

# Specialty Guideline Management

## Neulasta and pegfilgrastim biosimilars

### Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Neulasta	pegfilgrastim
Fulphila	pegfilgrastim-jmdb
Fylnetra	pegfilgrastim-pbbk
Nyvepria	pegfilgrastim-apgf
Stimufend	pegfilgrastim-fpgk
Udenyca	pegfilgrastim-cbqv
Ziextenzo	pegfilgrastim-bmez

### Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

#### FDA-approved Indications

##### Neulasta

##### **Patients with Cancer Receiving Myelosuppressive Chemotherapy**

Neulasta is indicated 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.

Reference number(s)
1931-A

### **Hematopoietic Subsyndrome of Acute Radiation Syndrome**

Neulasta is indicated to increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Subsyndrome of Acute Radiation Syndrome).

### **Fulphila**

#### **Patients with Cancer Receiving Myelosuppressive Chemotherapy**

Fulphila is indicated 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

### **Udenyca**

#### **Patients with Cancer Receiving Myelosuppressive Chemotherapy**

Udenyca is indicated 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.

### **Hematopoietic Subsyndrome of Acute Radiation Syndrome**

Udenyca is indicated to increase survival in patients acutely exposed to myelosuppressive doses of radiation.

### **Ziextenzo**

#### **Patients with Cancer Receiving Myelosuppressive Chemotherapy**

Ziextenzo is indicated 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.

### **Hematopoietic Subsyndrome of Acute Radiation Syndrome**

Ziextenzo is indicated to increase survival in patients acutely exposed to myelosuppressive doses of radiation.

### **Nyvepria**

#### **Patients with Cancer Receiving Myelosuppressive Chemotherapy**

Nyvepria is indicated 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.

### **Fylnetra**

#### **Patients with Cancer Receiving Myelosuppressive Chemotherapy**

Fylnetra is indicated 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.

## Stimufend

### **Patients with Cancer Receiving Myelosuppressive Chemotherapy**

Stimufend is indicated 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.

### **Hematopoietic Subsyndrome of Acute Radiation Syndrome**

Stimufend is indicated to increase survival in patients acutely exposed to myelosuppressive doses of radiation.

## Compendial Use

- Stem cell transplantation-related indications
- Prophylaxis for chemotherapy-induced febrile neutropenia in patients with solid tumors
- Hematopoietic Acute Radiation Syndrome
- Hairy cell leukemia, neutropenic fever

All other indications are considered experimental/investigational and not medically necessary.

## Documentation

### Primary Prophylaxis of Febrile Neutropenia

- Documentation must be provided of the member's diagnosis and chemotherapeutic regimen.
- If chemotherapeutic regimen has a low or intermediate risk of febrile neutropenia (less than 20%), documentation must be provided outlining the member's risk factors that confirm the member is at high risk for febrile neutropenia.

## Coverage Criteria

### Prevention of Neutropenia in Cancer Patients Receiving Myelosuppressive Chemotherapy

Authorization of 6 months may be granted for prevention of febrile neutropenia when all of the following criteria are met :

- The requested medication will not be used in combination with other colony stimulating factors within any chemotherapy cycle.
- The member will not receive chemotherapy at the same time as they receive radiation therapy.

- The requested medication will not be administered with weekly chemotherapy regimens.
- One of the following criteria is met :
  - The requested medication 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:
    - Myelosuppressive anti-cancer therapy that is expected to result in 20% or higher incidence of febrile neutropenia (FN) (See Appendix A).
    - Myelosuppressive anti-cancer therapy that is expected to result in 10 – 19% risk of FN (See Appendix B) and who are considered to be at high risk of FN because of bone marrow compromise, co-morbidities, or other patient specific risk factors (See Appendix 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).
  - The requested medication 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 scheduled planned for the current cycle (for which primary prophylaxis was not received).

## Other Indications

Authorization of 6 months may be granted for members with any of the following indications:

- Stem cell transplantation-related indications
  - Hematopoietic Subsyndrome of Acute Radiation Syndrome
  - Treatment for radiation-induced myelosuppression following a radiological/nuclear incident
  - Hairy cell leukemia
- Members with hairy cell leukemia with neutropenic fever following chemotherapy

## Continuation of Therapy

All members (including new members) requesting authorization for continuation of therapy must meet all requirements in the coverage criteria.

# Appendix

## APPENDIX A: Selected Chemotherapy Regimens with an Incidence of Febrile Neutropenia of 20% or Higher

This list is not comprehensive; there are other agents/regimens that have an intermediate/high risk for development of febrile neutropenia.

