

SPECIALTY GUIDELINE MANAGEMENT

NEULASTA (pegfilgrastim)
FULPHILA (pegfilgrastim-jmdb)
FYLNETRA (pegfilgrastim-pbbk)
NYVEPRIA (pegfilgrastim-apgf)
STIMUFEND (pegfilgrastim-fpgk)
UDENYCA (pegfilgrastim-cbqv)
ZIEXTENZO (pegfilgrastim-bmez)

POLICY

I. 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.

A. FDA-Approved Indication

Neulasta

1. 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.
2. 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).

Fulphila²

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

1. 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.
2. 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

Reference number(s)
1931-A

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.

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.

Fylmetra

Patients with Cancer Receiving Myelosuppressive Chemotherapy

Fylmetra 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.

B. Compendial Use

1. Stem cell transplantation-related indications
2. Prophylaxis for chemotherapy-induced febrile neutropenia in patients with solid tumors
3. Hematopoietic Subsyndrome of Acute Radiation Syndrome
4. Hairy cell leukemia, neutropenic fever

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

II. DOCUMENTATION

Primary Prophylaxis of Febrile Neutropenia

- A. Documentation must be provided of the member's diagnosis and chemotherapeutic regimen.
- B. 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.

III. CRITERIA FOR INITIAL APPROVAL

A. 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 (1, 2, 3, and 4):

1. The requested medication will not be used in combination with other colony stimulating factors within any chemotherapy cycle.
2. The member will not receive chemotherapy at the same time as they receive radiation therapy.
3. The requested medication will not be administered with weekly chemotherapy regimens.
4. One of the following criteria is met (i or ii):

- i. 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:
 - a. Myelosuppressive anti-cancer therapy that is expected to result in 20% or higher incidence of febrile neutropenia (FN) (*See Appendix A*).
 - b. 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*).
 - 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*).
- ii. 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).

B. Other indications

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

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

IV. CONTINUATION OF THERAPY

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

V. APPENDIX

A. APPENDIX A: Selected Chemotherapy Regimens with an Incidence of Febrile Neutropenia of 20% or Higher^{††}

1. Acute Lymphoblastic Leukemia:
Select ALL regimens as directed by treatment protocol (see NCCN guidelines ALL)
2. Bladder Cancer:
 - i. Dose dense MVAC (methotrexate, vinblastine, doxorubicin, cisplatin)
 - ii. CBDCA/Pac (carboplatin, paclitaxel)
3. Bone Cancer
 - i. VAI (vincristine, doxorubicin or dactinomycin, ifosfamide)
 - ii. VDC-IE (vincristine, doxorubicin or dactinomycin, and cyclophosphamide alternating with ifosfamide and etoposide)
 - iii. Cisplatin/doxorubicin
 - iv. VDC (cyclophosphamide, vincristine, doxorubicin or dactinomycin)
 - v. VIDE (vincristine, ifosfamide, doxorubicin or dactinomycin, etoposide)
4. Breast Cancer:
 - i. Docetaxel + trastuzumab
 - ii. Dose-dense AC (doxorubicin, cyclophosphamide) + paclitaxel (or dose dense paclitaxel)

Reference number(s)
1931-A

- iii. TAC (docetaxel, doxorubicin, cyclophosphamide)
- iv. AT (doxorubicin, docetaxel)
- v. Doc (docetaxel)
- vi. TC (docetaxel, cyclophosphamide)
- vii. TCH (docetaxel, carboplatin, trastuzumab)
- 5. Colorectal Cancer:
FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, irinotecan)
- 6. Esophageal and Gastric Cancers:
Docetaxel/cisplatin/fluorouracil
- 7. Head and Neck Squamous Cell Carcinoma
TPF (docetaxel, cisplatin, 5-fluorouracil)
- 8. Hodgkin Lymphoma:
 - i. Brentuximab vedotin + AVD (doxorubicin, vinblastine, dacarbazine)
 - ii. Escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone)
- 9. Kidney Cancer:
Doxorubicin/gemcitabine
- 10. Non-Hodgkin's Lymphoma:
 - i. CHP (cyclophosphamide, doxorubicin, prednisone) + brentuximab vedotin
 - ii. Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)
 - iii. ICE (ifosfamide, carboplatin, etoposide)
 - iv. Dose-dense CHOP-14 (cyclophosphamide, doxorubicin, vincristine, prednisone) ± rituximab
 - v. MINE (mesna, ifosfamide, mitoxantrone, etoposide)
 - vi. DHAP (dexamethasone, cisplatin, cytarabine)
 - vii. ESHAP (etoposide, methylprednisolone, cisplatin, cytarabine (Ara-C))
 - viii. HyperCVAD ± rituximab (cyclophosphamide, vincristine, doxorubicin, dexamethasone ± rituximab)
 - ix. VAPEC-B (vincristine, doxorubicin, prednisolone, etoposide, cyclophosphamide, bleomycin)
- 11. Melanoma:
Dacarbazine-based combination with IL-2, interferon alpha (dacarbazine, cisplatin, vinblastine, IL-2, interferon alfa)
- 12. Multiple Myeloma:
 - i. VTD-PACE (dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide + bortezomib)
 - ii. DT-PACE (dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide)
- 13. Ovarian Cancer:
 - i. Topotecan
 - ii. Docetaxel
- 14. Soft Tissue Sarcoma:
 - i. MAID (mesna, doxorubicin, ifosfamide, dacarbazine)
 - ii. Doxorubicin
 - iii. Ifosfamide/doxorubicin
- 15. Small Cell Lung Cancer:
 - i. Top (topotecan)
 - ii. CAV (cyclophosphamide, doxorubicin, vincristine)
- 16. Testicular Cancer:
 - i. VeIP (vinblastine, ifosfamide, cisplatin)
 - ii. VIP (etoposide, ifosfamide, cisplatin)
 - iii. TIP (paclitaxel, ifosfamide, cisplatin)
- 17. Gestational Trophoblastic Neoplasia:
 - i. EMA/CO (etoposide, methotrexate, dactinomycin/cyclophosphamide, vincristine)
 - ii. EMA/EP (etoposide, methotrexate, dactinomycin/etoposide, cisplatin)

