehensive Cancer Network. Myelodysplastic Syndromes, v3.2024. Available at http://www.nccn.org
10. Neupogen® (filgrastim) [Prescribing Information]. Thousand Oaks, CA: Amgen Inc.; 4/2023.
11. Nivestym™ (filgrastim-aafi) [Prescribing Information]. New York, NY: Pfizer, Inc.; 3/2023.
12. Releuko® (filgrastim-ayow) [Prescribing Information]. Bridgewater, NJ: Amneal Biosciences, LLC; 2/2022.
13. Zarxio® (filgrastim-sndz) [Prescribing Information]. Princeton, NJ: Sandoz Inc; 9/2022.

Review History

Date of Last Annual Review: 1Q2024
Changes from previous policy version:

- New Part B policy

Blue Shield of California Medication Policy to Determine Medical Necessity Reviewed by P&T Committee

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