Utilization Review Policy 256A

POLICY: Colony Stimulating Factors – Granix Utilization Management Medical Policy

- Granix® (tbo-filgrastim injection for subcutaneous use – Teva)

EFFECTIVE DATE: 9/1/2021
LAST REVISION DATE: 5/7/2025

COVERAGE CRITERIA FOR: UCare Medical Assistance and Exchange Plans Only (PMAP, Connect, MSC+, MnCare, all Individual and Family Plans)

OVERVIEW

Granix, a granulocyte colony stimulating factor (G-CSF), is indicated to reduce the duration of severe neutropenia in adults and pediatric patients ≥ 1 month of age with non-myeloid malignancies receiving myelosuppressive anti-cancer medications associated with a clinically significant incidence of febrile neutropenia.[1]

Guidelines

The National Comprehensive Cancer Network (NCCN) addresses the use of Granix in guidelines. Of note, throughout the recommendations, it is acknowledged that Granix is an appropriate substitute for filgrastim.

- **Hematopoietic Cell Transplantation:** Guidelines (version 2.2024 – August 30, 2024) recommend filgrastim for hematopoietic cell mobilization for allogeneic or autologous donors as a single agent or in combination with other treatments.[4]
- **Hematopoietic Growth Factors:** Guidelines (version 3.2024 – January 30, 2024) recommend Granix, 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.[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 CSFs in other scenarios in those given myelosuppressive chemotherapy. Granix is also recommended as an appropriate option for the treatment of patients with radiation-induced myelosuppression following a radiologic/nuclear incident (Hematopoietic Syndrome of Acute Radiation Syndrome [H-ARS]).
- **Myelodysplastic Syndromes (MDS):** Guidelines (version 3.2024 – July 25, 2024) recommend Granix for use in certain patients with MDS (e.g., neutropenic patients with recurrent or resistant infections, combination use with epoetin alfa or Aranesp® [darbepoetin alfa injection] in patients with anemia).[3]

The American Society of Clinical Oncology clinical practice guidelines for the use of white blood cell growth factors (2015) recommends CSFs to reduce the risk of febrile neutropenia in patients receiving cancer chemotherapy.[5] CSFs may be considered in patients receiving radiation therapy alone if prolonged delays secondary to neutropenia are expected. The guidelines state CSFs should be avoided in patients receiving concomitant chemotherapy and radiation therapy, particularly involving the mediastinum.

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 indications. 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 requires Granix to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Granix is recommended for requests meeting both the preferred product step therapy requirements and indication requirements.

Preferred Product(s): Zarxio
Non-Preferred Products(s): Granix

Step Therapy Requirements:

Authorization for a non-preferred biologic product or biosimilar will be granted if the patient has had *any one of the listed issues below (A, B, C, or D) with all preferred product(s)*. *Chart notes documenting* the issue must be provided at time of request:

A. Allergic reaction to a specific inactive ingredient in all preferred biologic products or biosimilars OR

B. Adverse reaction to a specific inactive ingredient in all preferred biologic products or biosimilars OR

C. Therapeutic success while taking a non-preferred biologic product or biosimilar and therapeutic failure during an adequate trial of all preferred biologic products or biosimilars which allowed sufficient time for a positive treatment outcome documented by medical chart notes OR

D. The patient has a diagnosis not included in the FDA-approved indications of all preferred products, but is included in the FDA-approved indications of the non-preferred product

Please note:

- Factors such as patient or prescriber preference or healthcare facility's or pharmacy's inability or unwillingness to order or stock the preferred product(s) will not be considered
- Common side effects to all products and infusion-related reactions are not considered documented allergic reactions to a preferred product as they would be expected with the innovator and biosimilar products
- Continuation of therapy overrides are not available to bypass required trial(s) of preferred biosimilar or biologic reference product
- Generally, an adequate trial of a drug is considered to be three months or longer in order to allow time for efficacy to be established

FDA-Approved Indications

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1. Cancer in a Patient Receiving Myelosuppressive Chemotherapy. Approve for 6 months if the patient meets BOTH of the following (A and B):

A) Patient meets ONE of the following (i, ii, iii, or iv):

i. 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. Patient meets BOTH of the following (a and b):

a) 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

b) Patient has at least one risk factor for febrile neutropenia according to the prescriber; OR

Note: Examples of risk factors include age > 65 year receiving full chemotherapy dose intensity; prior chemotherapy or radiation therapy; persistent neutropenia; bone marrow involvement by tumor; recent surgery and/or open wounds; liver dysfunction (bilirubin > 2.0 mg/dL); renal dysfunction (creatine clearance < 50 mL/min); poor performance status; human immunodeficiency virus (HIV) infection patients with low CD4 counts.

