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Section:	Prescription Drugs	**Effective Date:**	January 1, 2021
Subsection:	Hematological Agents	**Original Policy Date:**	December 7, 2011
Subject:	Neulasta Fulphila Nyvepria Udenyca Ziextenzo	**Page:**	1 of 6

Last Review Date: December 4, 2020

Neulasta Fulphila Nyvepria Udenyca Ziextenzo

Description

Neulasta, Neulasta Onpro (pegfilgrastim), **Fulphila** (pegfilgrastim-jmdb), **Nyvepria** (pegfilgrastim-apgf), **Udenyca** (pegfilgrastim-cbqv), **Ziextenzo** (pegfilgrastim-bmez)

Bolded medications are the preferred products

Background

Neutropenia (<500 neutrophils/mcl or <1,000 neutrophils/mcl and a predicted decline to ≤ 500/mcl over the next 48 hours) and resulting febrile neutropenia (≥ 38.3°C orally or ≥38.0°C over 1 hour) can be induced by myelosuppressive chemotherapy. Febrile neutropenia is a major dose-limiting toxicity of chemotherapy. Major infections, hospitalizations, dose reductions or treatment delays are resultant serious complications (1).

Neulasta (pegfilgrastim) and its biosimilars are granulocyte colony-stimulating factors (G-CSF) that act on hematopoietic cells by binding to specific cell surface receptors, thereby stimulating proliferation, differentiation, commitment, and end cell functional activation. The product is a covalent conjugate of recombinant methionyl human G-CSF (filgrastim) and monomethoxypolyethylene glycol. Fulphila, Nyvepria, Udenyca, and Ziextenzo are biosimilars to Neulasta (1-6).

Regulatory Status
FDA-approved indication:

Neulasta and its biosimilars are leukocyte growth factors indicated: (2-6)

- 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

Neulasta is indicated: (2)

- To increase survival in patients acutely exposed to myelosuppressive doses of radiation

Neulasta and its biosimilars are not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation (2-6).

The FDA defines biosimilar as a biological product that is highly similar to and has no clinically meaningful differences from an existing FDA-approved reference product. A manufacturer developing a proposed biosimilar demonstrates that its product is highly similar to the reference product by extensively analyzing the structure and function of both the reference product and the proposed biosimilar. Minor differences between the reference product and the proposed biosimilar in clinically inactive components are acceptable. Manufacturers must also demonstrate that its proposed biosimilar has no clinically meaningful differences from the reference product in terms of safety, purity, and potency (safety and effectiveness) (7).

Related policies
Leukine, Neupogen Granix Nivestym Zarxio

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Neulasta and its biosimilars may be considered **medically necessary** for the prophylaxis or treatment of chemotherapy induced febrile neutropenia and acute radiation syndrome and if the conditions indicated below are met.

Neulasta and its biosimilars may be considered **investigational** for all other indications.

Prior-Approval Requirements

Diagnoses

Patient must have **ONE** the following:

1. Prophylaxis for chemotherapy induced febrile neutropenia
2. Treatment of chemotherapy induced febrile neutropenia
3. Acute radiation syndrome

AND the following for **ALL** diagnoses:

a. **NOT** used in combination with another granulocyte colony-stimulating factor (G-CSF)
b. **Neulasta and Neulasta Onpro only:** Patient **MUST** have tried at least **TWO** of the preferred products (Fulphila, Nyvepria, Udenyca, Ziextenzo) unless the patient has a valid medical exception (e.g. inadequate treatment response, intolerance, contraindication)

Prior – Approval *Renewal* Requirements

Same as above

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 6 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Neutropenia (<500 neutrophils/mcl or <1,000 neutrophils/mcl and a predicted decline to ≤ 500/mcl over the next 48 hours) and resulting febrile neutropenia (≥ 38.3°C orally or ≥38.0°C over 1 hour) can be induced by myelosuppressive chemotherapy. Neulasta (pegfilgrastim) and

its biosimilars are granulocyte colony-stimulating factors (G-CSF) that act on hematopoietic cells by binding to specific cell surface receptors, thereby stimulating proliferation, differentiation, commitment, and end cell functional activation (1-6).

