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Policy Number: C10419-A

Rolvedon, Neulasta and Related Biosimilars

PRODUCTS AFFECTED

Neulasta (pegfilgrastim); Fylnetra (pegfilgrastim-pbbk), Fulphila (pegfilgrastim-jmdb), Udenyca (pegfilgrastim-cbqv), Ziextenzo (pegfilgrastim-bmez), Nyvepria (pegfilgrastim-apgf injection), Rolvedon (eflapegrastim-xnst), Stimufend (pegfilgrastim-fpgk)

COVERAGE POLICY

Coverage for services, procedures, medical devices, and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Patients with Cancer Receiving Myelosuppressive Chemotherapy, Patients with Hematopoietic Subsyndrome of Acute Radiation Syndrome

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review.

FOR ALL INDICATIONS:
1. IF THIS IS A NON-FORMULARY/NON-PREFERRED PRODUCT FOR INITIAL OR CONTINUATION OF THERAPY REQUEST: Documentation of trial/failure of or intolerance to a majority (not more than 3) of the preferred formulary BIOLOGIC/PDL alternatives for the given diagnosis. Submit

documentation including medication(s) tried, dates of trial(s) and reason for treatment failure(s)
OR
IF THIS IS FOR A MEDICAL BENEFIT REQUEST: BIOSIMILAR DRUGS are preferred when requested as a physician administered drug and/or pharmacy formulary product per applicable state regulations and there is a lack of data demonstrating clinical superiority of reference drugs over the FDA approved biosimilar drugs. A reference medication is approved under the following conditions: (a) Treatment with at least two (2) associated biosimilar drug(s) has been ineffective, not tolerated, or is contraindicated (i.e. an allergic reaction to a specific inactive ingredient in the preferred biologic product or biosimilar OR (b) an adverse reaction to a specific inactive ingredient in the preferred biologic product or biosimilar OR (c) therapeutic success while taking a non-preferred biologic productor biosimilar and therapeutic failure while taking the preferred biologic product or biosimilar documented by patient diary or medical charted notes)
[DOCUMENTATION REQUIRED-Document when the preferred biologic product or biosimilar was tried and the length of the trial period, Provide specific clinical documentation of therapeutic failure on the preferred biologic product or biosimilar whenever possible. Describe the medical problem caused by the preferred referenced biologic. Vague and non-descriptive symptoms are not adequate rationale (e.g., stomachache)]

A. FEBRILE NEUTROPENIA PROPHYLAXIS IN NON-MYELOID MALIGNANCIES:
1. Documented diagnosis of non-myeloid malignancy
   AND
2. Documentation that pegfilgrastim is being used following myelosuppressive chemotherapy [Documentation of current chemotherapy regimen, any previous chemotherapy regimens, and anticipated treatment plan] [DOCUMENTATION REQUIRED]
   AND
3. (a) Member has a risk of febrile neutropenia (FN) of greater than 20% based on current chemotherapy regimen (as listed in current ASCO and NCCN guidelines for myeloid growth factors [See Appendix]
   OR
   (b) Member has a risk of febrile neutropenia of 10-20% based on chemotherapy regimen, and at least ONE of the following risk factors apply:
   - (i) Prior chemotherapy or radiation therapy
   - (ii) Persistent neutropenia (defined as neutrophil count less than 500 neutrophils/mcL or less than 1,000 neutrophils/mcL and a predicted decline to less than or equal to 500 neutrophils/mcL over next 48 hours)
   - (iii) Bone marrow involvement by tumor
   - (iv) Recent surgery and/or open wounds
   - (v) Liver dysfunction (bilirubin greater than 2.0 mg/dL)
   - (vi) Renal dysfunction (creatinine clearance less than 50 mL/min)
   - (vii) Age greater than 65 receiving full chemotherapy dose intensity

   OR
   (c) Previous neutropenic fever complication from a prior cycle of similar chemotherapy
   OR
   (d) The member is receiving a dose-dense chemotherapy regimen
   AND
4. FOR PEDIATRIC MEMBERS: Documentation of member's current weight (within the last 30 days)

B. HEMATOPOIETIC SUB SYNDROME OF ACUTE RADIATION SYNDROME (Requests for Neulasta):
1. Documented diagnosis of member who has confirmed or suspected radiation injury due to accidental or intentional total body radiation of greater than 2 Grays (Gy) [DOCUMENTATION REQUIRED]

CONTINUATION OF THERAPY:

A. FEBRILE NEUTROPENIA PROPHYLAXIS IN NON-MYELOID MALIGNANCIES:
   1. Member is compliant with pegfilgrastim therapy as verified by prescriber and fill history
      AND
   2. Documentation of clinical benefits to support continuation of treatment including positive response to therapy (i.e., member did not become neutropenic mid-cycle requiring G-CFS) [DOCUMENTATION REQUIRED]
      AND
   3. Prescriber attests to regular lab monitoring (i.e., CBC and platelet count) as clinically appropriate
      AND
   4. Documentation of disease status/progression
      AND
   5. FOR PEDIATRIC MEMBERS: Documentation of member's current weight (within the last 30 days)

B. HEMATOPOIETIC SUB SYNDROME OF ACUTE RADIATION SYNDROME
   1. N/A; new authorization required.

DURATION OF APPROVAL:

For Febrile Neutropenia Prophylaxis in Non-Myeloid Malignancies:
Initial authorization: One chemotherapy cycle or 12 weeks, Continuation of Therapy: for up to 6 months

For Hematopoietic Subsyndrome of Acute Radiation Syndrome-Neulasta only:
Initial authorization: 1 month, Continuation of therapy: N/A

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with a board-certified hematologist, oncologist, or transplant specialist. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

Pegfilgrastim: None
Rolvedon (eflapegrastim-xnst): 18 years of age or older

QUANTITY:

Pegfilgrastim-

Febrile Neutropenia Prophylaxis: 6mg once per chemo cycle
Hematopoietic Sub Syndrome of Acute Radiation Syndrome: The recommended dose of Neulasta is two doses, 6 mg each, administered subcutaneously one week apart.
Dose is adjusted if weight is <45kg:
<10 kg: 0.1 mg/kg
10-20 kg: 1.5 mg
21-30 kg: 2.5 mg
31-44 kg: 4 mg

Up to 2 prefilled syringes (1.2mL) per 28 days (1 prefilled syringe per chemotherapy cycle), Up to 2 OnPro kits per 28 days (1 OnPro kit per chemotherapy cycle)

Rolvedon (eflapegrastim-xnst)

13.2 mg administered subcutaneously once per chemotherapy cycle

PLACE OF ADMINISTRATION:

The recommendation is that injectable medications in this policy will be for pharmacy or medical benefit coverage and the subcutaneous injectable products administered in a place of service that is a

non- hospital facility-based location as per the Molina Health Care Site of Care program.

Note: Site of Care Utilization Management Policy applies for Fulphila (pegfilgrastim), Fylnetra (pegfilgrastim-pbbk), Neulasta (pegfilgrastim), Udenyca (pegfilgrastim-cbqv), Ziextenzo (pegfilgrastim- bmez), Nyvepria (pegfilgrastim-apgf injection), Rolvedon (eflapegrastim-xnst), Stimufend (pegfilgrastim-fpgk) For information on site of care, See Specialty Medication Administration Site of Care Coverage Criteria (molinamarketplace.com)

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Subcutaneous

DRUG CLASS:
Granulocyte Colony-Stimulating Factors (G-CSF)

FDA-APPROVED USES:
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.

NEULASTA ONLY: Increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Sub syndrome of Acute Radiation Syndrome).

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
A biosimilar is highly similar version of a brand name biological drug that meets strict controls for structural, pharmaceutical, and clinical consistency. A biosimilar manufacturer must demonstrate that there are no meaningful clinical differences (i.e., safety and efficacy) between the biosimilar and the reference product. Clinical performance is demonstrated through human pharmacokinetic (exposure)and pharmacodynamic (response) studies, an assessment of clinical immunogenicity, and, if needed, additional clinical studies.[1] As costs for biological specialty drugs continue to rise, the growing biosimilar market will benefit providers and patients by broadening biological treatment options and expanding access to these medications at lower costs.
Molina Healthcare, Inc. continues to be committed to continually reevaluating Preferred strategies and applying innovative cost-controls to ensure patients receive safe, effective, and quality healthcare. This commitment includes potentially creating a preference for biosimilars when value can be added without compromising patient satisfaction and safety.

1. Food and Drug Administration. Biosimilar and Interchangeable Products. Retrieved from https://www.fda.gov/drugs/biosimilars/biosimilar-and-interchangeable-products. Accessed October 8, 2019.

