AETNA BETTER HEALTH®
Coverage Policy/Guideline

Name:	Neulasta and pegfilgrastim biosimilars	Page:	1 of 9
Effective Date:	12/10/2024	Last Review Date:	11/19/2024

Applies to:	☒Florida Kids	☒New Jersey	☒Maryland
	☒Pennsylvania Kids	☐Virginia	☒Kentucky PRMD

Intent:

The intent of this policy/guideline is to provide information to the prescribing practitioner outlining the coverage criteria for Neulasta and pegfilgrastim biosimilars under the patient's prescription drug benefit.

Description:

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).

Fulphila[2]

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.

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.

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.

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.

Applicable Drug List:

Neulasta
Fulphila
Fylnetra
Nyvepria
Stimufend
Udenyca
Ziextenzo

Policy/Guideline:

Documentation:

Primary Prophylaxis of Febrile Neutropenia

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

Note: Ziextenzo is the preferred agent. Requests for non-preferred agents require that the patient is unable to take Ziextenzo for the given diagnosis due to a trial and inadequate treatment response or intolerance, or a contraindication.

A. Prevention of neutropenia in cancer patients receiving myelosuppressive chemotherapy

Authorization of 6 months may be granted for prevention of febrile neutropenia when ALL 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

Continuation of Therapy:

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

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)
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. Dose-dense AC (doxorubicin, cyclophosphamide) + paclitaxel (or dose dense paclitaxel)
   ii. TAC (docetaxel, doxorubicin, cyclophosphamide)
   iii. TC (docetaxel, cyclophosphamide)
   iv. TCH (docetaxel, carboplatin, trastuzumab)

5. Head and Neck Squamous Cell Carcinoma
   TPF (docetaxel, cisplatin, 5-fluorouracil)
6. Hodgkin Lymphoma:
   i. Brentuximab vedotin + AVD (doxorubicin, vinblastine, dacarbazine)
   ii. Escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone)
7. Kidney Cancer:
   Doxorubicin/gemcitabine
8. 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. Pola-R-CHP (polatuzumab vedotin-piiq, rituximab, cyclophosphamide, doxorubicin, prednisone)
9. Melanoma:
   Dacarbazine-based combination with IL-2, interferon alpha (dacarbazine, cisplatin, vinblastine, IL-2, interferon alfa)
10. Multiple Myeloma:
    i. VTD-PACE (dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide + bortezomib)
    ii. DT-PACE (dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide)
11. Ovarian Cancer:
    i. Topotecan
    ii. Docetaxel
12. Soft Tissue Sarcoma:
    i. MAID (mesna, doxorubicin, ifosfamide, dacarbazine)

ii. Doxorubicin
iii. Ifosfamide/doxorubicin

13. Small Cell Lung Cancer:
    Topotecan
14. Testicular Cancer:
    i. VelP (vinblastine, ifosfamide, cisplatin)
    ii. VIP (etoposide, ifosfamide, cisplatin)
    iii. TIP (paclitaxel, ifosfamide, cisplatin)
15. Gestational Trophoblastic Neoplasia:
    i. EMA/CO (etoposide, methotrexate, dactinomycin/cyclophosphamide, vincristine
    ii. EMA/EP (etoposide, methotrexate, dactinomycin/etoposide, cisplatin)
    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)
16. 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 ± trastuzumab
   ii. AC (doxorubicin, cyclophosphamide) + sequential docetaxel (taxane portion only)
   iii. AC + sequential docetaxel + trastuzumab
   iv. Paclitaxel every 21 days ± trastuzumab
   v. TC (docetaxel, cyclophosphamide)

3. Cervical Cancer:
   i. Irinotecan
   ii. Cisplatin/topotecan
   iii. Paclitaxel/cisplatin ± bevacizumab
   iv. Topotecan
4. Colorectal Cancer:
   i. FOLFIRINOX (fluorouracil, leucovorin, oxaliplatin, irinotecan)
5. Esophageal and Gastric Cancers:
   i. Irinotecan/cisplatin
6. Non-Hodgkin's Lymphomas:
   i. GDP (gemcitabine, dexamethasone, cisplatin/carboplatin)
   ii. GDP (gemcitabine, dexamethasone, cisplatin/carboplatin) + rituximab
   iii. CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) including regimens with pegylated liposomal doxorubicin
   iv. CHOP + rituximab (cyclophosphamide, doxorubicin, vincristine, prednisone, rituximab) including regimens with pegylated liposomal doxorubicin
   v. 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, irinotecanSmall Cell Lung Cancer:
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

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

Approval Duration and Quantity Restrictions:

Approval: 6 months

Quantity Level Limit: Neulasta/Fulphila/Fylnetra/Nyvepria/Stimufend/ Udenyca/Ziextenzo (pegfilgrastim) injection 6 mg per 0.6 mL solution: 2 per 28 days

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