EXPRESS SCRIPTS®

PRIOR AUTHORIZATION POLICY

POLICY: Colony Stimulating Factors – Pegfilgrastim Products

- Fulphila™ (pegfilgrastim-jmdb injection for subcutaneous use – Mylan)
- Neulasta® (pegfilgrastim injection for subcutaneous use [includes single-dose prefilled syringes for manual use and single-dose prefilled syringe co-packaged with the On-body Injector] – Amgen)
- Udenyca™ (pegfilgrastim-cbqv injection for subcutaneous use – Coherus)

TAC APPROVAL DATE: 08/01/2018; selected revision 12/05/2018

OVERVIEW

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. 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 1 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. Give the second dose 1 week after the first dose. Fulphila and Udenyca are biosimilars to Neulasta.[23,24] Both 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. The dosing for this use is similar to the common indication for Neulasta.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of pegfilgrastim products. Due to the specialized skills required for evaluation and diagnosis of patients treated with pegfilgrastim, as well as the monitoring required for adverse events (AEs) and efficacy, initial approval requires pegfilgrastim to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indications

1. **Patients with Cancer Receiving Myelosuppressive Chemotherapy**. Approve for 6 months if the patient meets 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 (the risk 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 dysfunction; 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], and pegfilgrastim products [Neulasta, Fulphila]) and a reduced dose or frequency of chemotherapy may compromise treatment outcome.

   Pegfilgrastim products 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 G-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.

2. **Radiation Syndrome (Hematopoietic Syndrome of Acute Radiation Syndrome).** Approve for 1 month if 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 of 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 recommendations 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.[1] Fulphila is not specifically indicated for this use but it is the same chemical and, therefore, should act similarly.[23]

Other Uses with Supportive Evidence

3. **Patients with Cancer Following Peripheral Blood Progenitor Cell (PBPC) Transplantation.** Approve one dose if prescribed by, or in consultation with, an oncologist, a hematologist, or a physician that specializes in transplantation.[2,8-20]

Pegfilgrastim has been studied in patients with cancer undergoing high dose chemotherapy, followed by infusion of stem cell transplantation, which was usually autologous.[2,8-20] Results have been similar to those noted with use of daily filgrastim. 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 transplant.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Pegfilgrastim 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 pegfilgrastim 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.

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HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
Annual revision	Indication for radiation syndrome (hematopoietic syndrome of acute radiation syndrome) moved from the "Other Uses with Supportive Evidence" section to the "FDA-Approved Indications" section and the duration of therapy changed from one dose to 1 month. The wording of the examples of risk factors provided under the criteria for Patients with Cancer (Adults and Children) Receiving Myelosuppressive Chemotherapy (Criterion 1.B.ii.) were revised.	06/29/2016
Annual revision	No criteria changes.	07/12/2017
Not applicable	Noted in the Policy header that the injection for subcutaneous use includes the single-dose prefilled syringe for manual use and the single-dose prefilled syringe co-packaged with the On-body injector.	01/19/2018
Selected revision	Selected revision to add Fulphilia to the PA. Changed the PA policy to state "Pegfilgrastim Products" after "Colony Stimulating Factors".	06/13/2018
Annual revision	For the criteria regarding patients with cancer receiving myelosuppressive therapy in the criteria that reference a colony stimulating factor, the terminology of filgrastim and pegfilgrastim products were added, along with the listing of the individual products, which included adding Nivestym and Fulphila.	08/01/2018
DEU selected revision	For the indication regarding Patients with Cancer (Adults and Children) Receiving Myelosuppressive Chemotherapy, removed "(adults and children)".	08/08/2018
Selected revision	Selected revision to add Udenyca to the PA.	12/05/2018

TAC – Therapeutic Assessment Committee; TAC – Therapeutic Assessment Committee; * For a further summary of criteria changes, refer to respective TAC minutes available at: http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx.