Colony Stimulating Factors: Granix® (tbo-filgrastim)
(Subcutaneous/Intravenous)

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I. Length of Authorization

Coverage will be provided for four months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [Pharmacy Benefit]:

- Granix 300 mcg pre-filled syringe: 4 syringes per 1 day
- Granix 300 mcg single-dose vial: 4 vials per 1 day
- Granix 480 mcg pre-filled syringe: 3 syringes per 1 day
- Granix 480 mcg single-dose vial: 3 vials per 1 day

B. Max Units (per dose and over time) [Medical Benefit]:

BMT or PBSC:

- 1200 billable units per day

All Other indications:

- 600 billable units per day

III. Initial Approval Criteria

Coverage for Granix® (tbo-filgrastim) is provided in the following conditions:

Prophylactic use in patients with non-myeloid malignancy †

- Patient is undergoing myelosuppressive chemotherapy with an expected incidence of febrile neutropenia of 20% or greater §; OR
- Patient is undergoing myelosuppressive chemotherapy with an expected incidence of febrile neutropenia of 10% or greater § AND one or more of the following co-morbidities:
  - Elderly patients (age 65 or older) receiving full dose intensity chemotherapy
  - History of recurrent febrile neutropenia from chemotherapy
  - Extensive prior exposure to chemotherapy

- Previous exposure of pelvis, or other areas of large amounts of bone marrow, to radiation
- Pre-existing neutropenia (ANC ≤ 1000/mm^3) or bone marrow involvement with tumor
- Patient has a condition that can potentially increase the risk of serious infection (i.e. HIV/AIDS)
- Infection/open wounds
- Recent surgery
- Poor performance status
- Poor renal function (creatinine clearance <50)
- Liver dysfunction (elevated bilirubin >2.0)
- Chronic immunosuppression in the post-transplant setting including organ transplant

Treatment of chemotherapy-induced febrile neutropenia ‡

- Used for the treatment of chemotherapy induced febrile neutropenia; AND
  - Patient has been on prophylactic therapy with filgrastim; OR
  - Patient has not received prophylactic therapy with a granulocyte colony stimulating factor; AND
    - Patient has one or more of the following risk factors for developing infection-related complications:
      - Sepsis Syndrome
      - Age > 65
      - Absolute neutrophil count [ANC] <100/mcL
      - Duration of neutropenia expected to be greater than 10 days
      - Pneumonia or other clinically documented infections
      - Invasive fungal infection
      - Hospitalization at the time of fever
      - Prior episode of febrile neutropenia

Patient who experienced a neutropenic complication from a prior cycle of the same chemotherapy ‡

Bone Marrow Transplantation (BMT) failure or Engraftment Delay ‡

Peripheral Blood Stem Cell (PBSC) mobilization and transplant ‡

Myelodysplastic Syndromes (MDS) ‡

- Endogenous serum erythropoietin level of ≤500 mUnits/mL; AND
- Patient has lower risk disease (i.e., defined as IPSS-R [Very Low, Low, Intermediate], IPSS [Low/Intermediate-1], WPSS [Very Low, Low, Intermediate]); AND
- Used for treatment of symptomatic anemia in patients without del(5q); AND
- Patient is receiving concurrent therapy with an Erythropoiesis Stimulating Agent (ESA); AND
  - Patient has ring sideroblasts < 15% and will use in combination with lenalidomide following no response (despite adequate iron stores) or loss or response to an ESA alone; OR
  - Patient has ring sideroblasts ≥ 15%

Patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Subsyndrome of Acute Radiation Syndrome) ‡

† FDA-labeled indication(s); ‡ Compendia Recommended Indication(s)

§ Expected incidence of febrile neutropenia percentages for myelosuppressive chemotherapy regimens can be found in the NCCN Myeloid Growth Factors Clinical Practice Guideline at NCCN.org.

IV. Renewal Criteria

Same as initial prior authorization policy criteria.

V. Dosage/Administration

Indication	Dose
Prevention and treatment of febrile neutropenia in patients receiving myelosuppressive chemotherapy	5 mcg/kg daily for up to 14 days *Administer no earlier than 24 hours following myelosuppressive chemotherapy. Do not administer within 24 hours prior to chemotherapy.
PBPC/BMT	10 mcg/kg daily for up to 14 days
Other indications	5 mcg/kg daily for up to 14 days

VI. Billing Code/Availability Information

Jcode:

- J1447 - Injection, tbo-filgrastim, 1 microgram (1 microgram=1 billable unit)

NDC:

- Granix 300 mcg single-dose prefilled syringe: 63459-0910-xx
- Granix 480 mcg single-dose prefilled syringe: 63459-0912-xx
- Granix 300 mcg single-dose vial: 63459-0918-xx
- Granix 480 mcg single-dose vial: 63459-0920-xx

VII. References

1. Granix [package insert]. North Wales, PA; Teva Pharmaceuticals USA, Inc.; July 2018. Accessed March 2019.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Hematopoietic Growth Factors. Version 1.2019. National Comprehensive Cancer Network, 2017. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed March 2019.

3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) tbo-filgrastim. National Comprehensive Cancer Network, 2019. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed March 2019.
4. Elayan MM, Horowitz JG, Magraner JM, Shaughnessy PJ, Bachier C. Tbo-Filgrastim versus Filgrastim during Mobilization and Neutrophil Engraftment for Autologous Stem Cell Transplantation. Biol Blood Marrow Transplant. 2015 Nov; 21(11):1921-5. doi: 10.1016/j.bbmt.2015.05.024.
5. Trifilio S, Zhou Z, Galvin J, Fong JL, Monreal J, Mehta J. 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 Oct 22. doi: 10.1111/ctr.12637.
6. Kelaidi C Beyne-Rauzy O, Braun T, et al. High Response rate and improved exercise capacity and quality of life with a new regimen of darbepoetin alfa with or without filgrastim in lower-risk myelodysplastic syndromes: a phase II study by the GFM. Ann Hematol 2013; 92:621-631.
7. Wisconsin Physicians Service Insurance Corporation. Local Coverage Determination (LCD): Human Granulocyte/Macrophage Colony Stimulating Factors (L34699). Centers for Medicare & Medicaid Services, Inc. Updated on 01/24/2019 with effective date 02/01/2019. Accessed March 2019.
8. First Coast Service Options, Inc. Local Coverage Determination (LCD): G-CSF (Neupogen®, Granix™, Zarxio™) (L34002). Centers for Medicare & Medicaid Services, Inc. Updated on 10/12/2018 with effective date 10/01/2018. Accessed March 2019.
9. National Government Services, Inc. Local Coverage Article: Filgrastim, Pegfilgrastim, Tbo-filgrastim (e.g., Neupogen®, Neulasta™, Granix™, Zarxio™) - Related to LCD L33394 (A52408). Centers for Medicare & Medicaid Services, Inc. Updated on 12/28/2018 with effective date 01/01/2019. Accessed March 2019.
10. Palmetto GBA. Local Coverage Determination (LCD): White Cell Colony Stimulating Factors (L37176). Centers for Medicare & Medicaid Services, Inc. Updated on 02/22/2019 with effective date 01/01/2019. Accessed March 2019.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C93.10	Chronic myelomonocytic leukemia, not having achieved remission
D46.0	Refractory anemia without ring sideroblasts, so stated
D46.1	Refractory anemia with ring sideroblasts
D46.20	Refractory anemia with excess of blasts, unspecified
D46.21	Refractory anemia with excess of blasts 1
D46.4	Refractory anemia, unspecified

ICD-10	ICD-10 Description
D46.9	Myelodysplastic syndrome, unspecified
D46.A	Refractory cytopenia with multilineage dysplasia
D46.B	Refractory cytopenia with multilineage dysplasia and ring sideroblasts
D46.Z	Other myelodysplastic syndromes
D61.81	Pancytopenia
D70.1	Agranulocytosis secondary to cancer chemotherapy
D70.9	Neutropenia, unspecified
T45.1X5A	Adverse effect of antineoplastic and immunosuppressive drugs initial encounter
T45.1X5D	Adverse effect of antineoplastic and immunosuppressive drugs subsequent encounter
T45.1X5S	Adverse effect of antineoplastic and immunosuppressive drugs sequela
T66.XXXA	Radiation sickness, unspecified, initial encounter
T66.XXXD	Radiation sickness, unspecified, subsequent encounter
T66.XXXS	Radiation sickness, unspecified, sequela
W88.1	Exposure to radioactive isotopes
W88.8	Exposure to other ionizing radiation
Z41.8	Encounter for other procedures for purposes other than remedying health state
Z48.290	Encounter for aftercare following bone marrow transplant
Z51.11	Encounter for antineoplastic chemotherapy
Z51.12	Encounter for antineoplastic immunotherapy
Z51.89	Encounter for other specified aftercare
Z52.001	Unspecified donor, stem cells
Z52.011	Autologous donor, stem cells
Z52.091	Other blood donor stem cells
Z76.89	Persons encountering health services in other specified circumstances
Z94.81	Bone marrow transplant status
Z94.84	Stem cells transplant status

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD):

Jurisdiction(s): 5,8	NCD/LCD Document (s): L34699
https://www.cms.gov/medicare-coverage-database/search/lcd-date-search.aspx?DocID=L34699&bc=gAAAAAAAAAAA	

Jurisdiction(s): N	NCD/LCD Document (s): L34002
https://www.cms.gov/medicare-coverage-database/search/document-id-search-results.aspx?DocID=L34002&bc=gAAAAAAAAAAA&	

Jurisdiction(s): 6, K	NCD/LCD Document (s): A52408
https://www.cms.gov/medicare-coverage-database/search/document-id-search-results.aspx?DocID=A52408&bc=gAAAAAAAAAAA&	

Jurisdiction(s): J, M	NCD/LCD Document (s): L37176
https://www.cms.gov/medicare-coverage-database/search/lcd-date-search.aspx?DocID=L37176&bc=gAAAAAAAAAAA	

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC