Medical Policy

Colony Stimulating Factors – Long Acting [Neulasta® (pegfilgrastim), Udenyca® (pegfilgrastim-cbqv), Fulphila® (pegfilgrastim-jmdb), Ziextenzo™ (pegfilgrastim-bmez), Nyvepria™ (pegfilgrastim-apgf), Fylnetra® (pegfilgrastim-pbbk), Rolvedon™ (eflapegrastim-xnst)Stimufend (pegfligrastim-fpgk)]	
MEDICAL POLICY NUMBER	MED_Clin_Ops_048a
ORIGINAL EFFECTIVE DATE	7/1/2021
CURRENT VERSION NUMBER	3
CURRENT VERSION EFFECTIVE DATE	2/28/2023
APPLICABLE PRODUCT AND MARKET*	Individual Family Plan: ALL Small Group: ALL

IMPORTANT INFORMATION – PLEASE READ BEFORE USING THIS POLICY*: These services may or may not be covered by all Bright Health Plans. Please refer to the member's plan document for specific coverage information.*

Bright Health may use tools developed by third parties, such as MCG™ Care Guidelines and the ASAM Criteria™ to assist in administering health benefits. Bright Health Medical Policies, MCG™ Care Guidelines, and the ASAM Criteria™ are not intended to be used without the independent clinical judgment of a qualified health care provider considering the individual circumstances of each member's case. The treating health care providers are solely responsible for diagnosis, treatment, and medical advice. Members may contact Bright Health Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions about this Bright Health Medical Policy may visit Bright Health provider portal at brighthealthcare.com/provider

Before using this policy, please check the member benefit plan document and any federal or state mandates, if applicable. Bright Health policies and practices are compliant with all federal and state requirements, including mental health parity laws.

PURPOSE

To promote consistency between reviewers in clinical coverage decision-making by providing the criteria that generally determine the medical necessity of Long-Acting Colony Stimulating Factors therapy.

POLICY/CRITERA

Prior Authorization and Medical Review is required.

Coverage will be provided for four months and may be renewed unless otherwise specified.

Fulphila, Ziextenzo, Nyvepria, Rolvedon,Fylnetra, and Stimufend are Non-Preferred products.
The Preferred products are Neulasta and Udenyca.

Fulphila, Ziextenzo, Nyvepria, Rolvedon, Fylnetra, and Stimufend may be considered medically necessary if:

- The patient has a contraindication or severe intolerance to Neulasta and Udenyca

Coverage for Neulasta® (pegfilgrastim), Udenyca® (pegfilgrastim-cbqv), Fulphila® (pegfilgrastim-jmdb), Ziextenzo™ (pegfilgrastim-bmez), Nyvepria™ (pegfilgrastim-apgf), Fylnetra® (pegfilgrastim-pbbk), Rolvedon™ (eflapegrastim-xnst), Stimufend (pegfilgrastim-fpgk) is provided in the following conditions:

1. **Prophylactic use in patients with non-myeloid malignancy**
    - **a.** Patient is undergoing myelosuppressive chemotherapy with an expected incidence of febrile neutropenia* of greater than 20%; OR
    - **b.** Patient is undergoing myelosuppressive chemotherapy with an expected incidence of febrile neutropenia* of 10% to 20% AND one or more of the following co-morbidities:
        - **i.** Age >65 years receiving full dose intensity chemotherapy
        - **ii.** Extensive prior exposure to chemotherapy
        - **iii.** Previous exposure of pelvis, or other areas of large amounts of bone marrow, to radiation
        - **iv.** Persistent neutropenia (ANC ≤ 1000/mm3)
        - **v.** Bone marrow involvement by tumor
        - **vi.** Patient has a condition that can potentially increase the risk of serious infection (i.e., HIV/AIDS with low CD4 counts)
        - **vii.** Recent surgery and/or open wounds
        - **viii.** Poor performance status
        - **ix.** Renal dysfunction (creatinine clearance <50 mL/min)
        - **x.** Liver dysfunction (elevated bilirubin >2.0 mg/dL)
        - **xi.** Chronic immunosuppression in the post-transplant setting, including organ transplant

2. **Hematopoietic Subsyndrome of Acute Radiation Syndrome (Neulasta ONLY)**
    - a. Patient has been acutely exposed to myelosuppressive doses of radiation.

