

# Drug Therapy Guidelines

Colony Stimulating Factors (CSFs): Fulphila™ (pegfilgrastim-jmdb), Granix® (Tbo-filgrastim), Leukine® (sargramostim), Neupogen® (filgrastim), Neulasta® (pegfilgrastim), Nivestym™ (filgrastim-aafi), Udenyca™ (pegfilgrastim-cbqv), Zarxio™ (filgrastim-sndz)

*Applicable*

<b>Medical Benefit</b>		<b>Effective:</b> 8/15/19
<b>Pharmacy- Formulary 1</b>	x	<b>Next Review:</b> 6/20
<b>Pharmacy- Formulary 2</b>	x	<b>Date of Origin:</b> 10/06
<b>Pharmacy- Formulary 3/Exclusive</b>	x	<b>Review Dates:</b> 10/15/06, 11/5/07, 12/15/08, 12/09, 9/14/10, 9/11, 9/12, 9/13, 9/14, 6/15, 6/16, 6/17, 6/18, 12/18, 6/19
<b>Pharmacy- Formulary 4/AON</b>	x	

## I. Medication Description

CSFs are biosynthetic products that stimulate the development of white blood cells, such as neutrophils and macrophages (infection-fighting blood cells). Neutropenia is a severe drop in infection-fighting white blood cells (neutrophils). Neutrophils are measured in terms of “absolute neutrophil count” (ANC). A normal ANC is defined as being  $\geq 1500$  cells/mm<sup>3</sup>. CSF administration increases the number of infection-fighting cells in conditions such as chemotherapy-induced neutropenia (reduction in the neutrophil count after chemotherapy), bone marrow transplantation (BMT), severe chronic neutropenia (low white cell blood count), and myelodysplasia (disorder of blood cell production). When CSFs are used in conjunction with chemotherapy, it is possible to maintain or even increase doses of chemotherapeutic agents. The chemotherapy regimen, malignancy being treated, and patient risk factors are considered in assessing risk for development of febrile neutropenia and need for CSF prophylaxis. In patients with HIV infection, CSFs correct or minimize drug-induced or disease-induced neutropenia.

Fulphila™ (pegfilgrastim-jmdb) is biosimilar\*\* to Neulasta® (pegfilgrastim)  
 Udenyca™ (pegfilgrastim-cbqv) is biosimilar\*\* to Neulasta® (pegfilgrastim)

Nivestym™ (filgrastim-aafi) is biosimilar\*\* to Neupogen® (filgrastim)  
 Zarxio™ (filgrastim-sndz) is biosimilar\*\* to Neupogen® (filgrastim)

## II. Position Statement

Coverage under the medical benefit does not require prior authorization. Coverage is granted immediately under the pharmacy benefit when prescribed by an oncologist.

Coverage is determined through a prior authorization process with supporting clinical documentation for all other requests under the pharmacy benefit.

## III. Policy

- **Granix, Fulphila, Leukine, Neulasta, Neupogen, Nivestym, Udenyca, Zarxio** (non-oncology prescribers): coverage is provided for the following conditions:
  - Neutropenia due to:
    - Antineoplastic chemotherapy agents
    - Other chemotherapy agents

- Radiotherapy
- Malignancy
- AIDS/HIV
- Myelodysplasia
- Acute leukemia (AML, ALL)
- Severe chronic neutropenia (cyclic neutropenia)
- Primary or secondary prevention of antineoplastic chemotherapy-related neutropenia where the member is at high risk, for example:
  - Pre-existing neutropenia
  - Poor performance status
  - Renal or hepatic dysfunction
  - Extensive prior exposure to chemotherapy
  - Previous exposure of pelvis, or other areas of large amounts of bone marrow, to radiation
  - History of recurrent febrile neutropenia from chemotherapy
  - Elderly (>65 years old)
  - Member has a condition that can potentially increase the risk of serious infection (i.e. HIV/AIDS)
- Bone marrow transplant (BMT)
- Current or post-peripheral blood progenitor cell (PBPC) mobilization/transplantation
- Treatment of acute exposure to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome)
- **Granix** (non-oncology prescribers): coverage is provided for severe neutropenia in members with nonmyeloid malignancies receiving myelosuppressive chemotherapy associated with a clinically significant incidence of febrile neutropenia.

