Department:	Pharmacy Management	**Original Approval:**	01/20/2016
Policy #:	PM128	**Last Approval:**	12/12/2018
Title:	Pegfilgrastim Products (Neulasta, Fulphila)		
Approved By:	Medical Management Leadership Team		

REQUIRED CLINICAL DOCUMENTATION FOR REVIEW.

History and/or physical examination notes and relevant specialty consultation notes that address the problem and need for the service: -Diagnosis -Prescribed by or in consultation with an oncologist or hematologist or a physician that specializes in transplantation -Medication list (current and past) to include start and end dates of all chemotherapy agents -Age -Labs/diagnostics -Weight -Dosing and duration requested -Initial/extended approval.

BACKGROUND

Neulasta is a leukocyte growth factor, sometimes referred to as a granulocyte colony stimulating factor (G-CSF).[1] Neulasta is indicated 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.[1] For this indication, Neulasta is to be administered as a single subcutaneous (SC) injection (6 mg) once per chemotherapy cycle. The Neulasta prescribing information also gives dosing recommendations in pediatric patients weighing < 45 kg. Neulasta should not be administered in the period between 14 days before and 24 hours after administration of cytotoxic chemotherapy. Neulasta is also indicated to increase survival in patients acutely exposed to myelosuppressive doses of radiation (patients with hematopoietic subsyndrome of acute radiation syndrome). For this indication, the recommended dose of Neulasta is two doses, 6 mg each, given SC once week apart. Refer to the Neulasta prescribing information for pediatric patients < 45 kg. Administer the first dose as soon as possible after suspected or confirmed exposure to radiation levels greater than 2 gray.

DEFINITIONS

None.

INDICATIONS/CRITERIA

Medicaid Members	There is no preferred Pegfilgrastim on the WA HCA Single Preferred Drug list. Neulasta, Neulasta Onpro and Fulphila are not considered for approval unless member has tried and failed the preferred product (Neupogen). ***Continue to criteria for approval below.***

Medicare Members	***Step-utilization of Part D drugs not required.***

Coverage of pegfilgrastim is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. Patients with Cancer (Adults and Children) Receiving Myelosuppressive Chemotherapy.

Criteria. *The patient must meet the following criteria (A AND B):*

- **A)** The agent is prescribed by, or in consultation with, an oncologist or hematologist; AND
- **B)** The patient meets ONE of the following conditions (i, ii, or iii):
  - **i.** The patient is receiving myelosuppressive anti-cancer medications that are associated with a high risk of febrile neutropenia (i.e., the risk of febrile neutropenia is at least 20% based on the chemotherapy regimen); OR
  - **ii.** The patient is receiving myelosuppressive anti-cancer medications that are associated with a risk of febrile neutropenia but the risk is less than 20% based on the chemotherapy regimen and the patient has one or more risk factors for febrile neutropenia according to the prescribing physician (e.g., aged ≥ 65 years; prior chemotherapy or radiation therapy; persistent neutropenia; bone marrow involvement by tumor; recent surgery and/or open wounds; liver and/or renal function; poor performance status; or human immunodeficiency virus [HIV] infection); OR
  - **iii.** The patient has had a neutropenic complication from prior chemotherapy and did not receive prophylaxis with a colony stimulating factor (Leukine® [sargramostim injection], filgrastim products [Neupogen, Zarxio, Granix, Nivestym], pegfilgrastim products [Neulasta, Fulphila]) and a reduced dose or frequency of chemotherapy may compromise treatment outcome.

Neulasta and Fulphila are indicated 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.[1-3] The National Comprehensive Cancer Network (NCCN) guidelines for myeloid growth factors (version 1.2018), recommends use of CSF in various scenarios in patients with cancer receiving myelosuppressive chemotherapy.[2] Data are also available in children.[1,4-7] In the professional opinion of specialist physicians reviewing the data, we have adopted these criteria.