*Febrile neutropenia is defined as:

- Temperature: a single temperature ≥38.3 °C orally or ≥38.0 °C over 1 hour; AND
- Neutropenia: <500 neutrophils/mcL or <1,000 neutrophils/mcL and a predicted decline to ≤500 neutrophils/mcL over the next 48 hours

DOSING LIMITS

Max Units (per dose and over time) [Medical Benefit]:

Neulasta	Fulphila	Udenyca	Ziextenzo	Nyvepria	Fylnetra	Stimufend	Rolvedon
1 billable unit per 14 days	12 billable units per 14 days	12 billable units per 14 days	12 billable units per 14 days	12 billable units per 14 days	12billable units per 14 days	12 billable units per 14 days	13.2mg per 14 days

LIMITATIONS/EXCLUSIONS

1. Any indication other than those listed above due to insufficient evidence of therapeutic value
2. Patients with a history of serious allergic reactions to pegfilgrastim or filgrastim.
3. Use for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation.

DEFINITIONS

1. NEULASTA (pegfilgrastim) injection, for subcutaneous use. Initial U.S. Approval: 2002
    a. Neulasta injection is a clear, colorless solution supplied in a prefilled single-dose syringe for manual use containing 6 mg pegfilgrastim, supplied with a 27-gauge, 1/2-inch needle with an UltraSafe® Needle Guard.The needle cap of the prefilled syringe contains dry natural rubber (a derivative of latex).
    b. Neulasta is provided in a dispensing pack containing one sterile 6 mg/0.6 mL prefilled syringe.
    c. Neulasta prefilled syringe does not bear graduation marks and is intended only to deliver the entire contents of the syringe (6 mg/0.6 mL) for direct administration. Use of the prefilled syringe is not recommended for direct administration for pediatric patients weighing less than 45 kg who require doses that are less than the full contents of the syringe.
2. UDENYCA (pegfilgrastim-cbqv) injection, for subcutaneous use. INITIAL U.S. APPROVAL: 2018
    a. UDENYCA (pegfilgrastim-cbqv) is biosimilar* to Neulasta (pegfilgrastim)
    b. UDENYCA (pegfilgrastim-cbqv) injection is a clear, colorless, preservative-free solution supplied in a prefilled single-dose syringe with an UltraSafe Passive Needle Guard, containing 6mg of pegfilgrastim-cbqv.
    c. UDENYCA is provided in a dispensing pack containing one 6 mg/0.6 mL prefilled syringe
    d. UDENYCA prefilled syringe does not bear graduation marks and is intended only to deliver the entire contents of the syringe (6 mg/0.6 mL) for direct administration.

   e. Use of the prefilled syringe is not recommended for direct administration for pediatric patients weighing less than 45 kg who require doses that are less than the full contents of the syringe.
3. FULPHILA (pegfilgrastim-jmdb) injection, for subcutaneous use. Initial U.S. Approval: 2018
   a. FULPHILA (pegfilgrastim-jmdb) is biosimilar* to NEULASTA (pegfilgrastim).
   b. Fulphila (pegfilgrastim-jmdb) Injection is a clear, colorless solution supplied in a prefilled single-dose syringe for manual use containing 6 mg pegfilgrastim-jmdb, supplied with a 29 gauge, 1/2-inch needle with an UltraSafe Passive Plus™ Needle Guard.
   c. Fulphila is provided in a dispensing pack containing one sterile 6 mg/0.6 mL prefilled syringe.
   d. Fulphila prefilled syringe does not bear graduation marks and is intended only to deliver the entire contents of the syringe (6 mg/0.6 mL) for direct administration.
   e. Use of the prefilled syringe is not recommended for direct administration for pediatric patients weighing less than 45 kg who require doses that are less than the full contents of the syringe.
4. ZIEXTENZO™ (pegfilgrastim-bmez) injection, for subcutaneous use. Initial U.S. Approval: 2019
   a. ZIEXTENZO (pegfilgrastim-bmez) is biosimilar* to NEULASTA (pegfilgrastim).
   b. ZIEXTENZO injection is a clear, colorless to slightly yellowish solution supplied in a prefilled single-dose syringe for manual use containing 6 mg pegfilgrastim-bmez, supplied with a 27-gauge, 1/2-inch needle with an UltraSafe Passive Needle Guard.
   c. ZIEXTENZO is provided in a dispensing pack containing one sterile 6 mg/0.6 mL prefilled syringe.
   d. ZIEXTENZO prefilled syringe does not bear graduation marks and is intended only to deliver the entire contents of the syringe (6 mg/0.6 mL) for direct administration.
   e. Use of the prefilled syringe is not recommended for direct administration for pediatric patients weighing less than 45 kg who require doses that are less than the full contents of the syringe.
5. NYVEPRIA™ (pegfilgrastim-apgf) injection, for subcutaneous use. Initial U.S. Approval: 2020
   a. NYVEPRIA (pegfilgrastim-apgf) is biosimilar* to NEULASTA (pegfilgrastim)
   b. NYVEPRIA (pegfilgrastim-apgf) injection is a clear, colorless solution supplied in a prefilled single-dose syringe for manual use containing 6 mg pegfilgrastim-apgf, supplied with a 27-gauge 1/2-inch needle and a BD UltraSafe Plus™ Passive Needle Guard.
   c. NYVEPRIA is provided in a dispensing pack containing one sterile 6 mg/0.6 mL prefilled syringe.
   d. NYVEPRIA prefilled syringe does not bear graduation marks and is intended only to deliver the entire contents of the syringe (6 mg/0.6 mL) for direct administration.
   e. Use of the prefilled syringe is not recommended for direct administration for pediatric patients weighing less than 45 kg who require doses that are less than the full contents of the syringe.
6. FYLNETRA (pegfilgrastim-pbbk) injection, for subcutaneous use. Initial U.S. Approval: 2022
   a. FYLNETRA single-dose prefilled syringe for manual use
   b. FYLNETRA (pegfilgrastim-pbbk) injection is a clear, colorless to slightly yellow, preservative-free solution supplied in a prefilled single-dose syringe for manual use

