JOHNS HOPKINS MEDICINE / JOHNS HOPKINS HEALTHCARE	Johns Hopkins HealthCare LLC **Pharmacy Public** **Medical Management Drug Policies**	*Policy Number*	MMDP018
		Effective Date	01/01/2019
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	Subject **Pegfilgrastim Products: Neulasta, Fulphila, Udenyca, Ziextenzo, Nyvepria, Fylnetra, Stimufend**	*Revision Date*	04/19/2023
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This document applies to the following Participating Organizations:

US Family Health Plan

Keywords: Fulphila, Neulasta, Nyvepria, Udenyca, Ziextenzo

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I. POLICY

A. Neulasta (pegfilgrastim), Fulphila (pegfilgrastim-jmdb), Udenyca (pegfilgrastim-cbqv), Ziextenzo (pegfilgrastim-bmez), Nyvepria (pegfilgrastim-apgf), Fylnetra (pegfilgrastim-pbbk), and Stimufend (pegfilgrastim-fpgk) will require prior authorization for medical benefit coverage to ensure appropriate use. The process for initiating a prior authorization request can be found in policy PHARM 20.

B. Biosimilar and Interchangeable biosimilar Usage Notice: Current clinical evidence supports that biosimilars are highly similar, and do not have a clinically meaningful difference in terms of efficacy and safety when compared to their originator biologic product. In addition, the FDA has stated that biosimilars and interchangeable biosimilars can be used in patients previously treated with the originator product, as well as treatment-naïve patients. For Plan approval of therapy with the originator product, patients must first have trial and inadequate response to a preferred biosimilar medication when available.

II. POLICY CRITERIA

A. **Fulphila, Udenyca, Ziextenzo, Nyvepria, Fylnetra, or Stimufend** may be approved for patients who meet the following:

1. **Prevention of chemotherapy-induced neutropenia:**
   a. Documentation has been submitted showing the following:
      I. Patient will not be receiving myelosuppressive chemotherapy and radiation therapy at the same time
      II. Request meets one of the following:
         i. The pegfilgrastim product will be used for primary prophylaxis in a patient with a solid tumor or non-myeloid malignancy who has received, is currently receiving, or will be receiving either of the following:
            A. Myelosuppressive therapy is expected to result in 20% or higher incidence of febrile neutropenia (FN)

B. Myelosuppressive therapy is expected to result in 10 – 19% risk of FN, and patient is considered to be at high risk because of bone marrow compromise or co-morbidity, including, but not limited to the following:
1. Active infections, open wounds, or recent surgery
2. Age of 65 years old or greater
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

ii. The pegfilgrastim product will be used for secondary prophylaxis in patients with solid tumors or non-myeloid malignancies and the following:
A. Patient has 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
B. Patient will be receiving the same dose and schedule of therapy for the current cycle that used for the previous cycle, when primary prophylaxis was not received

III. Prescriber is, or in consultation with, an oncologist or hematologist

B. **Neulasta** may be approved for patients who meet the following:
1. **Prevention of chemotherapy-induced neutropenia**:
a. Documentation has been submitted showing the following:
I. Patient will not be receiving myelosuppressive chemotherapy and radiation therapy at the same time
II. Request meets one of the following:
i. The pegfilgrastim product will be used for primary prophylaxis in a patient with a solid tumor or non-myeloid malignancy who has received, is currently receiving, or will be receiving either of the following:
A. Myelosuppressive therapy is expected to result in 20% or higher incidence of febrile neutropenia (FN)
B. Myelosuppressive therapy is expected to result in 10 – 19% risk of FN, and patient is considered to be at high risk because of bone marrow compromise or co-morbidity, including, but not limited to the following:
1. Active infections, open wounds, or recent surgery
2. Age of 65 years old or greater
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

ii. The pegfilgrastim product will be used for secondary prophylaxis in patients with solid tumors or non-myeloid malignancies and the following:
A. Patient has 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
B. Patient will be receiving the same dose and schedule of therapy for the current cycle that used for the previous cycle, when primary prophylaxis was not received

