Policy Title:	Long-Acting Granulocyte Colony Stimulating Factor (G-CSFs) Policy: Fulphila (pegfilgrastim-jmdb), Fylnetra (pegfilgrastim-pbbk) Neulasta (pegfilgrastim), Neulasta (pegfilgrastim) Onpro, Nyvepria (pegfilgrastim-apgf), Rolvedon (eflapegrastim-xnst), Stimufend (pegfilgrastim-fpgk), Udenyca (Pegfilgrastim-cbqv), Ziextenzo (pegfilgrastim-bmez) (subcutaneous) **NON-ONCOLOGY POLICY**		
		Department:	PHA
Effective Date:	01/01/2020		
Review Date:	04/19/2019, 09/18/2019, 12/18/2019, 1/29/2020, 8/03/2020, 7/22/2021, 6/16/2022, 10/6/2022, 2/16/2023, 7/13/2023, 12/07/2023, 01/04/2024, 9/30/2025		

Purpose: To support safe, effective, and appropriate use of Long-Acting Granulocyte Colony Stimulating Factors.

Scope: Medicaid*, Commercial, Medicare

***Effective 8/1/2023: Medication is only available on the medical benefit**

Policy Statement:

Long-Acting Granulocyte Colony Stimulating Factors are covered under the Medical Benefit when used within the following guidelines for non-oncology indications. Use outside of these guidelines may result in non-payment unless approved under an exception process. Neulasta (pegfilgrastim), Neulasta Onpro (pegfilgrastim) or Ziextenzo (pegfilgrastim-bmez) are the preferred long-acting colony stimulating factors. **For oncology indications, please refer to Myeloid Growth Factors Policy.**

Procedure:

Coverage of Long-Acting Granulocyte Colony Stimulating Factors will be reviewed prospectively via the prior authorization process based on criteria below.

Criteria:

Member has one of the following conditions:

- Bone marrow transplantation (BMT) failure or engraftment delay; OR
- Peripheral blood progenitor cell (PBPC) mobilization and transplant; AND
- For members requesting Fulphila (pegfilgrastim-jmdb), Fylnetra (pegfilgrastim-pbbk), Rolvedon (eflapegrastim-xnst), Stimufend (pegfilgrastim-fpgk), Udenyca (Pegfilgrastim-cbqv); or Nyvepria (pegfilgrastim-apgf), they must have a documented failure, contraindication, or intolerance to Neulasta (pegfilgrastim), Neulasta (pegfilgrastim) Onpro, or Ziextenzo (pegfilgrastim-bmez);**OR**
- For members that are currently on treatment with Fulphila (pegfilgrastim-jmdb), Fylnetra (pegfilgrastim-pbbk), Rolvedon (eflapegrastim-xnst), Stimufend (pegfilgrastim-fpgk), Udenyca (Pegfilgrastim-cbqv) or Nyvepria (pegfilgrastim-apgf) they can remain on treatment **OR** Medicare

members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements.

Coverage durations: 4 months

Per §§ 42 CFR 422.101, this clinical medical policy only applies to Medicare in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD).

Policy Rationale:
Fulphila, Fylnetra, Neulasta, Neulasta Onpro, Nyvepria, Rolvedon, Stimufend, Udenyca, and Ziextenzo were reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Fulphilia, Fynetra, Neulasta, Neulasta Onpro, Nyvepria, Rolvedon, Stimufend, Udenyca, and Ziextenzo according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using these drugs for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For Medicare members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.

Dosage/Administration:

Indication	**Dosing**	**Maximum Dosing (1 billable unit = 0.5 mg)**
BMT failure or engraftment delay PBPC mobilization and transplant	<10kg = 0.1mg/kg 10-20 kg = 1.5 mg 21-30 kg = 2.5 mg 31-44 kg = 4 mg 45 kg and up = 6 mg Dosed no more frequently than every 14 days.	12 billable units per 14 days for Fulphila, Nyvepria, Udenyca & Ziextenzo 1 billable unit per 14 days for Neulasta

Investigational use: All therapies are considered investigational when used at a dose or for a condition other than those that are recognized as medically accepted indications as defined in any one of the following standard reference compendia: American Hospital Formulary Service Drug

information (AHFS-DI), Thomson Micromedex DrugDex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs, or Peer-reviewed published medical literature indicating that sufficient evidence exists to support use. Neighborhood does not provide coverage for drugs when used for investigational purposes.

Applicable Codes:

Below is a list of billing codes applicable for covered treatment options. The below tables are provided for reference purposes and may not be all-inclusive. Requests received with codes from tables below do not guarantee coverage. Requests must meet all criteria provided in the procedure section.

