

Department:	Pharmacy Management	Original Approval:	01/20/2016
Policy #:	PM131	Last Approval:	12/12/2018
Title:	Tbo-filgrastim (Granix)		
Approved By:	UM Committee		

REQUIRED CLINICAL DOCUMENTATION FOR REVIEW.

Documentation required to determine medical necessity for Tbo-filgrastim (Granix): History and/or physical examination notes and relevant specialty consultation notes that address the problem and need for the service: -Diagnosis -Prescribed by or in consultation with an oncologist, hematologist or a physician that specializes in transplantation -Medication list (current and past) to include start and end dates of all chemotherapy regimens -Age -Weight -Dosing and duration requested.

BACKGROUND

Granix, a granulocyte colony stimulating factor (G-CSF), is indicated for the reduction in the duration of severe neutropenia in adult and pediatric patients 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 in Granix in pediatric patients 1 month to < 17 years of age; no data are available for infants < 1 month of age. have not been established. Granix may be administered by a healthcare professional or by a patient or caregiver. Granix is available in single-use, preservative-free, prefilled syringes in strengths of 300 mcg/0.5 mL and 480 mcg/0.8 mL intended for single use only.

DEFINITIONS

None.

INDICATIONS/CRITERIA

Medicaid Members	Granix is preferred on the WA HCA Single Preferred Drug list. <i>Continue to criteria for approval below.</i>
Medicare Members	<i>Step-utilization of Part D drugs not required.</i>

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

FDA-Approved Indications

1. Cancer Patients Receiving Myelosuppressive Chemotherapy who are Adults.

Criteria. The patient must meet 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 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 (e.g., Granix, Neulasta® [pegfilgrastim injection], Neupogen® [filgrastim injection], Zarxio™ [filgrastim-sndz injection], Leukine® [sargramostim injection]) and a reduced dose or frequency of chemotherapy may compromise treatment outcome; OR
 - 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 prescribing physician (e.g., 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; prior episode of febrile neutropenia).

Granix is indicated for this condition to reduce the duration of severe neutropenia in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer medications associated with a clinically significant incidence of febrile neutropenia.¹ Guidelines from the National Comprehensive Cancer Network (NCCN) for myeloid growth factors (version 1.2018) recommend Granix, along with other colony stimulating factors, for prophylactic use if the patient is receiving anti-cancer medications that are associated with a high (> 20%) incidence of severe neutropenia with fever. 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 Granix in other scenarios in patients given myelosuppressive chemotherapy.²

Dosing in Adults with Cancer Receiving Myelosuppressive Chemotherapy. Dosing must meet the following: The dose is 5 mcg per kg per day by SC injection.¹

According to the NCCN guidelines for myeloid growth factors (version 1.2018), the SC route is preferred.² Granix is started the next day or up to 3 to 4 days after completion of chemotherapy and continued through post-nadir ANC recovery to normal levels.

Initial Approval/Extended Approval.

- A)** Initial Approval. Initial approval is for up to 6 months.

- B) Extended Approval. Extended approval is for up to 6-month intervals if the patient continues to receive myelosuppressive chemotherapy.

Duration of Therapy in Adults with Cancer Receiving Myelosuppressive Chemotherapy. Therapy may be continued as long as the patient is receiving myelosuppressive chemotherapy.

Labs/Diagnostics. None required.

Other Uses with Supportive Evidence

2. Patients (Adults and Children) Undergoing Peripheral Blood Progenitor Cell (PBPC) Collection and Therapy.

Criteria. *Patient must meet the following criteria:* Granix is prescribed by, or in consultation with, an oncologist, a hematologist, or a physician that specializes in transplantation.

Granix is not indicated in this scenario but other filgrastim products are indicated for the mobilization of hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.^{5-6,12} However, some data are available with Granix.^{6-9,13} The NCCN Panel in the guidelines for the myeloid growth factors recommends tbo-filgrastim (Granix) as an alternative for allogeneic hematopoietic cell mobilization and for granulocyte transfusion (category 2B).³ Also, tbo-filgrastim (Granix) is an alternative in the supportive care setting for post-autologous hematopoietic cell transplant (category 2A). Mobilization allows for the collection of increased numbers of progenitor cells capable of engraftment compared with collection by leukapheresis without mobilization or bone marrow harvest. After myeloablative chemotherapy, the transplantation of an increased number of progenitor cells can lead to a more rapid engraftment, which may result in a decreased need for supportive care. The scenarios where CSF is utilized includes patients with cancer or healthy donors undergoing mobilization of PBPC, as well as patients with cancer post autologous PBPC transplantation.^{1-3,10-11} This criterion is recommended based on the professional opinion of specialized and other physicians.

