# Colony Stimulating Factors

## NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

## BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

## DESCRIPTION

This policy informs prescribers of preferred products and provides an exception process for non-preferred products through prior authorization. The intent of the policy is to also provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines.

This program applies to the colony stimulating factor products specified in this policy. For the short-acting colony stimulating factors program Nivestym and Zarxio are the preferred products. For the long-acting colony stimulating factors program Fulphila, Neulasta and Neulasta Onpro are the preferred products. Coverage for targeted products (short-acting: Neupogen, Filkri, Granix, Leukine, Nypozi, and Releuko; long-acting: Armlupeg, Fylnetra, Nyvepria, Rolvedon, Stimufend, Udenyca, Udenyca Onbody, Ryzneuta, and Ziextenzo) is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to members requesting treatment with Leukine for an indication that is FDA-approved for the preferred product and to members requesting treatment with Neupogen or Granix for all indications.

**Table 1. Short-Acting Colony Stimulating Factors**

| Medication | Generic Name |
|---|---|
| **Preferred Products:** | |
| Nivestym | filgrastim-aafi |
| Zarxio | filgrastim-sndz |

| Targeted Products: | |
|---|---|
| Neupogen | filgrastim |
| Filkri | filgrastim-laha |
| Granix | TBO-filgrastim |
| Leukine | sargramostim |
| Nypozi | filgrastim-txid |
| Releuko | filgrastim-ayow |

**Table 2. Long-Acting Colony Stimulating Factors**

| Medication | Generic Name |
|---|---|
| **Preferred Products:** | |
| Fulphila | pegfilgrastim-jmdb |
| Neulasta syringe for manual injection | pegfilgrastim |
| Neulasta Onpro | pegfilgrastim |
| **Targeted Products:** | |
| Armlupeg | pegfilgrastim-unne |
| Fylnetra | pegfilgrastim-pbbk |
| Nyvepria | pegfilgrastim-apgf |
| Rolvedon | eflapegrastim-xnst |
| Stimufend | pegfilgrastim-fpgk |
| Udenyca | pegfilgrastim-cbqv |
| Udenyca Onbody | pegfilgrastim-cbqv |
| Ryzneuta | Efbemalenograstim Alfa |
| Ziextenzo | pegfilgrastim-bmez |

## EXCEPTION CRITERIA

Exception Criteria

1. Coverage for the targeted products, Neupogen, Filrki, Granix, Nypozi, or Releuko is provided when the member meets one of the following criteria:

A. Member has failed treatment with all of the preferred products due to a documented intolerable adverse event (e.g., rash, nausea, vomiting) and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information (i.e., known adverse reaction for both the brand and biosimilar medication)
B. Member has a documented latex allergy and the prescriber states that the member must use latex-free vials and the member had a documented inadequate response or intolerable adverse effect to Nivestym

**Approval** will be for **6 months**

2. Coverage for the targeted product, Leukine, is provided when the member meets one of the following criteria:
    A. Member has had a documented inadequate response or intolerable adverse effect to any of the preferred products
    B. Leukine is being requested for treatment of uveal melanoma with immunoembolization

**Approval** will be for **6 months**

3. Coverage for a targeted product, Armlupeg, Fylnetra, Nyvepria, Stimufend, Udenyca, Udenyca Onbody, or Ziextenzo is provided when the member meets the following criteria:
    A. Member has failed treatment with all of the preferred products due to a documented intolerable adverse effect (e.g., rash, nausea, vomiting) and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information (i.e., known adverse reaction for both the brand and biosimilar medication)

**Approval** will be for **6 months**

4. Coverage for the targeted products, Rolvedon and Ryzneuta, is provided when the member has had a documented inadequate response or intolerable adverse effect to any of the preferred products.

**Approval** will be for **6 months**

## POLICY (Note: applicable to Rolvedon only)

Member must meet BOTH the Exception Criteria for Rolvedon and Criteria for Initial Approval/Continuation of Therapy when both are applicable.