containing 6 mg pegfilgrastim-pbbk, supplied with a 27-gauge, 1/2-inch needle with an UltraSafe Plus Passive Needle Guard.

c. The needle cap on the prefilled syringe is not made with natural rubber latex.
d. FYLNETRA is provided in a dispensing pack containing one sterile 6 mg/0.6 mL prefilled syringe (NDC 70121-1627-1).
e. FYLNETRA prefilled syringe does not bear graduation marks and is intended only to deliver the entire contents of the syringe (6 mg/0.6 mL) for direct administration. Use of the prefilled syringe is not recommended for direct administration for pediatric patients weighing less than 45 kg who require doses that are less than the full contents of the syringe.

7. ROLVEDON™ (eflapegrastim-xnst) injection, for subcutaneous use Initial U.S. Approval: 2022
    a. Rolvedon (eflapegrastim-xnst) injection is a clear, colorless solution supplied in a singledose prefilled syringe containing 13.2 mg of eflapegrastim-xnst in 0.6 mL solution, with 29-gauge 1/2 inch pre-attached (staked) needle with a needle guard.
    b. Rolvedon is provided in a dispensing pack containing one sterile 13.2 mg/0.6 mL prefilled syringe (NDC 76961-101-01).
    c. Store refrigerated at 36°F to 46°F (2°C to 8°C) in the carton to protect from light. Do not shake. Discard syringes stored at room temperature for more than 12 hours. Do not freeze; discard syringe if frozen.

8. Stimufend (pegfilgrastim-fpgk) injection for subcutaneous use Initial U.S Approval: 2022
    a. STIMUFEND (pegfilgrastim-fpgk) injection is a single-dose prefilled syringe for manual use.
    b. STIMUFEND (pegfilgrastim-fpgk) injection is a clear, colorless, preservative-free solution containing 6mg pegfilgrastim-fpgk, supplied with a 27-guage, 1/2 -inch needle with a Safe-n-Sound passive needle Guard.
    c. The needle cap of the pre-filled syringe contains natural rubber (a derivative of latex).
    d. Stimufend pre-filled syringe does not bear graduation marks and is intended only to deliver the entire contents of the syringe (6 mg/0.6 mL) for direct administration. Use of the pre-filled syringe is not recommended for direct administration for pediatric patients weighing less than 45 kg who require doses that are less than the full contents of the syringe.

CODING

Applicable NDC Codes	
55513-0190-xx	Neulasta 6 mg prefilled syringe
55513-0192-xx	Neulasta 6 mg prefilled syringe Onpro Kit
67457-0833-xx	Fulphila 6 mg prefilled single-dose syringe
70114-0101-xx	Udenyca 6 mg prefilled single-dose syringe
61314-0866-xx	Ziextenzo 6 mg single-dose prefilled syringe

00069-0324-xx	Nyvepria 6 mg single-dose prefilled syringe
70121-1627-xx	Fylnetra 6 mg single-dose prefilled syringe
76961-0101-xx	Rolvedon 13.2 mg single-dose prefilled syringe
65219-0371-10	Stimufend 6mg single-dose prefilled syringe

Applicable Procedure Code	
J2506	Injection, pegfilgrastim, excludes biosimilar, 0.5 mg
Q5108	Injection, pegfilgrastim-jmdb, biosimilar, (Fulphila), 0.5 mg: 1 billable unit = 0.5 mg
Q5111	Injection, Pegfilgrastim-cbqv, biosimilar, (Udenyca), 0.5 mg; 1 billable unit = 0.5 mg
Q5120	Injection, pegfilgrastim-bmez, biosimilar, (Ziextenzo), 0.5 mg: 1 billable unit = 0.5 mg
Q5122	Injection, pegfilgrastim-apgf, biosimilar, (Nyvepria), 0.5 mg: 1 billable unit = 0.5 mg
J3590	Unclassified biologics

Applicable ICD-10 Codes	
D61.81	Pancytopenia
D70.1	Agranulocytosis secondary to cancer chemotherapy
D70.9	Neutropenia, unspecified
T45.1X5A	Adverse effect of antineoplastic and immunosuppressive drugs initial encounter
T45.1X5D	Adverse effect of antineoplastic and immunosuppressive drugs subsequent encounter
T45.1X5S	Adverse effect of antineoplastic and immunosuppressive drugs sequela
T66.XXXA	Radiation sickness, unspecified, initial encounter
T66.XXXD	Radiation sickness, unspecified, subsequent encounter
T66.XXXS	Radiation sickness, unspecified, sequela
W88.1	Exposure to radioactive isotopes
W88.8	Exposure to other ionizing radiation
Z41.8	Encounter for other procedures for purposes other than remedying health state
Z48.290	Encounter for aftercare following bone marrow transplant
Z51.11	Encounter for antineoplastic chemotherapy
Z51.12	Encounter for antineoplastic immunotherapy
Z51.89	Encounter for other specified aftercare
Z76.89	Persons encountering health services in other specified circumstances

EVIDENCE BASED REFERENCES

1. Neulasta [package insert]. Thousand Oaks, CA; Amgen Inc; February 2021. Accessed May 2021.
2. Fulphila [package insert]. Morgantown, WV; Mylan Pharmaceuticals; June 2020. Accessed May 2021.
3. Udenyca [package insert]. Redwood City, California; Coherus Biosciences; September 2019. Accessed May 2021.
4. Ziextenzo [package insert]. Princeton, NJ; Sandoz, Inc; September 2020. Accessed May 2021.
5. Nyvepria [package insert]. Lake Forest, IL; Pfizer Oncology; June 2020. Accessed May 2021.

6. Product Information: FYLNETRA(R) subcutaneous injection, pegfilgrastim-pbbk subcutaneous injection. Amneal Pharmaceuticals LLC (per FDA), Bridgewater, NJ, 2022.
7. Product Information: ROLVEDON(TM) subcutaneous injection, eflapegrastim-xnst subcutaneous injection. Spectrum Pharmaceuticals Inc (per manufacturer), Irvine, CA, 2022.
8. Product Information: STIMUFEND subcutaneous injection, pegfilgrastim-fpgk. Fresenius Kabi USA, LLC, Lake Zurich, Illinois, 2022.

POLICY HISTORY

Revision History	Month Day, Year	Updates
Original Effective Date	JULY 1, 2021	
Revision	JANUARY 1, 2022	New HCPCS code J2506 "Injection, pegfilgrastim, excludes biosimilar, 0.5 mg" - Effective January 1, 2022 Discontinue existing HCPCS J2505 "Injection, pegfilgrastim, 6 mg" - Effective December 31, 2021
	OCTOBER 25, 2022	Addition of non-preferred products Fylnetra & Rolvedon
	February 28th, 2023	Addition of non-preferred product Stimufend
P&T Committee Endorsement	MAY 24, 2021	
P&T Committee Endorsement	November 8th 2022	Addition of non-preferred products Fylnetra & Rolvedon
P&T Committee Endorsement	February 28th 2023	Addition of non-preferred product Stimufend