Dosing in Patients (Adults and Children) Undergoing PBPC Collection and Therapy. *Dosing must meet ONE of the following (A, B, OR C):*

- A) Patients with Cancer or Healthy Donors Undergoing Mobilization for PBPC: 10 mcg per kg per day SC for 5 to 7 days. Some patients may require up to 32 mcg per kg per day SC. Dosing can be once daily or twice daily.³ Alternate dosing will be assessed individually on a case-by-case basis.

In the autologous setting, Granix has been given as a dosage of 10 mcg/kg/day SC for 3 to 4 days prior to PBPC collection. Doses up to 32 mcg/kg/day SC have been used, in daily or twice daily dosing.^{2,6-9} The optimal duration has not been clearly established and some patients may require a longer duration of therapy.⁹⁻¹¹



- B) Patients Undergoing Mobilization of PBPC Who Are Poor Mobilizers:** 12.5 to 50 mcg per kg per day SC.¹¹ Dosing can be once daily or twice daily.² Alternate dosing will be assessed individually on a case-by-case basis.

Poor mobilizers (e.g., patients who fail to mobilize an adequate number of stem cells on the first attempt; patients with Hodgkin's lymphoma, non-Hodgkin's lymphoma, and preleukemic syndromes; recent chemotherapy or radiation), may use filgrastim or use other regimens that add Leukine to filgrastim, add Mozobil® (plerixafor injection), or mobilization with chemotherapy plus filgrastim.^{2,11}

- C) Patients with Cancer Post Autologous PBPC Transplantation:** 5 to 24 mcg per kg per day SC after reinfusion of the collected cells until a sustainable ANC is attained.⁴⁻⁵ Dosing can be once daily or twice daily.² Alternative dosing will be assessed individually on a case-by-case basis.

In clinical trials of filgrastim, the dose given to patients was 5 to 24 mcg/kg/day after reinfusion of the collected cells until a sustainable ANC ≥ 500 cells/mm³ was reached.⁴⁻⁵ Another recommendation for supportive care in patients post autologous stem cell or cord blood transplant, is to give filgrastim 5 mcg/kg/day beginning ≥ 5 days post transplant until recovery of ANC (e.g., $> 1,500$ cells/mm³ for 2 consecutive days).²

Initial Approval/Extended Approval.

Patients with Cancer or Healthy Donors Undergoing Mobilization of PBPC.

- A) Initial Approval.** For unrelated healthy donors, 5 days of therapy with Granix 10 mcg per kg per day are used.⁹⁻¹¹ For patients with cancer, 5 to 7 days of Granix 10 mcg per kg per day are usually given once daily; twice daily dosing may be used. Alternative regimens will be assessed individually on a case-by-case basis and may be extended for some patients (e.g., patients who are poor mobilizers).
- B) Extended Approval.** Not applicable.

Patients with Cancer Post Autologous PBPC Transplantation.

- A) Initial Approval.** 14 days or until the absolute neutrophil count (ANC) is $> 1,500$ cells/mm³ for 3 consecutive days. Usually the duration of therapy is 9 to 11 days but has ranged from 7 to 63 days. Alternative regimens will be assessed individually on a case-by-case basis.
- B) Extended Approval.** Not applicable.

Duration of Therapy in PBPC.

Patients with Cancer or Healthy Donors Undergoing Mobilization of PBPC. 5 days of Granix. Alternative durations will be assessed individually on a case-by-case basis and may be extended for some patients (e.g., patients who are poor mobilizers).

The National Marrow Donor Program protocol gives filgrastim for 4 consecutive days (in patients weighing < 35 kg) or 5 consecutive days in unrelated donors (allogeneic transplantation).⁵ In some instances, patients may require a longer duration of therapy (e.g., patients with cancer heavily

pretreated with chemotherapy, healthy patients in which a higher number of cells are needed due to the type of transplantation).