The following HCPCS/CPT code is:

HCPCS/CPT Code	Description
Q5108	Injection, pegfilgrastim-jmdb, biosimilar, (Fulphila), 0.5mg
Q5120	Injection, pegfilgrastim-bmez, biosimilar, (Ziextenzo), 0.5mg
Q5122	Injection, pegfilgrastim-apgf, biosimilar, (Nyvepria), 0.5mg
J2506	Injection, pegfilgrastim, 6mg
Q5111	Injection, pegfilgrastim-cbqv, biosimilar, (Udenyca), 0.5 mg
Q5130	Injection, pegfilgrastim-pbbk (Fylnetra), biosimilar, 0.5mg
J1449	Injection, eflapergrastim-xnst (Rolvedon), 0.1mg
Q5122	Injection, pegfilgrastim-fpgk (stimufend), biosimilar, 0.5mg

Summary of Evidence:

Fulphila (pegfilgrastim-jmdb)

Fulphila is a long-acting granulocyte colony-stimulating factor (G-CSF) biosimilar to Neulasta (pegfilgrastim). It 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 risk of febrile neutropenia. Fulphila is a G-CSF receptor agonist that stimulates proliferation, differentiation, and activation of neutrophils. Fulphila demonstrated efficacy equivalent to reference pegfilgrastim in reducing chemotherapy-induced neutropenia. In three randomized, double-blind clinical trials in patients with breast cancer receiving myelosuppressive chemotherapy (doxorubicin/docetaxel regimens), Fulphila significantly reduced the duration of severe neutropenia to a mean of 1.7-1.8 days versus 1.6 days with filgrastim, confirming non-inferiority. A separate placebo-controlled study showed that Fulphila reduced the incidence of febrile neutropenia from 17% to 1% ($p < 0.001$) and decreased hospitalizations and IV anti-infective use. Overall, Fulphila was well tolerated and clinically comparable in safety and efficacy to Neulasta. Common adverse reactions include bone pain and extremity pain.

Fylnetra (pegfilgrastim-pbbk)

Fylnetra is a long-acting granulocyte colony-stimulating factor (G-CSF) biosimilar to Neulasta (pegfilgrastim). It 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 risk of febrile neutropenia. Flynetra is a G-CSF receptor agonist that stimulates proliferation, differentiation, and activation of neutrophils. Fylnetra demonstrated clinical efficacy and safety equivalent to Neulasta in patients receiving myelosuppressive chemotherapy. In three randomized, double-blind trials in patients with breast cancer receiving doxorubicin and docetaxel, Fylnetra significantly reduced the duration of severe neutropenia to 1.7-1.8 days versus 1.6 days with filgrastim, meeting equivalence criteria. Overall, Fylnetra effectively shortened neutropenia duration, lowered febrile neutropenia risk, and demonstrated comparable efficacy and safety to the reference pegfilgrastim product. Common adverse reactions include bone pain and extremity pain.

Neulasta (pegfilgrastim)

Neulasta is a long-acting granulocyte colony-stimulating factor (G-CSF) indicated to (1) 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 risk of febrile neutropenia, and (2) increase survival after acute exposure to myelosuppressive doses of radiation (Hematopoietic Subsyndrome of Acute Radiation Syndrome, Heme-ARS). Neulasta is a G-CSF receptor agonist that stimulates proliferation, differentiation, and activation of neutrophils. Neulasta demonstrated significant efficacy in reducing chemotherapy-induced neutropenia. Across three pivotal randomized, double-blind studies in breast cancer patients receiving myelosuppressive chemotherapy (doxorubicin/docetaxel), Neulasta was shown to be non-inferior to daily filgrastim in shortening the duration of severe neutropenia, with mean durations of 1.7-1.8 days vs 1.6 days, respectively. In a placebo-controlled study of 928 patients, Neulasta reduced the incidence of febrile neutropenia from 17% to 1% ($p < 0.001$), and also decreased hospitalizations (1% vs 14%) and IV anti-infective use (2% vs 10%) compared to placebo. Overall, Neulasta consistently demonstrated robust clinical efficacy and safety, significantly reducing neutropenia duration and infection-related complications across indications. Common adverse reactions include bone pain and pain in extremity.

Nyvepria (pegfilgrastim-apgf)

Nyvepria is a long-acting granulocyte colony-stimulating factor (G-CSF) biosimilar to Neulasta (pegfilgrastim). It 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. Nyvepria is a G-CSF receptor agonist that stimulates proliferation, differentiation, and activation of neutrophils. Nyvepria demonstrated comparable efficacy and safety to reference pegfilgrastim (Neulasta) in patients with breast cancer receiving myelosuppressive chemotherapy. In three randomized, double-blind studies, Nyvepria significantly reduced the duration of severe neutropenia to a mean of 1.7-1.8 days vs. 1.6 days with daily filgrastim, meeting equivalence criteria. Overall, Nyvepria effectively shortened neutropenia duration, reduced infection risk, and showed equivalent clinical efficacy and safety to Neulasta. The most common adverse reactions are bone pain and pain in extremity.

