 Draft Revision Policy: Do Not Implement

Colony Stimulating Factors - Pegfilgrastim (Neulasta®); Pegfilgrastim-jmdb (Fulphila®); Pegfilgrastim-pbbk (Fylnetra®); Pegfilgrastim-apgf (Nyvepria™); Pegfilgrastim-fpgk (Stimufend®); Pegfilgrastim-cbqv (Udenyca®); Pegfilgrastim-bmez (Ziextenzo™)

Some agents on this policy may require step therapy *See* "Step Therapy Requirements for Provider Administered Specialty Medications" Document at:
https://www.bcbst.com/docs/providers/Comm_BC_PAD_Step_Therapy_Guide.pdf

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the medical policy and a health plan or government program (e.g., TennCare), the express terms of the health plan or government program will govern.

The proposal is to add text/statements in red and to delete text/statements with strikethrough:

POLICY

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.

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

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 ~~Subsyndrome of~~ 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% and less), 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 greater than 20% ~~or higher~~ incidence of febrile neutropenia (FN) (See Appendix A).
    - Myelosuppressive anti-cancer therapy that is expected to result in 10 – ~~19~~20% 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 ~~initial authorization~~ requirements in the coverage criteria.

APPENDIX

APPENDIX A: **Selected Chemotherapy Regimens with an Incidence of Febrile Neutropenia of Greater than 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)
- Nivolumab + AVD (doxorubicin, vinblastine, dacarbazine)
- Escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone)
- BrECADD (brentuximab vedotin, etoposide, cyclophosphamide, doxorubicin, dacarbazine, dexamethasone)

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
- CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone)
- 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
- Carboplatin/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)
- TIP (Paclitaxel, ifosfamide, cisplatin)
- VIP (etoposide, ifosfamide, cisplatin)
- ICE (ifosfamide, carboplatin, etoposide)

Wilms Tumor
- Regimen M (vincristine, dactinomycin, doxorubicin, cyclophosphamide, etoposide)
- Regimen I (vincristine, doxorubicin, cyclophosphamide, etoposide)
- Revised Regimen UH-1 (vincristine, doxorubicin, cyclophosphamide, carboplatin, etoposide)
- Revised Regimen UH-2 (vincristine, doxorubicin, cyclophosphamide, carboplatin, etoposide, irinotecan)

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~~20%

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
- Sacituzumab govitecan-hziy
- 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

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

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EFFECTIVE DATE

ID_CHS_2025