Reference number(s)
1931-A

- iii. EP/EMA (etoposide, cisplatin/etoposide, methotrexate, dactinomycin)
 - iv. TP/TE (paclitaxel, cisplatin/paclitaxel, etoposide)
 - v. BEP (bleomycin, etoposide, cisplatin)
 - vi. VIP (etoposide, ifosfamide, cisplatin)
 - vii. ICE (ifosfamide, carboplatin, etoposide)
18. Wilms Tumor:
- i. Regimen M (vincristine, dactinomycin, doxorubicin, cyclophosphamide, etoposide)
 - ii. 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.

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

- 1. Occult Primary – Adenocarcinoma:
Gemcitabine/docetaxel
- 2. Breast Cancer:
 - i. Docetaxel
 - ii. CMF classic (cyclophosphamide, methotrexate, fluorouracil)
 - iii. CA (doxorubicin, cyclophosphamide) (60 mg/m²) (hospitalized)
 - iv. AC (doxorubicin, cyclophosphamide) + sequential docetaxel (taxane portion only)
 - v. AC + sequential docetaxel + trastuzumab
 - vi. A (doxorubicin) (75 mg/m²)
 - vii. AC (doxorubicin, cyclophosphamide)
 - viii. CapDoc (capecitabine, docetaxel)
 - ix. Paclitaxel every 21 days
- 3. Cervical Cancer:
 - i. Irinotecan
 - ii. Cisplatin/topotecan
 - iii. Paclitaxel/cisplatin
 - iv. Topotecan
- 4. Colorectal Cancer:
 - i. FL (fluorouracil, leucovorin)
 - ii. CPT-11 (irinotecan) (350 mg/m² q 3 wk)
 - iii. FOLFOX (fluorouracil, leucovorin, oxaliplatin)
 - iv. FOLFIRINOX (fluorouracil, leucovorin, oxaliplatin, irinotecan)
- 5. Esophageal and Gastric Cancers:
 - i. Irinotecan/cisplatin
 - ii. Epirubicin/cisplatin/5-fluorouracil
 - iii. Epirubicin/cisplatin/capecitabine
- 6. Non-Hodgkin's Lymphomas:
 - i. EPOCH-IT chemotherapy
 - ii. GDP (gemcitabine, dexamethasone, cisplatin/carboplatin)
 - iii. GDP (gemcitabine, dexamethasone, cisplatin/carboplatin) + rituximab
 - iv. FMR (fludarabine, mitoxantrone, rituximab)
 - v. CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) including regimens with pegylated liposomal doxorubicin
 - vi. CHOP + rituximab (cyclophosphamide, doxorubicin, vincristine, prednisone, rituximab) including regimens with pegylated liposomal doxorubicin

Reference number(s)
1931-A

- vii. Bendamustine
- 7. Non-Small Cell Lung Cancer:
 - i. Cisplatin/paclitaxel
 - ii. Cisplatin/vinorelbine
 - iii. Cisplatin/docetaxel
 - iv. Cisplatin/etoposide
 - v. Carboplatin/paclitaxel
 - vi. Docetaxel
- 8. Ovarian Cancer:
 - Carboplatin/docetaxel
- 9. Pancreatic Cancer:
 - FOLFIRINOX (fluorouracil, leucovorin, oxaliplatin, irinotecan)
- 10. Prostate Cancer:
 - Cabazitaxel
- 11. Small Cell Lung Cancer:
 - Etoposide/carboplatin
- 12. Testicular Cancer:
 - i. BEP (bleomycin, etoposide, cisplatin)
 - ii. Etoposide/cisplatin
- 13. Uterine Sarcoma:
 - 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.

C. APPENDIX C: Patient Risk Factors*

- 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

*This list is not all-inclusive.

VI. REFERENCES

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