### Acute Lymphoblastic Leukemia

Select ALL regimens as directed by treatment protocol (see NCCN guidelines ALL)

### Bladder Cancer

Dose dense MVAC (methotrexate, vinblastine, doxorubicin, cisplatin)

### Bone Cancer

- VAIA (vincristine, doxorubicin, ifosfamide, and dactinomycin)
- VDC-IE (vincristine, doxorubicin or dactinomycin, and cyclophosphamide alternating with ifosfamide and etoposide)
- Cisplatin/doxorubicin
- VDC (cyclophosphamide, vincristine, doxorubicin or dactinomycin)
- VIDE (vincristine, ifosfamide, doxorubicin or dactinomycin, etoposide)

### Breast Cancer

- Dose-dense AC (doxorubicin, cyclophosphamide) followed by dose-dense paclitaxel
- TAC (docetaxel, doxorubicin, cyclophosphamide)
- TC (docetaxel, cyclophosphamide)
- TCH (docetaxel, carboplatin, trastuzumab)

### Head and Neck Squamous Cell Carcinoma

TPF (docetaxel, cisplatin, 5-fluorouracil)

### Hodgkin Lymphoma

- Brentuximab vedotin + AVD (doxorubicin, vinblastine, dacarbazine)
- Escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone)

### Kidney Cancer

Doxorubicin/gemcitabine

### Non-Hodgkin's Lymphoma

- CHP (cyclophosphamide, doxorubicin, prednisone) + brentuximab vedotin

Reference number(s)
1931-A

- Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) ± rituximab
- ICE (ifosfamide, carboplatin, etoposide) ± rituximab
- Dose-dense CHOP-14 (cyclophosphamide, doxorubicin, vincristine, prednisone) ± rituximab
- MINE (mesna, ifosfamide, mitoxantrone, etoposide) ± rituximab
- DHAP (dexamethasone, cisplatin, cytarabine) ± rituximab
- ESHAP (etoposide, methylprednisolone, cisplatin, cytarabine) ± rituximab
- HyperCVAD ± rituximab (cyclophosphamide, vincristine, doxorubicin, dexamethasone ± rituximab)
- Pola-R-CHP (polatuzumab vedotin-piiq, rituximab, cyclophosphamide, doxorubicin, prednisone)

## Melanoma

Dacarbazine-based combination with IL-2, interferon alpha (dacarbazine, cisplatin, vinblastine, IL-2, interferon alfa)

## Multiple Myeloma

- VTD-PACE (dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide + bortezomib)
- DT-PACE (dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide)

## Ovarian Cancer

- Topotecan ± bevacizumab
- Docetaxel

## Soft Tissue Sarcoma

- MAID (mesna, doxorubicin, ifosfamide, dacarbazine)
- Doxorubicin
- Ifosfamide/doxorubicin

## Small Cell Lung Cancer

Topotecan

## Testicular Cancer

- VelP (vinblastine, ifosfamide, cisplatin)
- VIP (etoposide, ifosfamide, cisplatin)
- TIP (paclitaxel, ifosfamide, cisplatin)

## Gestational Trophoblastic Neoplasia

- EMA/CO (etoposide, methotrexate, dactinomycin/cyclophosphamide, vincristine)
- EMA/EP (etoposide, methotrexate, dactinomycin/etoposide, cisplatin)
- EP/EMA (etoposide, cisplatin/etoposide, methotrexate, dactinomycin)
- TP/TE (paclitaxel, cisplatin/paclitaxel, etoposide)

Reference number(s)
1931-A

- BEP (bleomycin, etoposide, cisplatin)
- VIP (etoposide, ifosfamide, cisplatin)
- ICE (ifosfamide, carboplatin, etoposide)

## Wilms Tumor

- Regimen M (vincristine, dactinomycin, doxorubicin, cyclophosphamide, etoposide)
- Regimen I (vincristine, doxorubicin, cyclophosphamide, etoposide)

Applies to chemotherapy regimens with or without monoclonal antibodies (e.g., trastuzumab, rituximab)

## APPENDIX B: Selected Chemotherapy Regimens with an Incidence of Febrile Neutropenia of 10% to 19%

This list is not comprehensive; there are other agents/regimens that have an intermediate/high risk for development of febrile neutropenia.