Dosing in Patients with Cancer Receiving Myelosuppressive Chemotherapy: *Dosing must meet ONE of the following (A, B OR C)*:

- **A)** In adults, the dose is a single SC injection of 6 mg administered once per chemotherapy cycle[1]; OR
- **B)** In children, a single 100 mcg per kg dose is given SC once per chemotherapy cycle; maximum dose is 6 mg.[1-2,4-7]
- **C)** For pediatric patients < 45 kg give a single SC dose once per chemotherapy cycle as follows: 4 mg (0.4 mL) is recommended in patients 31 to 44 kg; 2.5 mg (0.25 mL) is recommended for patients 21 to 30 kg; 1.5 mg (0.15 mL) is recommended for patients 10 to 20 kg; and 0.1 mg/kg

(0.01 mL/kg) is recommended for patients < 10 kg. Of note, the Neulasta/Fulphila prefilled syringe is not designed to allow for direct administration of doses < 0.6 mL (6 mg). The syringe does not bear graduation marks, which are needed to accurately measure doses of Neulasta/Fulphila < 0.6 mL (6 mg) for direct administration to patients. Thus, the direct administration to patients requiring dosing of < 0.6 mL (6 mg) is not recommended due to the potential for errors.

According to the NCCN guidelines for myeloid growth factors (version 1.2018), Pegfilgrastim should be administered the day after chemotherapy but Pegfilgrastim can also be administered up to 3 to 4 days after chemotherapy.[2] For patients who cannot return to the clinic for next-day administration, alternative options exist. Evidence is available to support use for chemotherapy regimens given once every 3 weeks. Phase II data demonstrate efficacy for chemotherapy regimens given every 2 weeks. In sufficient data support use for cytotoxic chemotherapy regimens given once every week; therefore, Pegfilgrastim should not be used.

Initial Approval/Extended Approval.

A) *Initial Approval*. Approval is for up to 6 months at one dose per each chemotherapy cycle. Multiple doses in the same cycle are not recommended.

B) *Extended Approval*. Approval is for up to 6-month intervals if the patient continues to receive myelosuppressive chemotherapy.

Duration of Therapy in Patients with Cancer Receiving Myelosuppressive Chemotherapy. Therapy may continue as long as the patient is receiving myelosuppressive chemotherapy with one dose per cycle.

Labs/Diagnostics. None required.

2. Radiation Syndrome (Hematopoietic Syndrome of Acute Radiation Syndrome).

Criteria. *The patient must meet the following criteria*: The agent is prescribed by, or in consultation with, a physician with expertise in treating acute radiation syndrome.

Neulasta is indicated to increase survival in patients acutely exposed to myelosuppresive doses or radiation (hematopoietic subsyndrome of acute radiation syndrome).[1] The recommended dose of Neulasta is two doses, 6 mg each, given SC 1 week apart. Dosing in pediatric patients < 45 kg is cited in the Neulasta prescribing information. Give the first Neulasta dose as soon as possible after suspected or confirmed exposure to radiation levels > 2 gray. Administer the second dose 1 week after the first dose. Fulphila is not specifically indicated for this use but it is the same chemical and, therefore, should act similarly.[23]

Dosing in Radiation Syndrome (Hematopoietic Syndrome of Acute Radiation Syndrome): *Dosing must meet ONE of the following (A OR B)*:

A) Two doses, 6 mg each, given SC 1 week apart;[1] OR

B) For pediatric patients < 45 kg give two doses SC 1 week apart as follows: 4 mg (0.4 mL) for patients 31 to 44 kg; 2.5 mg (0.25 mL) for patients 21 to 30 kg; 1.5 mg (0.15 mL) for patients 10

to 20 kg; and 0.1 mg/kg (0.01 mL/kg) is recommended for pediatric patients < 10 kg. Of note, the Neulasta/ Fulphila prefilled syringes are not designed to allow for direct administration of doses < 0.6 mL (6 mg). The syringe does not bear graduation marks, which are needed to accurately measure doses of Neulasta/Fulphila < 0.6 mL (6 mg) for direct administration to patients. Thus, the direct administration to patients requiring dosing of < 0.6 mL (6 mg) is not recommended due to the potential for errors.

Initial Approval/Extended Approval.

A) *Initial Approval*. Initial approval is for 1 month.

B) *Extended Approval*. Not applicable.