iii. Patient meets BOTH of the following (a and b):

a) Patient has had a neutropenic complication from a prior chemotherapy cycle and did not receive prophylaxis with a colony stimulating factor; AND

Note: Examples of colony stimulating factors include filgrastim products, pegfilgrastim products, Ryzneuta (efbemalenograstim alfa-vuxw subcutaneous injection), Rolvedon (eflapegrastim-xnst subcutaneous injection).

b) A reduced dose or frequency of chemotherapy may compromise treatment outcome; OR

iv. 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; AND

Note: Examples of risk factors include sepsis syndrome; age > 65 years; severe neutropenia (absolute neutrophil count [ANC] < 100 cells/mm^3); neutropenia expected to be > 10 days in duration; pneumonia or other clinically documented infections; invasive fungal infection; hospitalization at the time of fever; prior episode of febrile neutropenia.

B) The medication is prescribed by or in consultation with an oncologist or hematologist.

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. Myelodysplastic Syndromes (MDS). Approve for 3 months if prescribed by or in consultation with an oncologist or hematologist.

Dosing. Approve up to 5 mcg/kg per day by subcutaneous injection.

3. 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 10 mcg/kg per day by subcutaneous injection.

4. Radiation Syndrome (Hematopoietic Syndrome of Acute Radiation Syndrome [H-ARS]). Approve for 1 month if prescribed by or in consultation with a physician who has expertise in treating acute radiation syndrome.

Dosing. Approve up to 10 mcg/kg per day as a subcutaneous injection.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Granix is not recommended in the following situations:

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® subcutaneous injection [prescribing information]. North Wales, PA: Teva; November 2023.
2. The NCCN Hematopoietic Growth Factors Clinical Practice Guidelines in Oncology (version 3.2024 – January 30, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on September 18, 2024.
3. The NCCN Myelodysplastic Syndromes Clinical Practice Guidelines in Oncology (version 3.2024 – July 25, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on September 18, 2024.

4. The NCCN Hematopoietic Cell Transplantation Clinical Practice Guidelines in Oncology (version 2.2024 – August 30, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on September 18, 2024.
5. 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.

HISTORY

Type of Revision	Summary of Changes	Review 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 of cancer patients receiving myelosuppressive chemotherapy, removed the notation "who are adults" to reflect FDA-approval of Granix in children.	08/08/2018
Annual Revision	The following changes per the specific indications are cited below: **1. Cancer in Patients Receiving Myelosuppressive Chemotherapy:** CSFs 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
Annual Revision	Myelodysplastic Syndromes, criteria, and dosing were added as an approval condition.	08/19/2020
Annual Revision	No criteria changes.	08/18/2021
Annual Revision	No criteria changes.	08/31/2022
UCare Revision	Combined Medicare Policy with Health Exchange and Medicaid Policy due to retirement of Local Coverage Article A52408 (L33394). Update Biosimilar Step Therapy Requirement section to include lookback period for both Medicare (365 days) and Medicaid and Commercial patients (180 days).	7/28/2023
Annual Revision	No criteria changes	09/20/2023
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	09/16/2024
Annual Revision	**Cancer in a Patient Receiving Myelosuppressive Chemotherapy**: The Note providing examples of risk factors for febrile neutropenia was updated from "≥ 65 years" to "> 65 years of age receiving full chemotherapy dose intensity", liver dysfunction was defined as "bilirubin > 2.0 mg/dL", renal dysfunction was defined as "creatine clearance < 50 mL/min", and human immunodeficiency infection patients was clarified by adding "with low CD4 counts." The requirement for a patient to have had a neutropenic complication from "prior chemotherapy" was updated to add "cycle." The Note providing examples of colony stimulating factors was updated to add Ryzneuta and Rolvedon and remove Leukine. The Note providing examples of risk factors associated with poor clinical outcomes for patients who have febrile neutropenia was updated to include pneumonia, hospitalization at the time of fever, and prior episode of febrile neutropenia. **Peripheral Blood Progenitor Cell (PBPC) Collection and Therapy:** The dosing limitation was lowered from 32 mcg/kg to 10 mcg/kg. **Radiation Syndrome (Hematopoietic Syndrome of Acute Radiation Syndrome [H-ARS]):** This Other Uses with Supportive Evidence was added to the policy. A new dosing limitation was added.	10/09/2024
UCare Update	Updated step therapy criteria to require clinical need for non-preferred product over the preferred products including chart note documentation to support the need for a non-preferred product.	05/07/2025