



IEHP UM Subcommittee Approved Authorization Guideline			
Guideline	Reference Product Pegfilgrastim and Biosimilar Products	Guideline #	UM_OTH 19
		Original Effective Date	11/13/2019
Section	Other	Revision Date	

COVERAGE POLICY

A. Neulasta (pegfilgrastim)

Requests may be approved if all of the following criteria are met:

1. Treatment with **Fulphila** (pegfilgrastim-jmdb) and **Udenyca** (pegfilgrastim-cbqv) has been ineffective, not tolerated, or both are contraindicated; and
2. Requested dosage is consistent with FDA approved labeling

B. Neulasta Onpro (pegfilgrastim autoinjector device)

Requests may be approved if all of the following criteria are met:

1. Documentation that patient is not able to return to provider office (due to significant behavioral issues, physical difficulties or cognitive impairment) for administration of **Fulphila** (pegfilgrastim-jmdb) or **Udenyca** (pegfilgrastim-cbqv); and
2. Milliman Care Guidelines (MCG) criteria for Granulocyte Colony-Stimulating Factor (G-CSF) are met; and
3. Requested dosage is consistent with FDA approved labeling

C. Fulphila (pegfilgrastim-jmdb)

Requests may be approved if all of the following criteria are met:

1. Pegfilgrastim-jmdb is reimbursable when used to reduce the incidence of neutropenia-related infection in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.
1. Requested dosage is consistent with FDA approved labeling

D. Udenyca (pegfilgrastim-cbqv)

Requests may be approved if all of the following criteria are met:

1. Milliman Care Guidelines (MCG) for Granulocyte Colony-Stimulating Factor (G-CSF) or Granulocyte Macrophage Colony Stimulating Factor (GM-CSF) A-0314 is met
2. Requested dosage is consistent with FDA approved labeling

E. Continued Therapy

Re-authorization may be reviewed every 6 months. Clinical documentation (including, but not limited to chart notes) must be provided to confirm that current medical necessity criteria are met.

COVERAGE LIMITATIONS AND EXCLUSIONS

Request for investigational indications that lack established clinical benefits and safety are not covered.

ADDITIONAL INFORMATION

The Biological Price Competition and Innovation Act passed in 2009 established the pathway for approval of biosimilars with the goal of reducing expenditure for costly biologic drug. A biosimilar is a biological product that demonstrates high similarity to the FDA-approved originator (reference) product by extensive comparative analysis of the products, such as purity, chemical identity and bioactivity. The FDA may approve biosimilars for the same indications as the originator product when human pharmacokinetic and pharmacodynamic studies also demonstrated no clinically meaningful differences from the reference product in terms of safety, purity and potency⁵.

In 2018, the U.S. Food and Drug Administration (FDA) approved the first pegfilgrastim biosimilars, pegfilgrastim-jmdb (**Fulphila**) and pegfilgrastim-cbqv (**Udenyca**), for the same indications as their reference product pegfilgrastim (**Neulasta**). They are the long-acting granulocyte-colony stimulating factors (G-CSFs) that help reduce the risk of febrile neutropenia in patients with non-myeloid malignancies receiving myelosuppressive chemotherapy.

Applicable Codes

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement policy.

HCPCS Code	Description
J2505	Injection, pegfilgrastim, 6mg
Q5108	Injection, pegfilgrastim-jmdb, biosimilar, (fulphila), 0.5mg
Q5111	Injection, pegfilgrastim-cbqv, biosimilar, (udenyca), 0.5mg

CLINICAL/REGULATORY RESOURCE

B. Department of Health Care Services Medi-Cal Provider Manual:

1. Pegfilgrastim-jmdb is reimbursable when used to reduce the incidence of neutropenia-related infection in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

C. Milliman Care Guidelines (MCG) 22nd Edition 2019:

1. Granulocyte colony-stimulating factor (G-CSF) or granulocyte-macrophage colony-stimulating factor (GM-CSF) may be indicated for 1 or more of the following:
 - a. Acute myeloid leukemia and 1 or more of the following:
 - i. Induction chemotherapy using filgrastim
 - ii. Induction chemotherapy using sargramostim and ALL of the following:

- Age 55 years or older
 - Less than 10% blasts in bone marrow or blood
- iii. Consolidation chemotherapy using filgrastim
 - iv. Salvage chemotherapy following relapse
- b. Acute radiation exposure and 1 or more of the following:
 - i. Absolute neutrophil count less than 500/mm³ (0.5 x10⁹/L) and expected to persist for 1 week or more
 - ii. Lymphocyte count less than 1400/mm³ (1.4 x10⁹/L) at 48 hours
 - iii. Radiation dose (confirmed or suspected) of greater than 2 Gy
 - c. Myelodysplastic syndrome and ALL of the following:
 - i. Absolute neutrophil count less than 1500/mm³ (1.5 x10⁹/L)
 - ii. History of recurrent or resistant infections
 - d. Myeloid engraftment for hematopoietic stem cell transplant and 1 or more of the following
 - i. Hematopoietic stem cell transplant failure or delay in engraftment
 - ii. Mobilization of peripheral blood progenitor cell prior to stem cell transplant
 - iii. Nonmyeloid malignancy undergoing myeloablative chemotherapy followed by bone marrow or peripheral blood progenitor cell transplant
 - e. Myelosuppressive chemotherapy for nonmyeloid malignancy (first cycle) and 1 or more of the following
 - i. Administration of 3 or more myelosuppressive agents
 - ii. Age 65 years or older
 - iii. Chemotherapy regimen has historical risk of febrile neutropenia of greater than 20%
 - iv. Elevated alkaline phosphatase
 - v. Elevated bilirubin
 - vi. Elevated lactate dehydrogenase
 - vii. Glomerular filtration rate less than 30 mL/min/1.73m² (0.50 mL/sec/1.73m²)
 - viii. HIV infection with low CD4 counts
 - ix. Low serum albumin
 - x. Low serum hemoglobin
 - xi. Pre-existing bone marrow involvement with tumor
 - xii. Pre-existing infection
 - xiii. Pre-existing neutropenia
 - xiv. Pre-existing open wound
 - xv. Previous chemotherapy
 - xvi. Previous radiation therapy
 - xvii. Recent surgery
 - f. Myelosuppressive chemotherapy for nonmyeloid malignancy (subsequent cycle) and ALL of the following:
 - i. Chemotherapy dose delay or reduction is not desirable
 - ii. History of neutropenia, as indicated by 1 or more of the following:
 - Febrile neutropenia with prior chemotherapy cycle
 - Prolonged neutropenia with prior chemotherapy cycle