III. Patient has had trial and inadequate response to at least one preferred pegfilgrastim biosimilar product
IV. Prescriber is, or in consultation with, an oncologist or hematologist

2. **Acute Hematopoietic radiation injury syndrome**:
a. Documentation has been submitted showing that the patient was acutely exposed to myelosuppressive doses of radiation
b. Requested quantity is not greater than two doses, which will be taken 1 week apart

III. AUTHORIZATION PERIOD/LIMITATIONS

A. Initial approval will be limited to 6 months of therapy for prophylaxis of chemotherapy-induced neutropenia (dosed no more frequently than every 14 days).
B. Initial approval of Neulasta will be restricted to 2 doses when used for acute radiation exposure.
C. Continuation of therapy may be approved for neutropenia prophylaxis in 6-month intervals with documentation showing a beneficial response to treatment.

IV. EXCLUSIONS

A. Pegfilgrastim and pegfilgrastim biosimilars will not be covered for the following:
1. Concurrent use with other colony stimulating factors within any chemotherapy cycle
2. Co-administration with weekly chemotherapy regimens
3. Use in patients with history of serious allergic reaction to human granulocyte colony-stimulating factors
4. Any indications or uses that are not FDA-approved or guideline-supported including, but not limited to:
a. Acute myeloid leukemia,
b. Aplastic anemia
c. Hepatitis C treatment-induced neutropenia,
d. HIV-associated neutropenia
e. Agranulocytosis

V. RECOMMENDED DOSAGE

Prevention of chemotherapy-induced neutropenia: 6mg subcutaneously once per chemotherapy cycle, beginning at least 24 hours after completion of chemotherapy; should NOT be administered in the period between 14 days before and 24 hours after administration of cytotoxic chemotherapy

- *For pediatric patients with a weight of less than 45 kilograms*, dosing is weight-based once per chemotherapy cycle, beginning at least 24 hours after completion of chemotherapy:
  - Patients <10 kg: 0.1 mg/kg (0.01 mL/kg volume)

- Patients 10 to 20 kg: 1.5 mg (0.15 mL volume)
- Patients 21 to 30 kg: 2.5 mg (0.25 mL volume)
- Patients 31 to 44 kg: 4 mg (0.4 mL volume)

Acute Hematopoietic radiation injury syndrome: 6 mg subcutaneously once weekly for 2 doses.

- *For pediatric patients with a weight of less than 45 kilograms,* dosing is weight-based for two doses one week apart:
  - Patients <10 kg: 0.1 mg/kg (0.01 mL/kg volume)
  - Patients 10 to 20 kg: 1.5 mg (0.15 mL volume)
  - Patients 21 to 30 kg: 2.5 mg (0.25 mL volume)
  - Patients 31 to 44 kg: 4 mg (0.4 mL volume)

VI. CODES

Note: The following CPT/HCPCS codes are included below for informational purposes. Inclusion or exclusion of a CPT/HCPCS code(s) below does not signify or imply member coverage or provider reimbursement. The member's specific benefit plan determines coverage.

Medication	HCPCS/CPT Code
Neulasta 6 MG/0.6ML SOSY Injection, pegfilgrastim, 6 mg	J2505
Neulasta Onpro 6 MG/0.6ML PSKT Injection, pegfilgrastim, 6 mg	J2505
Fulphila Injection, pegfilgrastim-jmdb, biosimilar,0.5 mg	Q5108
Udenyca 6 MG/0.6ML SOSY Injection, pegfilgrastim-cbqv, biosimilar, 0.5 mg	Q5111
Ziextenzo Injection, pegfilgrastim-bmez, biosimilar, 0.5 mg	Q5120
Nyvepria 6MG/0.6ML SOSY Injection, pegfilgrastim-apgf, biosimilar, 0.5 mg	Q5122
Fylnetra Injection, pegfilgrastim-pbbk, biosimilar, 0.5 mg	Q5130
Stimufend Injection, pegfilgrastim-fpgk, biosimilar, 0.5 mg	Q5127

Examples of Disease Settings and Chemotherapy Regimens* with an Incidence of Febrile Neutropenia of 20% or Higher*:

1. Acute Lymphoblastic Leukemia:
   a. Select ALL regimens as directed by treatment protocol (see NCCN guidelines ALL)

2. Bladder Cancer:
   a. Dose dense MVAC (methotrexate, vinblastine, doxorubicin, cisplatin)
   b. CBDCa/Pac (carboplatin, paclitaxel)
3. Bone Cancer
   a. VAI (vincristine, doxorubicin or dactinomycin, ifosfamide)
   b. VDC-IE (vincristine, doxorubicin or dactinomycin, and cyclophosphamide alternating with ifosfamide and etoposide)
   c. Cisplatin/doxorubicin
   d. VDC (cyclophosphamide, vincristine, doxorubicin or dactinomycin)
   e. VIDE (vincristine, ifosfamide, doxorubicin or dactinomycin, etoposide)
4. Breast Cancer:
   a. Docetaxel + trastuzumab
   b. Dose-dense AC (doxorubicin, cyclophosphamide) + paclitaxel (or dose dense paclitaxel)
   c. TAC (docetaxel, doxorubicin, cyclophosphamide)
   d. AT (doxorubicin, docetaxel)
   e. Doc (docetaxel)
   f. TC (docetaxel, cyclophosphamide)
   g. TCH (docetaxel, carboplatin, trastuzumab)
5. Colorectal Cancer:
   a. FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, irinotecan)
6. Esophageal and Gastric Cancers:
   a. Docetaxel/cisplatin/fluorouracil
7. Head and Neck Squamous Cell Carcinoma
   a. TPF (docetaxel, cisplatin, 5-fluorouracil)
8. 8. Hodgkin Lymphoma:
   a. Brentuximab vedotin + AVD (doxorubicin, vinblastine, dacarbazine)
   b. Escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone)
9. Kidney Cancer:
   a. Doxorubicin/gemcitabine
10. Non-Hodgkin's Lymphoma:
    a. CHP (cyclophosphamide, doxorubicin, prednisone) + brentuximab vedotin
    b. Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)
    c. ICE (ifosfamide, carboplatin, etoposide)
    d. Dose-dense CHOP-14 (cyclophosphamide, doxorubicin, vincristine, prednisone) ± rituximab
    e. MINE (mesna, ifosfamide, mitoxantrone, etoposide)
    f. DHAP (dexamethasone, cisplatin, cytarabine)
    g. ESHAP (etoposide, methylprednisolone, cisplatin, cytarabine (Ara-C))
    h. HyperCVAD ± rituximab (cyclophosphamide, vincristine, doxorubicin, dexamethasone ± rituximab)
    i. VAPEC-B (vincristine, doxorubicin, prednisolone, etoposide, cyclophosphamide, bleomycin)
11. Melanoma:
    a. Dacarbazine-based combination with IL-2, interferon alpha (dacarbazine, cisplatin, vinblastine, IL-2, interferon alfa)
12. Multiple Myeloma:
    a. VTD-PACE (dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide + bortezomib)
    b. DT-PACE (dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide)

13. Ovarian Cancer:
    a. Topotecan
    b. Docetaxel
14. Pancreatic Cancer:
    a. FOLFIRINOX (fluorouracil, leucovorin, irinotecan, oxaliplatin)
15. Soft Tissue Sarcoma:
    a. MAID (mesna, doxorubicin, ifosfamide, dacarbazine)
    b. Doxorubicin
    c. Ifosfamide/doxorubicin
16. Small Cell Lung Cancer:
    a. Top (topotecan)
    b. CAV (cyclophosphamide, doxorubicin, vincristine)
17. Testicular Cancer:
    a. VelP (vinblastine, ifosfamide, cisplatin)
    b. VIP (etoposide, ifosfamide, cisplatin)
    c. TIP (paclitaxel, ifosfamide, cisplatin)
18. Gestational Trophoblastic Neoplasia:
    a. EMA/EP (etoposide, methotrexate, dactinomycin/etoposide, cisplatin)
    b. EP/EMA (etoposide, cisplatin/etoposide, methotrexate, dactinomycin)
    c. TP/TE (paclitaxel, cisplatin/paclitaxel, etoposide)
    d. BEP (bleomycin, etoposide, cisplatin)
    e. VIP (etoposide, ifosfamide, cisplatin)
    f. ICE (ifosfamide, carboplatin, etoposide)
19. Wilms Tumor:
    a. Regimen M (vincristine, dactinomycin, doxorubicin, cyclophosphamide, etoposide)
    b. Regimen I (vincristine, doxorubicin, cyclophosphamide, etoposide)