Required Documentation

**Primary Prophylaxis of Febrile Neutropenia**

1. Documentation must be provided of the member's diagnosis and chemotherapeutic regimen.
2. If chemotherapeutic regimen has an intermediate risk of febrile neutropenia (10-19% [See Appendix B]), documentation must be provided outlining the patient's risk factors that confirm the member is at high risk for febrile neutropenia.

Criteria for Initial Approval

**Prevention of neutropenia in cancer patients receiving myelosuppressive chemotherapy**

1. Authorization of 6 months may be granted for prevention of febrile neutropenia when ALL of the following criteria are met:
    A. Rolvedon will not be used in combination with other colony stimulating factors within any chemotherapy cycle.

B. Member will not be receiving chemotherapy and radiation therapy at the same time.
C. Rolvedon will not be administered with weekly chemotherapy regimens.
D. One of the following criteria is met:
    1) Rolvedon will be used for primary prophylaxis in members with a solid tumor or non-myeloid malignancies who have received, are currently receiving, or will be receiving any of the following:
        a. Myelosuppressive anti-cancer therapy that is expected to result in greater than 20% incidence of febrile neutropenia (FN) (see Appendix A)
        b. Myelosuppressive anti-cancer therapy that is expected to result in 10-20% risk of FN (see Appendix B) and who are considered to be at high risk of FN because of bone marrow compromise, comorbidities, or other patient specific risk factors (see appendix C)
        c. Myelosuppressive anti-cancer therapy that is expected to result in less than 10% risk of FN and who have at least 2 patient-related risk factors (See Appendix C).
    2) Rolvedon will be used for secondary prophylaxis in members with solid tumors or non-myeloid malignancies who experienced a febrile neutropenic complication or a dose-limiting neutropenic event (a nadir or day of treatment count impacting the planned dose of chemotherapy) from a prior cycle of similar chemotherapy, with the same dose and schedule planned for the current cycle (for which primary prophylaxis was not received).

**Other Indications**

1. Authorization of 6 months may be granted for members with any of the following indications:
    A. Stem cell transplantation-related indications
    B. Hematopoietic Acute Radiation Syndrome
        1) Treatment for radiation-induced myelosuppression following a radiological/nuclear incident
    C. Hairy cell leukemia
        1) Members with hairy cell leukemia with neutropenic fever following chemotherapy

Continuation of Therapy

All members (including new members) requesting authorization for continuation of therapy with Rolvedon must meet all initial authorization criteria.

Rolvedon is considered **not medically necessary** for patients who do not meet the criteria set forth above.

Dosing and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

## APPENDICES

Appendix A: Selected Chemotherapy Regimens with an Incidence of Febrile Neutropenia of greater than 20%* †

1. Acute Lymphoblastic Leukemia:
    A. Select ALL regimens as directed by treatment protocol (see NCCN guidelines ALL)
2. Bladder Cancer:
    A. Dose dense MVAC (methotrexate, vinblastine, doxorubicin, cisplatin)
3. Bone Cancer:
    A. VAIA (vincristine, doxorubicin, ifosfamide, and dactinomycin)

B. VDC-IE (vincristine, doxorubicin or dactinomycin, and cyclophosphamide alternating with ifosfamide and etoposide)
C. Cisplatin/doxorubicin
D. VDC (cyclophosphamide, vincristine, doxorubicin or dactinomycin)
E. VIDE (vincristine, ifosfamide, doxorubicin or dactinomycin, etoposide)