Prior authorization is required to ensure the safe, clinically appropriate and cost-effective use of Neulasta and its biosimilars while maintaining optimal therapeutic outcomes.

References

1. NCCN Clinical Practice Guidelines in Oncology® Hematopoietic Growth Factors (Version 2.2020). National Comprehensive Cancer Network, Inc. January 2020.
2. Neulasta [package insert]. Thousand Oaks, CA: Amgen Inc.; January 2020.
3. Fulphila [package insert]. Zurich, Switzerland: Mylan GmbH; June 2020.
4. Nyvepria [package insert]. New York, NY: Pfizer Inc.; June 2020.
5. Udenyca [package insert]. Redwood City, CA: Coherus BioSciences, Inc.; September 2019.
6. Ziextenzo [package insert]. Princeton, NJ: Sandoz Inc.; September 2020.
7. Biosimilar and Interchangeable Products. U.S. Food & Drug Administration. October 23, 2017. https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/ucm580419.htm#generic

Policy History

Date	Reason
July 2010	ICD-9 code was removed for myelosuppressive chemotherapy, to decrease the incidence of infection as manifested by febrile neutropenia (various), bone marrow transplantation (996.85), peripheral blood progenitor cell collection (various), acceleration of myeloid recovery in patients with non-Hodgkin's lymphoma, ALL or Hodgkin's disease undergoing bone marrow transplantation (various), induction chemotherapy in acute myelogenous leukemia (various), mobilization and following transplantation of autologous PBPC (various), myeloid reconstitution after allogenic bone marrow transplantation (various), severe chronic neutropenia (various) and bone marrow transplantation failure or engraftment delay (996.0-996.5). ICD-9 code was updated for bone marrow transplantation failure or engraftment delay (996.82). ICD-10 code

	was added for bone marrow transplantation failure or engraftment delay (T86.02).
November 2010	Separation of colony stimulating factors to improve functionality and workflow; remove non-FDA approved indications (including ICD-9 and 10 codes) as follows: Myelodysplastic Syndrome (MDS), Myeloid engraftment following bone marrow transplantation, Myeloid engraftment following hematopoietic stem cell transplantation, Congenital, Cyclic, or Idiopathic Neutropenia, Neutropenia associated with AIDS treatment, and Peripheral progenitor cell yield.
September 2011	Separation of the colony stimulating agents' criterion; Neulasta is not FDA approved for the same indications as Leukine and Neupogen. Removal of ICD-9 and 10 codes due to lack of specificity.
December 2011	Aligned with Medical Policy
December 2012	Annual Review-editorial updates
March 2014	Annual review and decreased approval and renewal limits to 6 months
March 2015	Annual editorial review and reference update Addition of not used in combination with another granulocyte colony-stimulating factor (G-CSF)
December 2015	Addition of new indication acute radiation syndrome
March 2016	Annual editorial review Policy number changed from 5.10.09 to 5.85.09
December 2016	Annual editorial review and reference update
September 2017	Annual review and reference update
July 2018	Addition of Fulphila biosimilar to criteria
September 2018	Annual review Addition of off-label indications to Fulphila per SME
November 2018	Annual review and reference update. Addition of Udenyca biosimilar to criteria
March 2019	Annual review. Revised regulatory status section to separate indications based on medication per SME
December 2019	Annual review. Addition of requirement to trial preferred products. Addition of Ziextenzo biosimilar to criteria. Renamed policy Neulasta Fulphila Udenyca Ziextenzo
March 2020	Annual review and reference update
July 2020	Addition of Nyvepria biosimilar
September 2020	Annual review
December 2020	Annual review and reference update. Added Ziextenzo and Nyvepria as preferred products

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 4, 2020 and is effective on January 1, 2021.