Policy and Procedure	
PHARMACY STEP THERAPY POLICY AND CRITERIA ORPTCHEM039.1225	**HEMOTOLOGICAL AGENTS** **GRANULOCYTE COLONY STIMULATING FACTORS (G-CSF)** See Table 2 for Applicable Medications
Effective Date: 2/1/2026	**Review/Revised Date**: 10/24, 08/25, 10/25, 11/25 (JEF)
Original Effective Date: 09/24	**P&T Committee Meeting Date**: 06/24, 12/24, 08/25, 10/25, 12/25
Approved by: Oregon Region Pharmacy and Therapeutics Committee	

SCOPE:
Providence Health Plan and Providence Health Assurance as applicable (referred to individually as "Company" and collectively as "Companies").

APPLIES TO:
Commercial
Medicare Part B
Medicaid

POLICY CRITERIA:

COVERED USES:
All medically accepted indications not otherwise excluded from the benefit

REQUIRED MEDICAL INFORMATION:
Documented trial and failure, intolerance or contraindication to Neulasta and Fulphila.

EXCLUSION CRITERIA: N/A

AGE RESTRICTIONS: N/A

PRESCRIBER RESTRICTIONS: N/A

COVERAGE DURATION:
Authorization will be approved until no longer eligible with the plan, subject to formulary and/or benefit changes.

Requests for indications that were approved by the FDA within the previous six (6) months may not have been reviewed by the health plan for safety and effectiveness and inclusion on this policy document. These requests will be reviewed using the New Drug and or Indication Awaiting P&T Review; Prior Authorization Request ORPTCOPS047.

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Requests for a non-FDA approved (off-label) indication requires the proposed indication be listed in either the American Hospital Formulary System (AHFS), Drugdex, or the National Comprehensive Cancer Network (NCCN) and is considered subject to evaluation of the prescriber's medical rationale, formulary alternatives, the available published evidence-based research and whether the proposed use is determined to be experimental/investigational.

Coverage for Medicaid is limited to a condition that has been designated a covered line item number by the Oregon Health Services Commission listed on the Prioritized List of Health Care Services.

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case.

INTRODUCTION: Granulocyte colony stimulating factor (G-CSF) is a class of biological medication that boosts white blood cell count. G-CSF stimulates the bone marrow to produce more neutrophils. Pegfilgrastim is a pegylated formulation of G-CSF, a long-acting formulation of G-CSF.

FDA APPROVED INDICATIONS:

Table 1. Granulocyte Colony Stimulating Factors (G-CSF) applicable to this policy

Generic Name	Brand Name	FDA Indication
pegfilgrastim-pbbk	Fylnetra®	• Patients with Hematopoietic Subsyndrome of Acute Radiation Syndrome: Indicated to increase survival in patients acutely exposed to myelosuppressive doses of radiation
pegfilgrastim-pbbk	Fylnetra®	• 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 Limitations of Use: not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation.
pegfilgrastim-apgf	Nyvepria®	
pegfilgrastim-bmez	Ziextenzo®	
efbemalenograstim alfa-vuxw	Ryzneuta®	
pegfilgrastim-fpgk	Stimufend®	• 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 Limitations of Use:
pegfilgrastim-cbqv	Udenyca®	

		not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation. • Indicated to increase survival in patients acutely exposed to myelosuppressive doses of radiation

Table 2. Applicable medications for step therapy policy

Generic Name	Brand Name
pegfilgrastim-pbbk	Fylnetra®
pegfilgrastim-apgf	Nyvepria®
pegfilgrastim-fpgk	Stimufend®
pegfilgrastim-cbqv	Udenyca®
pegfilgrastim-bmez	Ziextenzo®
efbemalenograstim alfa-vuxw	Ryzneuta®

Table 3. Preferred and non-preferred pegfilgrastim and pegfilgrastim biosimilars

HCPCS	Coding Description	Brand Name
Preferred Products		
Q5108	Injection, pegfilgrastim-jmdb (fulphila), biosimilar, 0.5 mg	Fulphila
J2506	Injection, pegfilgrastim, excludes biosimilar, 0.5 mg	Neulasta
Non-preferred Products		
Q5130	Injection, pegfilgrastim-pbbk (fylnetra), biosimilar, 0.5 mg	Fylnetra
Q5122	Injection, pegfilgrastim-apgf (nyvepria), biosimilar, 0.5 mg	Nyvepria
J9361	Injection, efbemalenograstim alfa-vuxw, 0.5 mg	Ryzneuta
Q5127	Injection, pegfilgrastim-fpgk (stimufend), biosimilar, 0.5 mg	Stimufend
Q5111	Injection, pegfilgrastim-cbqv (udenyca), biosimilar, 0.5 mg	Udenyca
Q5120	Injection, pegfilgrastim-bmez (ziextenzo), biosimilar, 0.5 mg	Ziextenzo
ADMINISTRATION CODES◊		
96372	Ther/proph/diag inj sc/im	
96401	Chemo anti-neopl sq/im	