### Occult Primary – Adenocarcinoma

Gemcitabine/docetaxel

### Breast Cancer

- Docetaxel ± trastuzumab
- AC (doxorubicin, cyclophosphamide) + sequential docetaxel (taxane portion only)
- AC + sequential docetaxel + trastuzumab
- Paclitaxel every 21 days ± trastuzumab
- TC (docetaxel, cyclophosphamide)

### Cervical Cancer

- Irinotecan
- Cisplatin/topotecan
- Paclitaxel/cisplatin ± bevacizumab
- Topotecan

### Colorectal Cancer

FOLFIRINOX (fluorouracil, leucovorin, oxaliplatin, irinotecan)

### Esophageal and Gastric Cancers

Irinotecan/cisplatin

### Non-Hodgkin's Lymphomas

- GDP (gemcitabine, dexamethasone, cisplatin/carboplatin)
- GDP (gemcitabine, dexamethasone, cisplatin/carboplatin) + rituximab
- CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) including regimens with pegylated liposomal doxorubicin

- CHOP + rituximab (cyclophosphamide, doxorubicin, vincristine, prednisone, rituximab) including regimens with pegylated liposomal doxorubicin
- Bendamustine

## Non-Small Cell Lung Cancer

- Cisplatin/paclitaxel
- Cisplatin/vinorelbine
- Cisplatin/docetaxel
- Cisplatin/etoposide
- Carboplatin/paclitaxel
- Docetaxel

## Ovarian Cancer

Carboplatin/docetaxel

## Pancreatic Cancer

FOLFIRINOX (fluorouracil, leucovorin, oxaliplatin, irinotecan)

## Prostate Cancer

Cabazitaxel

## Small Cell Lung Cancer

Etoposide/carboplatin

## Testicular Cancer

- BEP (bleomycin, etoposide, cisplatin)
- Etoposide/cisplatin

## Uterine Sarcoma

Docetaxel

Applies to chemotherapy regimens with or without monoclonal antibodies (e.g., trastuzumab, rituximab)

## APPENDIX C: Patient Risk Factors

This list is not all-inclusive.

- Active infections, open wounds, or recent surgery
- Age greater than or equal to 65 years
- Bone marrow involvement by tumor producing cytopenias
- Previous chemotherapy or radiation therapy
- Poor nutritional status
- Poor performance status
- Previous episodes of FN

- Other serious co-morbidities, including renal dysfunction, liver dysfunction, HIV infection, cardiovascular disease
- Persistent neutropenia

## References

1. Neulasta [package insert]. Thousand Oaks, CA: Amgen Inc.; February 2021.
2. Fulphila [package insert]. Cambridge, MA: Biocon Biologics Inc.; June 2023.
3. Udenyca [package insert]. Redwood City, CA: Coherus BioSciences, Inc.; December 2023.
4. Ziextenzo [package insert]. Princeton, NJ: Sandoz Inc.; February 2024.
5. Nyvepria [package insert]. Lake Forest, IL: Hospira, Inc.; March 2023.
6. Fylnetra [package insert]. Piscataway, NJ: Kashiv BioSciences, LLC; May 2022.
7. Stimufend [package insert]. Lake Zurich, IL: Fresenius Kabi USA, LLC; September 2023.
8. The NCCN Drugs & Biologics Compendium © 2024 National Comprehensive Cancer Network, Inc. Available at: <https://www.nccn.org> Accessed June 5, 2024.
9. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Hematopoietic Growth Factors. Version 3.2024. [https://www.nccn.org/professionals/physician\\_gls/pdf/growthfactors.pdf](https://www.nccn.org/professionals/physician_gls/pdf/growthfactors.pdf) Accessed June 6, 2024.
10. IBM Micromedex® DRUGDEX® (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at <https://www.micromedexsolutions.com> (Accessed: June 6, 2024).
11. Smith TJ, Bohlke K, Lyman GH, et al. Recommendations for the use of white blood cell growth factors: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol. 2015;33(28):3199-3212.
12. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Hairy Cell Leukemia. Version 2.2024. [https://www.nccn.org/professionals/physician\\_gls/pdf/hairy\\_cell.pdf](https://www.nccn.org/professionals/physician_gls/pdf/hairy_cell.pdf) Accessed June 6, 2024.
13. Smith TJ, Khatcheressian J, Lyman GH, et al. 2006 update of recommendations for the use of white blood cell growth factors: an evidence-based clinical practice guideline. J Clin Oncol. 2006;24(19):3187-3205.
14. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Gestational Trophoblastic Neoplasia. Version 1.2024. [https://www.nccn.org/professionals/physician\\_gls/pdf/gtn.pdf](https://www.nccn.org/professionals/physician_gls/pdf/gtn.pdf) Accessed June 5, 2024.
15. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Wilms Tumor (Nephroblastoma). Version 1.2023. [https://www.nccn.org/professionals/physician\\_gls/pdf/wilms\\_tumor.pdf](https://www.nccn.org/professionals/physician_gls/pdf/wilms_tumor.pdf) Accessed June 6, 2024.