CVS Caremark®

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| Reference number(s) |
| 1931-A |

# 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.

##### 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
* 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)
* 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

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