Duration of Therapy in Radiation Syndrome (Hematopoietic Syndrome of Acute Radiation Syndrome). Two doses of Neulasta are given 1 week apart until the ANC is adequate.

Labs/Diagnostics. None required.

Other Uses with Supportive Evidence

3. Patients with Cancer Following Peripheral Blood Progenitor Cell (PBPC) Transplantation.

Criteria. *The patient must meet the following criteria*: The agent is prescribed by, or in consultation with, an oncologist, a hematologist, or a physician that specializes in transplantation.

Pegfilgrastim has been studied in patients with cancer undergoing high dose chemotherapy, followed by infusion of stem cell transplantation, which was usually autologous.[8-20] Results have been similar to that noted with use of daily Neupogen. Pegfilgrastim was usually administered on Day 1 and sometimes up to Day 5 after stem cell transplantation. The NCCN guidelines for myeloid growth factors (version 1.2018) note that pegfilgrastim has been utilized for post autologous hematopoietic cell transplantation.

Dosing in Patients with Cancer Following PBPC Transplantation. *Dosing must meet ONE of the following (A OR B):*[8-20]

A) The dose in adults is 6 mg SC on Day +1 or up to Day +5 after PBPC transplantation; OR

B) The dose in children is 100 mcg per kg or 200 mcg per kg SC one time.

Initial Approval/Extended Approval.

A) *Initial Approval*. Initial approval is for one dose.

B) *Extended Approval*. Not applicable.

Duration of Therapy in Patients with Cancer Following PBPC Transplantation. Usually only one dose of pegfilgrastim is needed until the absolute neutrophil count (ANC) is adequate.[8-20]

Labs/Diagnostics. None required.

Waste Management for All Indications.

Neulasta and Fulphilaare available as a 6 mg syringe. This dose should be sufficient in most situations.

Conditions Not Recommended For Approval.
Neulasta has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.).

1. **Myelodysplastic syndrome (MDS).** Only limited data report use of pegflgrastim for patients with MDS.[21] Guidelines from the NCCN for MDS (version 1.2019) do not mention use of pegfilgrastim in this patient population.[22]

2. Coverage is not recommended for circumstances *not* listed in the *Recommended Authorization Criteria*. Criteria will be updated as new published data are available.

SPECIAL CONSIDERATIONS
None.

LIMITATIONS/EXCLUSIONS
Please refer to a product line's certificate of coverage for benefit limitations and exclusions for these services:

PRODUCT LINE	LINK TO CERTIFICATE OF COVERAGE
MEDICARE ADVANTAGE	http://healthfirst.chpw.org/for-members/resource-library/handbooks-and-guides
WASHINGTON APPLE HEALTH	http://chpw.org/our-plans/apple-health/
INTEGRATED MANAGED CARE	http://chpw.org/our-plans/apple-health/

Citations & References

References	1. Neulasta® injection for subcutaneous use [prescribing information]. Thousand Oaks, CA: Amgen, Inc.; June 2018. 2. The NCCN Myeloid Growth Factors Clinical Practice Guidelines in Oncology (Version 1.2018 – March 2, 2018). ® 2018 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on July 30, 2018.

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OTHER REFERENCES UTILIZED

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CFR		
WAC	WAC 284-43-2050	
RCW		
Contract Citation	☐ WAH	
	☐ IMC	
	☐ MA	
Other Requirements		
NCQA Elements		

Revision History

Revision Date	Revision Description	Revision Made By
01/13/2016	New	Kelly Force; Yusuf Rashid, RPh
01/20/2016	Approval	MMLT
01/12/2017	No revisions	Fran McGaugh
01/13/2017	Approval	MMLT
07/24/2017	Criteria completely updated and revised	Michael Sporck, Pharmacy Intern Sophia Yun, PharmD
07/25/2017	Approved	MMLT
03/09/2018	Reassigned from UM139 to PM128	Cindy Bush
04/27/2018	Transferred to new template	Cindy Bush

05/25/2018	No revisions	Jennifer Farley, PharmD
06/14/2018	Approval	UM Committee
11/28/2018	Revisions from ESI annual update	Jennifer Farley, PharmD
12/12/2018	Approval	UM Committee