◊ Coding/Administration Notes:
• The above code list is provided as a courtesy and may not be all-inclusive. Inclusion or omission of a code from this policy neither implies nor guarantees reimbursement or coverage. Some codes may not require routine review for medical necessity, but they are subject to provider contracts, as well as member benefits, eligibility and potential utilization audit.
• HCPCS/CPT code(s) may be subject to National Correct Coding Initiative (NCCI) procedure-to-procedure (PTP) bundling edits and daily maximum edits known as “medically unlikely edits” (MUEs) published by the Centers for Medicare and Medicaid Services (CMS). This policy does not take precedence over NCCI edits or MUEs. Please refer to the CMS website for coding guidelines and applicable code combinations.

POSITION STATEMENT:

Six biosimilar forms of pegfilgrastim (pegfilgrastim-jmdb [Fulphila®], pegfilgrastim-cbqv [Udenyca®], pegfilgrastim-bmez [Ziextenzo®], pegfilgrastim-apgf [Nyvepria®]), Pegfilgrastim-fpgk [Stimufend®], and pegfilgrastim-pbbk [Fylnetra®] were approved in the United States between 2018 and 2022.[1]

Current treatment guidelines published by the American Society of Clinical Oncology Clinical Practice in 2015 state pegfilgrastim, filgrastim, tbo-filgrastim, and filgrastim-sndz (and other biosimilars, as they become available) can be used for the prevention of treatment-related febrile neutropenia." Guidelines state that choice of therapy depends on various factors including convenience, cost, and clinical situation.[2]

A meta-analysis by *Rastogi et al.* evaluated the efficacy and safety of filgrastim in head-to-head trials with placebo/no treatment, pegfilgrastim, and biosimilar filgrastim. A total of 56 studies were reviewed in the meta-analysis reviewing data from 13,058 cancer patients. Filgrastim was found to be more effective and safer in reducing febrile neutropenia compared to placebo/no treatment, no notable difference found for efficacy and safety between pegfilgrastim and filgrastim, and a similar efficacy profile was found with filgrastim and its biosimilars.[3]

No meta-analyses or head-to-head trials were found for pegfilgrastim and its biosimilars.

Efbemalenograstim alfa-vuxw is the first non-PEGylated long-acting granulocyte colony-stimulating factor (G-CSF) approved in the United States. PEGylation can provide advantages like increased half-life; however, non-PEGylation may provide an advantage as PEGylation has been associated with pharmacologic limitations, such as inducing an anti-PEG immune response, potential loss of biological activity, and reduced cellular uptake. Prior to its approval, efbemalenograstim alfa-vuxw was anticipated to be considered a "biobetter" of Amgen's Neulasta (pegfilgrastim); however, available data have not demonstrated clinical superiority.

Efbemalenograstim alfa-vuxw was approved by the FDA based on two phase 3, multicenter, randomized trials evaluating safety and efficacy of efbemalenograstim alfa-vuxw in reducing the risk for febrile neutropenia in breast cancer patients receiving myelosuppressive chemotherapy. The primary endpoint was duration of severe neutropenia (DSN) in cycle 1:

- Study GC-627-04 mean [SD] DSN: 1.3 [1.19] days with efbemalenograstim alfa-vuxw and 3.9 [1.44] days with placebo

- Study GC-627-05 DSN: 0.2 days in both the efbemalenograstim alfa and pegfilgrastim arms (mean difference 0.0 days [95% CI -0.1, 0.1]), demonstrating non-inferiority.

REFERENCE/RESOURCES:

1. Relevant and current package inserts
2. Smith T. MD, Bohlke K., and Armitage J. MD. Recommendations for the use of white blood cell growth factors: American society of clinical oncology clinical practice guideline update. *Journal of Oncology Practice*. 2015;11(6). Available at: https://ascopubs.org/doi/full/10.1200/JOP.2015.006742
3. Rastogi S, Kalaiselvan, Ali S, et al. Efficacy and safety of filgrastim and its biosimilars to prevent febrile neutropenia in cancer patients: a prospective study and meta-analysis. *Biology (Basel).* 2021;10(10):1069. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8533340/.