Patients with Cancer Post Autologous PBPC Transplantation. 14 days of Granix. Approve for another 14 days if ANC is not at a sustainable level. Most patients have a response after 28 days of Granix. Alternative durations will be assessed individually on a case-by-case basis.

Labs/Diagnostics. None required.

Waste Management for All Indications.

Single dose pre-filled syringes are in strengths of 300 mcg/0.5 mL and 480 mcg/0.5 mL. Single-dose vials are available in 300 mcg/mL and 480/1.6 mL. The dose is based on a mcg per kg body weight basis. Use the most efficient formulation that delivers the needed dose.

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).

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

SPECIAL CONSIDERATIONS

None.

LIMITATIONS/EXCLUSIONS

Please refer to a product line's certificate of coverage for benefit limitations and exclusions for these services:

PRODUCT LINE	LINK TO CERTIFICATE OF COVERAGE
MEDICARE ADVANTAGE	http://healthfirst.chpw.org/for-members/resource-library/handbooks-and-guides
WASHINGTON APPLE HEALTH	http://chpw.org/our-plans/apple-health/
INTEGRATED MANAGED CARE	http://chpw.org/our-plans/apple-health/

Citations & References

References	
	<ol style="list-style-type: none"> 1. Granix® injection [prescribing information]. North Wales, PA: Teva Pharmaceuticals; July 2018. 2. The NCCN Myeloid Growth Factors Clinical Practice Guidelines in Oncology (Version 1.2018 – March 2, 2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on July 27, 2018. 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. <i>J Clin Oncol</i>. 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 July 27, 2018. 4. Neupogen® injection for subcutaneous or intravenous use [prescribing information]. Thousand Oaks, CA: Amgen, Inc.; June 2018. 5. Zarxio™ injection for subcutaneous or intravenous use [prescribing information]. Princeton, NJ: Sandoz; February 2017. 6. 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. <i>Bone Marrow Transplant</i>. 2013;48:922-925. 7. Elayan MM, Horowitz JG, Magraner JM, et al. Tbo-filgrastim versus filgrastim during mobilization and neutrophil engraftment for autologous stem cell transplantation. <i>Biol Blood Marrow Transplant</i>. 2015;21:1921-1925. 8. 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. <i>Clin Transplant</i>. 2015;29:1128-1132. 9. Blair HA, Scott LJ. Tbo-filgrastim: a review in neutropenia conditions. <i>BioDrugs</i>. 2016;30:153-160. 10. Pulsipher MA, Chitphakdithai P, Miller JP, et al. Adverse events among 2408 unrelated donors of peripheral blood stem cells: results of a prospective trial from the National Marrow Donor Program. <i>Blood</i>. 2009;113:3604-3611. 11. Pusic I, DiPersio JF. The use of growth factors in hematopoietic stem cell transplantation. <i>Curr Pharm Des</i>. 2008;14(20):1950-1961. 12. Nivestym™ injection for subcutaneous or intravenous use [prescribing information]. Lake Forest, IL: Hospira/Pfizer; July 2018.

	13. 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. <i>Biol Blood Marrow Transplant.</i> 2017;23(12):2065-2069.
CFR	
WAC	WAC 284-43-2050
RCW	
Contract Citation	<input type="checkbox"/> WAH
	<input type="checkbox"/> IMC
	<input type="checkbox"/> MA
Other Requirements	
NCQA Elements	

Revision History

Revision Date	Revision Description	Revision Made By
01/13/2016	New	Kelly Force; Yusuf Rashid, RPh
01/20/2016	Approval	MMLT
01/12/2017	No revisions	Fran McGaugh
01/13/2017	Approval	MMLT
07/24/2017	Criteria completely updated and revised	Michael Sporck, Pharmacy Intern Sophia Yun, PharmD
07/25/2017	Approved	MMLT
03/09/2018	Reassigned from UM142 to PM131	Cindy Bush
04/27/2018	Transferred to new template	Cindy Bush
05/23/2018	No revisions	Jennifer Farley, PharmD
06/14/2018	Approval	UM Committee
11/28/2018	Revisions from ESI annual update	Jennifer Farley, PharmD
12/12/2018	Approval	UM Committee