Rolvedon (eflapegrastim-xnst)

Rolvedon is a long-acting granulocyte colony-stimulating factor (G-CSF) indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in adult patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia. Rolvedon is a G-CSF receptor agonist that stimulates proliferation, differentiation, and activation of neutrophils. Rolvedon demonstrated efficacy equivalent to pegfilgrastim in patients with early-stage breast cancer receiving myelosuppressive chemotherapy. In two randomized, open-label, active-controlled phase 3 studies (NCT02643420 and NCT02953340) enrolling 643 patients, Rolvedon (13.2 mg SC once per cycle) was compared to pegfilgrastim (6 mg SC). The mean duration of severe neutropenia (DSN) in cycle 1 was 0.20 vs

0.35 days in Study 1 and 0.31 vs 0.39 days in Study 2, confirming non-inferiority to pegfilgrastim. Overall, Rolvedon effectively reduced the duration of severe neutropenia, demonstrating comparable efficacy and safety to pegfilgrastim.. Common adverse reactions (≥20%) include fatigue, nausea, diarrhea, bone pain, headache, pyrexia, anemia, rash, myalgia, arthralgia, and back pain.

Stimufend (pegfilgrastim-fpgk)

Stimufend is a long-acting granulocyte colony-stimulating factor (G-CSF) biosimilar to Neulasta (pegfilgrastim). It 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. Stimufend is a G-CSF receptor agonist that stimulates proliferation, differentiation, and activation of neutrophils. Stimufend demonstrated equivalent efficacy and safety to reference pegfilgrastim (Neulasta) in patients with breast cancer receiving myelosuppressive chemotherapy. Across three randomized, double-blind clinical trials, Stimufend reduced the mean duration of severe neutropenia to 1.7-1.8 days versus 1.6 days with filgrastim, confirming non-inferiority. Overall, Stimufend effectively shortened neutropenia duration and reduced febrile neutropenia incidence, demonstrating clinical equivalence to Neulasta. The most common adverse reactions are bone pain and pain in extremity.

Udenyca (pegfilgrastim-cbqv)

Udenyca is a long-acting granulocyte colony-stimulating factor (G-CSF) biosimilar to Neulasta indicated to (1) 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 risk of febrile neutropenia, and (2) increase survival after acute exposure to myelosuppressive doses of radiation (Hematopoietic Subsyndrome of Acute Radiation Syndrome, Heme-ARS). Udencya is a G-CSF receptor agonist that stimulates proliferation, differentiation, and activation of neutrophils. Udenyca (pegfilgrastim-cbqv) demonstrated efficacy and safety comparable to the reference pegfilgrastim product in patients with breast cancer receiving myelosuppressive chemotherapy. In two randomized, double-blind studies ($n \approx 467$ per arm), the mean duration of severe neutropenia in cycle 1 was 1.7-1.8 days with pegfilgrastim vs. 1.6 days with filgrastim, confirming equivalence. In a placebo-controlled trial of 928 patients, pegfilgrastim reduced the incidence of febrile neutropenia from 17% to 1% ($p<0.001$), with associated decreases in hospitalization (1% vs. 14%) and IV anti-infective use (2% vs. 10%). Overall, Udenyca effectively shortened neutropenia duration and reduced infection-related complications, demonstrating clinical equivalence to Neulasta. The most common adverse reactions are bone pain and pain in extremity.

Ziextenzo (pegfilgrastim-bmez)

Ziextenzo is a long-acting granulocyte colony-stimulating factor (G-CSF) biosimilar to Neulasta indicated to (1) 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 risk of febrile neutropenia; and (2) increase survival after acute exposure to myelosuppressive doses of radiation (Hematopoietic Subsyndrome of Acute Radiation Syndrome, Heme-ARS). Ziextenzo is a G-CSF receptor agonist that stimulates proliferation, differentiation, and activation of neutrophils. Ziextenzo demonstrated efficacy and safety comparable to Neulasta in patients with breast cancer receiving myelosuppressive chemotherapy. In two randomized, double-blind studies using doxorubicin/docetaxel regimens, Ziextenzo showed mean durations of severe neutropenia of 1.7-1.8 days versus 1.6 days with daily filgrastim, confirming clinical equivalence. Overall, Ziextenzo effectively shortened neutropenia duration and reduced infection risk,

confirming equivalence to reference pegfilgrastim. The most common adverse reactions are bone pain and pain in extremity

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