Drug and Biologic Coverage Policy

Effective Date **06/01/2025**
Coverage Policy Number **IP0528**

Filgrastim

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Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for formulary exceptions for the following filgrastim products:

- **Granix®** (tbo-filgrastim subcutaneous injection)
- **Neupogen®** (filgrastim intravenous or subcutaneous injection)
- **Nypozi™** (filgrastim-txid intravenous or subcutaneous injection)
- **Releuko®** (filgrastim-ayow intravenous or subcutaneous injection)

Medical Necessity Criteria

Coverage criteria are listed for products **in the below table**:

Product	Criteria
Granix (tbo-filgrastim)	**Granix is considered medically necessary when ONE of the following is met (1 or 2):** 1. Patient meets BOTH of the following (A and B): A. The patient has tried BOTH Nivestym AND Zarxio B. Patient cannot continue to use each of the formulary alternatives due to a formulation difference in the inactive ingredient(s) [e.g., differences in stabilizing agent, buffering agent, and/or surfactant] which, according to the prescriber, would result in a significant allergy or serious adverse reaction 2. Patients requiring a dose < 180 mcg AND the patient meets BOTH of the following (A and B): A. The patient has tried Nivestym B. Patient cannot continue to use the formulary alternative due to a formulation difference in the inactive ingredient(s) [e.g., differences in stabilizing agent, buffering agent, and/or surfactant] which, according to the prescriber, would result in a significant allergy or serious adverse reaction
Neupogen (filgrastim)	**Neupogen is considered medically necessary when ONE of the following is met (1, 2, or 3):** 1. Patient meets BOTH of the following (A and B): A. The patient has tried BOTH Nivestym) AND Zarxio B. Patient cannot continue to use each of the formulary alternatives due to a formulation difference in the inactive ingredient(s) [e.g., differences in stabilizing agent, buffering agent, and/or surfactant] which, according to the prescriber, would result in a significant allergy or serious adverse reaction 2. Patients who require administration by intravenous infusion AND the patient meets BOTH of the following (A and B): A. The patient has tried ONE of Nivestym or Zarxio B. Patient cannot continue to use the formulary alternative due to a formulation difference in the inactive ingredient(s) [e.g., differences in stabilizing agent, buffering agent, and/or surfactant] which, according to the prescriber, would result in a significant allergy or serious adverse reaction 3. Patients requiring a dose < 180 mcg AND the patient meets BOTH of the following (A and B): A. The patient has tried Nivestym B. Patient cannot continue to use the formulary alternative due to a formulation difference in the inactive ingredient(s) [e.g., differences in stabilizing agent, buffering agent, and/or surfactant] which, according to the prescriber, would result in a significant allergy or serious adverse reaction
Nypozi (filgrastim-txid)	**Nypozi is considered medically necessary when ONE of the following is met (1 or 2):** 1. Patient meets BOTH of the following (A and B): A. The patient has tried BOTH Nivestym AND Zarxio B. Patient cannot continue to use each of the formulary alternatives due to a formulation difference in the inactive ingredient(s) [e.g., differences in stabilizing agent, buffering agent, and/or surfactant] which, according to the prescriber, would result in a significant allergy or serious adverse reaction 2. Patients who require administration by intravenous infusion AND the patient meets BOTH of the following (A and B):

Product	Criteria
	A. The patient has tried ONE of Nivestym or Zarxio B. Patient cannot continue to use the formulary alternative due to a formulation difference in the inactive ingredient(s) [e.g., differences in stabilizing agent, buffering agent, and/or surfactant] which, according to the prescriber, would result in a significant allergy or serious adverse reaction
Releuko (filgrastim-ayow)	**Releuko is considered medically necessary when ONE of the following is met (1 or 2):** 1. Patient meets BOTH of the following (A and B): A. The patient has tried BOTH Nivestym) AND Zarxio B. Patient cannot continue to use each of the formulary alternatives due to a formulation difference in the inactive ingredient(s) [e.g., differences in stabilizing agent, buffering agent, and/or surfactant] which, according to the prescriber, would result in a significant allergy or serious adverse reaction 2. Patients who require administration by intravenous infusion AND the patient meets BOTH of the following (A and B): A. The patient has tried ONE of Nivestym or Zarxio B. Patient cannot continue to use the formulary alternative due to a formulation difference in the inactive ingredient(s) [e.g., differences in stabilizing agent, buffering agent, and/or surfactant] which, according to the prescriber, would result in a significant allergy or serious adverse reaction

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Reauthorization Criteria

Continuation of filgrastim products (Granix, Neupogen, or Releuko) is considered medically necessary when the above medical necessity criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial and reauthorization is up to 1 month

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven (criteria will be updated as new published data are available).

