

POLICY: Colony Stimulating Factors – Granix™ (tbo-filgrastim injection – Teva)

APPROVAL DATE: 08/21/2019

OVERVIEW

Granix, a leukocyte growth factor, is indicated to reduce the duration of severe neutropenia in adults and pediatric patients 1 month of age and older with non-myeloid malignancies receiving myelosuppressive anti-cancer medications associated with a clinically significant incidence of febrile neutropenia.¹ The recommended dose is 5 mcg/kg per day given as a subcutaneous (SC) injection. The safety and effectiveness of Granix in pediatric patients have been established for pediatric patients 1 month to < 17 years of age; no data are available for infants < 1 month old. Granix may be administered by a healthcare professional or by a patient or caregiver. Granix is available in prefilled syringes and vials.

Guidelines

The National Comprehensive Cancer Network (NCCN) guidelines for hematopoietic growth factors (version 2.2019 – March 27, 2019) recommend filgrastim, along with other granulocyte colony-stimulating factors (CSFs), for prophylactic use if the patient is receiving anti-cancer medications that are associated with a high (> 20%) incidence of severe neutropenia with fever (category 1).² Consider CSF therapy for patients with an intermediate (10% to 20%) probability of developing febrile neutropenia based on risk factors. The NCCN guidelines also recommend therapy with a CSFs in other scenarios in those given myelosuppressive chemotherapy. The American Society of Clinical Oncology (ASCO) also has clinical practice guidelines for the use of white blood cell growth factors (2015) that also recommends CSFs to reduce the risk of febrile neutropenia in patients receiving cancer chemotherapy.³ The NCCN guidelines for hematopoietic growth factors (version 2.2019 – March 27, 2019) recommend filgrastim products, including Granix, for mobilization and following hematopoietic cell transplant.² Data are also available in this clinical scenario with Granix.⁴⁻⁷

Dosing

The NCCN guidelines for hematopoietic growth factors (version 2.2019 – March 27, 2019) recommend filgrastim products for the mobilization and following hematopoietic cell transplant.² Doses for mobilization of hematopoietic progenitor cells in the autologous setting are up to 32 mcg/kg per day of SC injection, in daily or twice-daily dosing.

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of Granix. Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). 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. Because of the specialized skills required for evaluation and diagnosis of patients treated with Granix as well as the monitoring required for adverse events and long-term efficacy, approval for some conditions requires Granix to be prescribed by or in consultation with a physician who specializes in the condition being treated.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indications

1. Cancer in Patients 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, iii, or iv):

- i. The patient is receiving myelosuppressive anti-cancer medications that are associated with a high risk of febrile neutropenia (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 at least one risk factor for febrile neutropenia according to the prescriber. Note: Examples of risk factors include age ≥ 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 and a reduced dose or frequency of chemotherapy may compromise treatment outcome; OR Note: Examples of colony-stimulating factors include filgrastim products, pegfilgrastim products, and sargramostim products (e.g., Leukine[®]).
- iv. The patient who has received chemotherapy has febrile neutropenia and has at least one risk factor for poor clinical outcomes or for developing infection-associated complications according to the prescriber. Note: Examples of risk factors include sepsis syndrome; age > 65 years; severe neutropenia (absolute neutrophil count < 100 cells/mm³); neutropenia expected to be > 10 days in duration; invasive fungal infection; other clinically documented infections; or prior episode of febrile neutropenia.

Dosing. Approve up to 5 mcg/kg per day by subcutaneous injection given for up to 14 days per month.

Other Uses with Supportive Evidence

2. Peripheral Blood Progenitor Cell (PBPC) Collection and Therapy. Approve for 1 month if prescribed by or in consultation with an oncologist, a hematologist or a physician who specializes in transplantation.

Dosing. Approve up to 32 mcg/kg per day by intravenous or subcutaneous injection.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

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

REFERENCES

1. Granix® injection [prescribing information]. North Wales, PA: Teva Pharmaceuticals; March 2019.
2. The NCCN Hematopoietic Growth Factors Clinical Practice Guidelines in Oncology (version 2.2019 – March 27, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on August 9, 2019.
3. Smith TJ, Bohlke K, Lyman GH, Carson KR, et al. Recommendations for the use of WBC growth factors: American Society of Clinical Oncology Clinical Practice Guideline Update. *J Clin Oncol*. 2015;33(28):3199-3212. Available at: <http://jco.ascopubs.org/content/early/2015/07/08/JCO.2015.62.3488.full.pdf+html> Accessed on August 9, 2019.
4. Schmitt M, Xu X, Hilgendorf I, et al. Mobilization of PBSC for allogeneic transplantation by the use of G-CSF biosimilar XM02 in healthy donors. *Bone Marrow Transplant*. 2013;48:922-925.
5. Elayan MM, Horowitz JG, Magraner JM, et al. Tbo-filgrastim versus filgrastim during mobilization and neutrophil engraftment for autologous stem cell transplantation. *Biol Blood Marrow Transplant*. 2015;21:1921-1925.
6. Trifilio S, Zough Z, Galvin J, et al. Filgrastim versus TBO-filgrastim to reduce the duration of neutropenia after autologous hematopoietic stem cell transplantation: TBO, or not TBO, that is the question. *Clin Transplant*. 2015;29:1128-1132.
7. Bhamidipati PK, Tiala MA, Grossman BJ, et al. Results of a prospective, open-label, non-inferiority study of tbo-filgrastim (Granix) versus filgrastim (Neupogen) in combination with plerixafor for autologous stem cell mobilization in patients with multiple myeloma and Non-Hodgkin lymphoma. *Biol Blood Marrow Transplant*. 2017;23(12):2065-2069.

HISTORY

Type of Revision	Summary of Changes	Approval Date
Annual revision	For the criteria regarding patients with cancer receiving myelosuppressive therapy who are adults 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
Selected revision	For the indication in cancer patients receiving myelosuppressive chemotherapy, removed the notation “who are adults” to reflect Food and Drug Administration-approval of Granix in children. Also, for this indication of use, removed “adults” in the dosing section so it applies children as well.	08/08/2018
Annual revision	For all conditions, the Dosing sections were revised to provide for the maximum range of dosing (see Policy). Additionally, the following sections were removed: initial/extended approval, duration of therapy, and labs/diagnostics. The waste management section was also deleted. Additional changes per the specific indications were as follows: 1. Cancer in Patients Receiving Myelosuppressive Chemotherapy: Colony stimulating factors are now provided as examples in a Note rather than as part of the criterion. Also, risk factors are now listed as Notes rather than as part of the criterion. The wording in reference to “according to the prescribing physician” was changed to “according to the prescriber”. 2. Peripheral Blood Progenitor Cell Collection and Therapy: The qualifier of “adults and children” was removed from the indication.	08/21/2019