High risk for chemotherapy induced FN infectious complications because of bone marrow compromise OR co-morbidity with any of the following risk factors (not an all-inclusive list):
Age >65 years
Poor performance status
Previous episodes of FN
History of previous chemotherapy or radiation
therapy Completion of combined chemoradiotherapy
Bone marrow involvement by tumor producing
cytopenia Pre-existing neutropenia
Poor nutritional status

Poor renal function
Liver dysfunction (i.e., elevated bilirubin)
Presence of open wound(s) or active infection Recent surgery (within the past 12 weeks) More advanced cancer
Other serious co-morbidities

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
None

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of pegfilgrastim and its biosimilars are considered experimental/investigational and therefore, will follow Molina's Off-Label policy [Use in routine infection prophylaxis (e.g., adjunctive therapy to antibiotics in a member with uncomplicated febrile neutropenia, afebrile neutropenia). Continued use beyond 42 days with no response. Concurrent use with other CSF agents (Neupogen, Leukine). Known hypersensitivity to pegfilgrastim or any ingredient in the requested formulation. E. coli protein hypersensitivity. Receiving chemotherapy with a risk of febrile neutropenia <20% and no significant high risk for complications. Pegfilgrastim will be administered in the period between 14 days before and 24 hours after administration of cytotoxic chemotherapy]. Contraindications to pegfilgrastim and eflapegrastim include: Patients with a history of serious allergic reactions to human granulocyte colony-stimulating factors such as eflapegrastim, pegfilgrastim or filgrastim.

OTHER SPECIAL CONSIDERATIONS:
None

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
Q5111	Inj, pegfilgrastim-cbqv, biosimilar, (udenyca) 0.5mg
Q5108	Inj, pegfilgrastim-jmdb, biosimilar, (fulphila), 0.5mg
J2506	Injection, pegfilgrastim, excludes biosimilar, 0.5mg
Q5120	Injection, pegfilgrastim-bmez, biosimilar, (ziextenzo)0.5 mg
Q5122	Injection, pegfilgrastim-apgf, biosimilar, (nyvepria), 0.5 mg
Q5130	Unclassified biologics (Fylnetra)
J1449	Unclassified biologics (Rolvedon)
Q5127	Unclassified biologics (Stimufend)

AVAILABLE DOSAGE FORMS:
Neulasta (pegfilgrastim) 6mg/0.6mL prefilled syringe, 6mg/0.6mL OnPro kit
Fulphila (pegfilgrastim-jmdb) 6mg/0.6mL prefilled syringe
Udenyca 6mg/0.6mL prefilled syringe
Ziextenzo SOSY 6MG/0.6ML prefilled syringe
NYVEPRIA 6 mg/0.6 mL prefilled syringe
Rolvedon 13.2 mg/0.6 mL solution in a single dose prefilled syringe
Stimufend SOSY 6MG/0.6ML solution in a single dose prefilled syringe

REFERENCES

1. Neulasta [package insert]. Thousand Oaks, CA; Amgen Inc; February 2021.
2. Fulphila [package insert]. Morgantown, WV; Mylan GmbH; October 2021
3. Udenyca [package insert]. Coherus Biosciences. Redwood City, CA; June 2021.
4. Ziextenzo [package insert]. Princeton, NJ; Sandoz Inc.; March 2021.
5. NYVEPRIA [package insert]. Lake Forest, IL; Hospira Inc., a Pfizer Company; April 2021.
6. Fylnetra [package insert]. Piscataway, NJ; Amneal Pharmaceuticals LLC; May 2022.
7. Rolvedon (eflapegrastim) [prescribing information]. Irvine, CA: Spectrum Pharmaceuticals Inc; September 2022.
8. Stimufend (pegfilgrastim-fpgk) [prescribing information]. Lake Zurich, IL: Fresenius Kabi USA, LLC; September 2022.
9. National Comprehensive Cancer Network. 2022. Hematopoietic Growth Factors (Version 1.2023). [online] Available at: < growthfactors.pdf (nccn.org)> [Accessed 8 December 2022]
10. Chemoradiotherapy with or without granulocyte-macrophage colony-stimulating factor in the treatment of limited-stage small-cell lung cancer: a prospective phase III randomized study of the Southwest Oncology Group Bunn PA Jr, Crowley J, Kelly K, Hazuka MB, Beasley K, Upchurch C, Livingston R, Weiss GR, Hicks WJ, Gandara DR. J Clin Oncol. 1995;13(7):1632
11. Intensified hyperfractionated accelerated radiotherapy limits the additional benefit of simultaneous chemotherapy--results of a multicentric randomized German trial in advanced head-and-neck cancer. Staar S, Rudat V, Stuetzer H, Dietz A, Volling P, Schroeder M, Flentje M, Eckel HE, Mueller RP. Int J Radiat Oncol Biol Phys. 2001;50(5):1161

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Title Products Affected Age Restrictions Quantity Contraindications/Exclusions/Discontinuation Coding/Billing Information Available Dosage Forms References	Q1 2023
REVISION- Notable revisions: Products Affected Required Medical Information Continuation of Therapy Duration of Approval Quantity Contraindications/Exclusions/Discontinuation References	Q4 2022
Q2 2022 Established tracking in new format	Historical changes on file