Coding

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J1442	Injection, filgrastim (g-csf), excludes biosimilars, 1 microgram
J1447	Injection, tbo-filgrastim, 1 mcg
Q5101	Injection, filgrastim-sndz, biosimilar, (Zarxio), 1 microgram
Q5110	Injection, filgrastim-aafi, biosimilar, (Nivestym), 1 microgram
C9173	Injection, filgrastim-aafi, biosimilar, (Nypozi), 1 microgram
Q5125	Injection, filgrastim-ayow, biosimilar, (Releuko), 1 microgram

Background

OVERVIEW

Filgrastim, a granulocyte colony stimulating factor (G-CSF), is indicated for the following uses:[1-5]

- **Decrease the incidence of infection, as manifested by febrile neutropenia**, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever.
- **Mobilization of hematopoietic progenitor cells,** into the peripheral blood for collection by leukapheresis.
- **Reduce the time to neutrophil recovery and the duration of fever,** following induction or consolidation chemotherapy treatment of adults with acute myeloid leukemia (AML).
- **Reduce the duration of neutropenia and neutropenia-related clinical sequelae** (e.g., febrile neutropenia), in patients with non-myeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation (BMT).
- **Reduce the incidence and duration of sequelae of 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 [H-ARS])

Nivestym, Nypozi, Releuko, and Zarxio are biosimilars to Neupogen.[1-5] Releuko indication labeling does not include mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.[4] Neupogen, Nypozi, and Zarxio labeling include the indication for treatment of H-ARS.[1,2,5]

Guidelines

The National Comprehensive Cancer Network (NCCN) addresses the use of filgrastim products in several guidelines. Of note, throughout the recommendations, it is acknowledged that an FDA-approved biosimilar is an appropriate substitute for filgrastim.

- **Acute Lymphoblastic Leukemia (ALL):** Guidelines (version 2.2024 **–** July 19, 2024) recommend granulocyte colony stimulating factors (CSFs) as supportive care for myelosuppressive blocks of therapy or as directed by treatment protocol.[6]
- **Acute Myeloid Leukemia (AML):** Guidelines (version 3.2024 **–** May 17, 2024) recommend granulocyte colony stimulating factors (CSFs) as supportive care for myelosuppressive blocks of therapy or as directed by treatment protocol.[23]
- **Hematopoietic Cell Transplantation:** Guidelines (version 2.2024 – August 30, 2024) recommend filgrastim for hematopoietic cell mobilization for allogeneic or autologous donors as a single agent or in combination with other treatments.[7]
- **Hematopoietic Growth Factors:** Guidelines (version 3.2024 – January 30, 2024) recommend filgrastim, along with other CSFs, for prophylactic use if the patient is receiving anti-cancer medications that are associated with a high (> 20%) incidence of severe neutropenia with fever.[8] Consider CSF therapy for patients with an intermediate (10% to 20%) probability of developing febrile neutropenia based on risk factors. The NCCN guidelines also recommend therapy with CSFs in other scenarios in those given myelosuppressive chemotherapy.

- **Management of Immunotherapy-Related Toxicities:** Guidelines (version 1.2024 – December 7, 2023) recommend granulocyte CSFs as supportive care for neutropenic patients with Grade 1 cytokine release syndrome resulting from chimeric antigen receptor T-cell therapy.[9]
- **Myelodysplastic Syndromes (MDS):** Guidelines (version 3.2024 – July 25, 2024) consider filgrastim for use in certain patients (e.g., neutropenic patients with recurrent or resistant infections, combination use with epoetin alfa or Aranesp® [darbepoetin alfa injection] in patients with anemia).[10]

The American Society of Clinical Oncology clinical practice guidelines for the use of white blood cell growth factors (2015) recommend CSFs to reduce the risk of febrile neutropenia in patients receiving cancer chemotherapy.[11] CSFs may be considered in patients receiving radiation therapy alone if prolonged delays secondary to neutropenia are expected. The guidelines state CSFs should be avoided in patients receiving concomitant chemotherapy and radiation therapy, particularly involving the mediastinum.

Other Uses with Supportive Evidence
Neutropenia occurs in patients with human immunodeficiency virus (HIV) and may be caused by medications or due to the disease process. Studies have demonstrated positive outcomes with the use of filgrastim for the treatment of neutropenia in this patient population.[12-15]

Filgrastim has been used for agranulocytosis caused by non-cytotoxic medications, primarily described in case series, case reports and literature reviews.[16-22]

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Revision Details

Type of Revision	Summary of Changes	Date
Selected Revision	No criteria changes	12/15/2024
Selected Revision	**Nypozi** (filgrastim-txid) added to the policy. **Updated** criteria for Granix, Neupogen and Releuko.	06/01/2025

The policy effective date is in force until updated or retired.