- g. Severe chronic neutropenia, as indicated by 1 or more of the following:
 - i. Diagnosis of congenital neutropenia confirmed
 - ii. Diagnosis of cyclic neutropenia confirmed
 - iii. Diagnosis of idiopathic neutropenia confirmed

D. National Comprehensive Cancer Network (NCCN) Drugs & Biologics Compendium 2019:

NCCN Recommended Use	Neulasta (pegfilgrastim)	Fulphila (pegfilgrastim- jmdb)	Udenyca (pegfilgrastim- cbqv)
Treatment for patients who present with acute exposure to myelosuppressive doses of RT	2A	2A	2A
Prophylaxis of chemotherapy-induced febrile neutropenia or other dose-limiting neutropenic events in intermediate-risk (10% to 20% overall risk of febrile neutropenia) patients with solid tumors and nonmyeloid malignancies receiving treatment in the curative/adjuvant or palliative settings who have one or more patient risk factors	2A	2A	2A
Prophylaxis of chemotherapy-induced febrile neutropenia or other dose-limiting neutropenic events in high-risk (>20% overall risk of febrile neutropenia) patients with solid tumors and nonmyeloid malignancies receiving treatment in the curative/adjuvant or palliative settings	1	2A	2A
Used for supportive care post autologous hematopoietic cell transplant	2A	--	--

E. National Comprehensive Cancer Network (NCCN) Hematopoietic Growth Factor Clinical Practice Guidelines 2019:

1. In 2018, the FDA approved the first pegfilgrastim biosimilars, pegfilgrastim-jmdb and pegfilgrastim-cbqv, for the same indications as their reference products. The FDA’s approval of these biosimilars was based on review of evidence including structural and functional characterization, animal study data, human pharmacokinetic and pharmacodynamic data, clinical immunogenicity data and other clinical safety and effectiveness data.
2. Pegfilgrastim-jmdb
 - a. Pegfilgrastim-jmdb has been shown to have high analytical and functional similarity to pegfilgrastim, with similar structure, molecular mass, physiochemical characteristics, impurities and G-CSF receptor binding affinity. A phase I randomized equivalence trial concluded that pegfilgrastim-jmdb demonstrated similar pharmacokinetics, pharmacodynamics and safety to pegfilgrastim in healthy volunteers.
 - b. In a multicenter randomized phase III efficacy and safety trial, breast cancer patients receiving myelosuppressive chemotherapy with pegfilgrastim-jmdb

support showed no difference in the duration of severe neutropenia, time to ANC nadir, duration of post-nadir recovery, or treatment-related adverse events compared to patients receiving reference pegfilgrastim.

3. Pegfilgrastim-cbqv

- a. Although data are limited, pegfilgrastim-cbqv was shown to have a similar safety profile and bioequivalent pharmacokinetics and pharmacodynamics to pegfilgrastim in 122 healthy volunteers in a multicenter randomized crossover study. No serious treatment-related adverse events were observed with the use of pegfilgrastim-cbqv.

DEFINITION OF TERMS

1. Biosimilar – A biological product that is highly similar to the FDA-approved originator (reference) product with the exception of minor differences in clinically inactive components and no differences in efficacy, safety and purity⁴.

REFERENCES

1. Department of Health Care Services Medi-Cal Provider Manual. Available at: http://files.medi-cal.ca.gov/pubsdoco/Manuals_menu.asp. Accessed on October 8, 2019.
2. Milliman Care Guidelines (MCG) 22nd Edition [database online]. Seattle, WA: MCG Health, 2019. Available at: <https://cgi.careguidelines.com/login-careweb.htm>. Updated periodically.
3. National Comprehensive Cancer Network (NCCN) Drugs & Biologics Compendium [database online]. Plymouth Meeting, PA: National Comprehensive Cancer Network, Inc., 2019. Available at: www.NCCN.org. Updated periodically.
4. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology, Hematopoietic Growth Factors. Version 2.2019. Available at: www.NCCN.org. Last revised on March 27, 2019. Accessed on October 9, 2019.
5. U.S. Food and Drug Administration. Biosimilar and Interchangeable Products. Available at: <https://www.fda.gov/drugs/biosimilars/biosimilar-and-interchangeable-products>. Accessed October 9, 2019.

DISCLAIMER

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