Examples of Disease Settings and Chemotherapy Regimens* with an Incidence of Febrile Neutropenia of 10% to 19%*:

1. Occult Primary – Adenocarcinoma:
    a. Gemcitabine/docetaxel
2. Breast Cancer:
    a. Docetaxel
    b. CMF classic (cyclophosphamide, methotrexate, fluorouracil)
    c. CA (doxorubicin, cyclophosphamide) (60 mg/m2) (hospitalized)
    d. AC (doxorubicin, cyclophosphamide) + sequential docetaxel (taxane portion only)
    e. AC + sequential docetaxel + trastuzumab
    f. A (doxorubicin) (75 mg/m2)
    g. AC (doxorubicin, cyclophosphamide)
    h. CapDoc (capecitabine, docetaxel)
    i. Paclitaxel every 21 days

3. Cervical Cancer:
    a. Irinotecan
    b. Cisplatin/topotecan
    c. Paclitaxel/cisplatin
    d. Topotecan
4. Colorectal Cancer:
    a. FL (fluorouracil, leucovorin)
    b. CPT-11 (irinotecan) (350 mg/m2 q 3 wk)
    c. FOLFOX (fluorouracil, leucovorin, oxaliplatin)
5. Esophageal and Gastric Cancers:
    a. Irinotecan/cisplatin
    b. Epirubicin/cisplatin/5-fluorouracil
    c. Epirubicin/cisplatin/capecitabine
6. Non-Hodgkin's Lymphomas:
    a. EPOCH-IT chemotherapy
    b. GDP (gemcitabine, dexamethasone, cisplatin/carboplatin)
    c. GDP (gemcitabine, dexamethasone, cisplatin/carboplatin) + rituximab
    d. FMR (fludarabine, mitoxantrone, rituximab)
    e. CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) including regimens with pegylated liposomal doxorubicin
    f. CHOP + rituximab (cyclophosphamide, doxorubicin, vincristine, prednisone, rituximab) including regimens with pegylated liposomal doxorubicin
    g. Bendamustine
7. Non-Small Cell Lung Cancer:
    a. Cisplatin/paclitaxel
    b. Cisplatin/vinorelbine
    c. Cisplatin/docetaxel
    d. Cisplatin/etoposide
    e. Carboplatin/paclitaxel
    f. Docetaxel
8. Ovarian Cancer:
    a. Carboplatin/docetaxel
9. Prostate Cancer:
    a. Cabazitaxel
10. Small Cell Lung Cancer:
    a. Etoposide/carboplatin
11. Testicular Cancer:
    a. BEP (bleomycin, etoposide, cisplatin)
    b. Etoposide/cisplatin
12. Uterine Sarcoma:
    a. Docetaxel

**Please Note: This is not an all-inclusive list, as additional regimens may be listed in current NCCN guidelines.*

VII. REFERENCES

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VIII. APPROVALS

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DATE OF REVISION	SUMMARY OF CHANGE
12/19/2018	Policy Creation
01/16/2019	Added clinical criteria for Udenyca
07/17/2019	Modified clinical criteria to reflect Fulphila and Udenyca as preferred Nuelasta-biosimilar products
01/15/2020	No policy changes-presented policy for USFHP adoption effective 3/1/2020
05/04/2020	Added biosimilar usage notice
07/15/2020	Added clinical criteria for Ziextenzo
02/17/2021	Added Nyvepria as an applicable drug
11/10/2021	Removed Priority Partners as an applicable LOB
04/19/2023	Added Fylnetra and Stimufend; revised criteria

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