#### IV. Quantity Limitations

Coverage is available for quantities sufficient to allow for FDA-approved dosing.

#### V. Coverage Duration

- BMT or PBPC mobilization/transplantation – 1 month
- Myelodysplasia or AIDS/HIV-related neutropenia – 4 months
- All other situations – 6 months

#### VI. Coverage Renewal Criteria

Coverage can be renewed based upon the following criteria:

- Same as initial prior authorization policy criteria **AND**
- Absence of unacceptable toxicity from the drug

#### VII. Billing/Coding Information

- Pertinent indications:
  - Chemotherapy induced neutropenia: D70.1, D70.2, Z41.8, Z51.11, Z51.89
  - Acute myelogenous leukemia (following induction therapy): D70.1, D70.2, Z41.8, Z94.81, Z94.84, Z51.11, Z51.89
  - Peripheral blood progenitor cell collection (PBPC): Z94.84
  - Bone marrow transplant: Z94.81
  - Bone marrow transplantation failure or engraftment delay: D70.1, D70.2, T86.00 – T86.09, Z41.8, Z94.81, Z94.84, Z51.11, Z51.89
  - Severe chronic neutropenia: D70.1, D70.2, Z41.8, Z58.11, Z51.89
  - Myelodysplastic syndrome: C92.10, D46.0 – D46.21, D46.A, D46.B, D46.22, D46.c, D46.9
  - Neutropenia associated with HIV/AIDS: B20
  - Effects of radiation: T66.XXXA

#### VIII. Summary of Policy Changes

- 1/1/12: renewal criteria specified as same as initial criteria
- 12/15/12: added need to review for lack of unacceptable toxicity to renewal criteria
- 12/15/13: removed specific ANC levels needed for coverage
- 1/1/15: no policy changes
- 7/1/15: formulary distinctions made
- 9/10/15: biosimilar Zarxio added to policy
- 9/15/15: addition of coverage for treatment of Hematopoietic Syndrome of Acute Radiation Syndrome.
- 7/19/16: no policy changes
- 6/21/17: clarified Neulasta use; added Granix coverage
- 6/15/18: no policy changes
- 2/15/19: added biosimilars Udenyca, Fulphila, and Nivestym to policy
- 8/15/19: updated coverable indications for biosimilar and follow-on biologic products

#### IX. References

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16. Holmes FA, et al. A single dose of pegylated filgrastim is as effective as daily filgrastim for hematologic support of chemotherapy in breast cancer patients: results of a randomized, doubleblind, phase III trial. *Proc Annu Meet Am Soc Clin Oncol* 2001:27.
17. Package Insert: Zarxio™ (filgrastim-sndz). Sandoz Inc., Princeton, NJ 08540. Revised 12/2017.
18. Package Insert: Granix (Tbo-filgrastim). Teva Pharmaceuticals. North Wales, PA 19454. Revised 3/2019
19. Package Insert: Udenyca™ (pegfilgrastim-cbqv). Coherus BioSciences, Inc., Redwood City, CA 94065. Revised 11/2018.
20. Fulphila™ (pegfilgrastim-jmdb injection for subcutaneous injection) [prescribing information]. Zurich, Switzerland: Mylan GmbH; June 2018.
21. Nivestym™ (filgrastim-aafi) injection [prescribing information]. Lake Forest, IL: Hospira, Inc.; July 2018.

*\*\* Biosimilar means that the biological product is approved based on data demonstrating that it is highly similar to an FDA-approved biological product, known as a reference product, and that there are no clinically meaningful differences between the biosimilar product and the reference product. Biosimilarity of MVASI has been demonstrated for the condition(s) of use (e.g. indication(s), dosing regimen(s)), strength(s), dosage form(s), and route(s) of administration described in its Full Prescribing Information.*

*The Plan fully expects that only appropriate and medically necessary services will be rendered. The Plan reserves the right to conduct pre-payment and post-payment reviews to assess the medical appropriateness of the above-referenced therapies.*

*The preceding policy applies only to members for whom the above named pharmacy benefit medications are included on their covered formulary. Members with closed formulary benefits are subject to trying all appropriate formulary alternatives before a coverage exception for a non-formulary medication will be considered.*

*The preceding policy is a guideline to allow for coverage of the pertinent medication/product, and is not meant to serve as a clinical practice guideline.*