4. Breast Cancer:
   A. Dose-dense AC (doxorubicin, cyclophosphamide) followed by dose-dense paclitaxel
   B. TAC (docetaxel, doxorubicin, cyclophosphamide)
   C. TC (docetaxel, cyclophosphamide)
   D. TCH (docetaxel, carboplatin, trastuzumab)
5. Head and Neck Squamous Cell Carcinoma:
   A. TPF (docetaxel, cisplatin, 5-fluorouracil)
6. Hodgkin Lymphoma:
   A. Brentuximab vedotin + AVD (doxorubicin, vinblastine, dacarbazine)
   B. Escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone)
7. Kidney Cancer:
   A. Doxorubicin/gemcitabine
8. Non-Hodgkin's Lymphoma:
   A. CHP (cyclophosphamide, doxorubicin, prednisone) + brentuximab vedotin
   B. Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) ± rituximab
   C. ICE (ifosfamide, carboplatin, etoposide) ± rituximab
   D. Dose-dense CHOP-14 (cyclophosphamide, doxorubicin, vincristine, prednisone) ± rituximab
   E. MINE (mesna, ifosfamide, mitoxantrone, etoposide) ± rituximab
   F. DHAP (dexamethasone, cisplatin, cytarabine) ± rituximab
   G. ESHAP (etoposide, methylprednisolone, cisplatin, cytarabine (Ara-C))
   H. HyperCVAD ± rituximab (cyclophosphamide, vincristine, doxorubicin, dexamethasone ± rituximab)
   I. Pola-R-CHP (polatuzumab vedotin-piiq, rituximab, cyclophosphamide, doxorubicin, prednisone)
9. Melanoma:
   A. Dacarbazine-based combination with IL-2, interferon alpha (dacarbazine, cisplatin, vinblastine, IL-2, interferon alfa)
10. Multiple Myeloma:
    A. VTD-PACE (dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide + bortezomib)
    B. DT-PACE (dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide)
11. Ovarian Cancer:
    A. Topotecan ± bevacizumab
    B. Docetaxel
12. Pancreatic Cancer:
    A. FOLFIRINOX (fluorouracil, leucovorin, irinotecan, oxaliplatin)
13. Soft Tissue Sarcoma:
    A. MAID (mesna, doxorubicin, ifosfamide, dacarbazine)
    B. Doxorubicin
    C. Ifosfamide/doxorubicin
14. Small Cell Lung Cancer:
    A. Top (topotecan)

15. Testicular Cancer:
    A. VeIP (vinblastine, ifosfamide, cisplatin)
    B. VIP (etoposide, ifosfamide, cisplatin)
    C. TIP (paclitaxel, ifosfamide, cisplatin)
16. Gestational Trophoblastic Neoplasia:
    A. EMA/CO (etoposide, methotrexate, dactinomycin/cyclophosphamide, vincristine)
    B. EMA/EP (etoposide, methotrexate, dactinomycin/etoposide, cisplatin)
    C. EP/EMA (etoposide, cisplatin/etoposide, methotrexate, dactinomycin)
    D. TP/TE (paclitaxel, cisplatin/paclitaxel, etoposide)
    E. BEP (bleomycin, etoposide, cisplatin)
    F. VIP (etoposide, ifosfamide, cisplatin)
    G. ICE (ifosfamide, carboplatin, etoposide)
17. Wilms Tumor:
    A. Regimen M (vincristine, dactinomycin, doxorubicin, cyclophosphamide, etoposide)
    B. Regimen I (vincristine, doxorubicin, cyclophosphamide, etoposide)

* Applies to chemotherapy regimens with or without monoclonal antibodies (e.g., trastuzumab, rituximab)
† This list is not comprehensive; there are other agents/regimens that have an intermediate/high risk for development of febrile neutropenia.

Appendix B: Selected Chemotherapy Regimens with an Incidence of Febrile Neutropenia of 10% to 20%*†

1. Occult Primary – Adenocarcinoma:
    A. Gemcitabine/docetaxel
2. Breast Cancer:
    A. Docetaxel ± trastuzumab
    B. AC (doxorubicin, cyclophosphamide) + sequential docetaxel (taxane portion only)
    C. AC + sequential docetaxel + trastuzumab
    D. TC (docetaxel, cyclophosphamide)
3. Cervical Cancer:
    A. Irinotecan
    B. Cisplatin/topotecan
    C. Paclitaxel/cisplatin ± bevacizumab
    D. Topotecan
4. Colorectal Cancer:
    A. FOLFIRINOX (fluorouracil, leucovorin, oxaliplatin, irinotecan)
5. Esophageal and Gastric Cancers:
    A. Irinotecan/cisplatin
6. Non-Hodgkin’s Lymphomas:
    A. GDP (gemcitabine, dexamethasone, cisplatin/carboplatin)
    B. GDP (gemcitabine, dexamethasone, cisplatin/carboplatin) + rituximab
    C. CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) including regimens with pegylated liposomal doxorubicin
    D. CHOP + rituximab (cyclophosphamide, doxorubicin, vincristine, prednisone, rituximab) including regimens with pegylated liposomal doxorubicin
    E. Bendamustine
7. Non-Small Cell Lung Cancer:
    A. Cisplatin/paclitaxel
    B. Cisplatin/vinorelbine
    C. Cisplatin/docetaxel
    D. Cisplatin/etoposide
    E. Carboplatin/paclitaxel

F. Docetaxel
8. Ovarian Cancer:
    A. Carboplatin/docetaxel
9. Prostate Cancer:
    A. Cabazitaxel
10. Small Cell Lung Cancer:
    A. Etoposide/carboplatin
11. Testicular Cancer:
    A. BEP (bleomycin, etoposide, cisplatin)
    B. Etoposide/cisplatin
12. Uterine Sarcoma:
    A. Docetaxel

* Applies to chemotherapy regimens with or without monoclonal antibodies (e.g., trastuzumab, rituximab).
† This list is not comprehensive; there are other agents/regimens that have an intermediate/high risk for development of febrile neutropenia.

Appendix C: Patient Risk Factors
This list is not all-inclusive.

1. Active infections, open wounds, or recent surgery
2. Age greater than or equal to 65 years
3. Bone marrow involvement by tumor producing cytopenias
4. Previous chemotherapy or radiation therapy
5. Poor nutritional status
6. Poor performance status
7. Previous episodes of FN
8. Other serious co-morbidities, including renal dysfunction, liver dysfunction, HIV infection, cardiovascular disease
9. Persistent neutropenia

## PROCEDURES AND BILLING CODES

***To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.***

- C9399 – Unclassified drugs or biologicals
- C9173 – Injection, filgrastim-txid (Nypozi), biosimilar, 1 microgram (cancelled 7/1/2025)
- J1442 – Injection, filgrastim (g-csf), excludes biosimilars, 1 microgram (Neupogen)
- J1447 – Injection, tbo-filgrastim, 1 mcg
- J1449 – Injection, eflapegrastim-xnst, (Rolvedon) 0.1 mg (effective 4/1/2023)
- J2820 – Injection, sargramostim (gm-csf), 50 micrograms (Leukine)
- J3590 – Unclassified biologicals
- J9361 – Injection, efbemalenograstim alfa-vuxw, 0.5 mg (Ryzneuta)
- Q5108 – Injection, pegfilgrastim-jmdb, biosimilar, (Fulphila), 0.5mg
- Q5111 – Injection, pegfilgrastim-cbqv, biosimilar, (Udenyca), 0.5mg
- Q5120 – Injection, pegfilgrastim-bmez, biosimilar, (Ziextenzo), 0.5mg
- Q5122 – Injection, pegfilgrastim-apgf (Nyvepria), biosimilar, 0.5 mg
- Q5125 – Injection, filgrastim-ayow, biosimilar, (Releuko), 1 microgram
- Q5127 – Injection, pegfilgrastim-fpgk, biosimilar, (Stimufend), 0.5 mg (effective 4/1/2023)
- Q5130 – Injection, pegfilgrastim-pbbk, biosimilar, (Fylnetra), 0.5 mg (effective 4/1/2023)
- Q5148 – Injection, filgrastim-txid (Nypozi), biosimilar, 1 microgram (effective 4/1/2025)

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## POLICY HISTORY

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