BlueCross BlueShield
Federal Employee Program

Neupogen (filgrastim), Granix (tbo-filgrastim), **Nivestym** (filgrastim-aafi), Nypozi* (filgrastim-txid), Releuko (filgrastim-ayow), **Zarxio** (filgrastim-sndz)

*Prior authorization for specific formulations applies only to formulary exceptions due to being a non-covered medication.
Preferred products: Nivestym, Zarxio

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Colony stimulating factors are medications used to stimulate the production of neutrophils, a type of white blood cells important in fighting off infections. Granix (tbo-filgrastim), Neupogen (filgrastim) and Neupogen biosimilars are granulocyte colony-stimulating factors (G-CSF) that act on hematopoietic cells by binding to specific cell surface receptors, thereby stimulating proliferation, differentiation, commitment, and end cell functional activation. Zarxio (filgrastim-sndz), Nivestym (filgrastim-aafi), Releuko (filgrastim-ayow), Nypozi (filgrastim-txid) are biosimilars to Neupogen and approved for most indications of Neupogen (1-6).

Regulatory Status

FDA-approved indications:

1. Cancer patients receiving myelosuppressive chemotherapy
   Filgrastim is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anticancer drugs associated with a significant incidence of severe neutropenia with fever (1-6).

2. Patients with acute myeloid leukemia receiving induction or consolidation chemotherapy
   Filgrastim is indicated for reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of adults with AML (1-3, 5-6).

3. Cancer patients receiving bone marrow transplant
   Filgrastim is indicated to reduce the duration of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by marrow transplantation (1-3, 5-6).

4. Patients undergoing peripheral blood progenitor cell collection and therapy
   Filgrastim is indicated for the mobilization of hematopoietic progenitor cells into the peripheral

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blood for collection by leukapheresis (1-3, 6).

5. Patients with severe congenital, cyclic or idiopathic neutropenia

   Filgrastim is indicated for chronic administration to reduce the incidence and duration of sequelae of neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia (1-3, 5-6).

6. Patients acutely exposed to myelosuppressive doses of radiation

   Increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic syndrome of acute radiation syndrome) (1, 6).

Off-Label Uses: (7-11)

1. Agranulocytosis
2. AIDS associated
3. Aplastic anemia
4. Ganciclovir-induced neutropenia
5. Hairy cell leukemia
6. Hematopoietic stem cell transplantation
7. Umbilical cord stem cell transplantation
8. Hepatitis C therapy associated (ANC < 750 mm^3)
9. Myelodysplastic syndrome in neutropenic patients with recurrent or resistant infections

Granix is not technically considered a biosimilar to Neupogen because it was filed as a Biologics License Application since a biosimilars approval pathway had not been established at the time of FDA submission. Although these two drugs have slight structural differences, the pharmacokinetic parameters, safety, and efficacy between the two biologics do not significantly differ (12).

Splenic rupture, including fatal cases, can occur following the administration of filgrastim. Patients who report left upper abdominal or shoulder pain after receiving filgrastim should be evaluated for

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an enlarged spleen or splenic rupture (1-6).

Acute respiratory distress syndrome (ARDS) can occur in patients receiving filgrastim. Patients should be evaluated for ARDS if they develop fever and lung infiltrates or respiratory distress after receiving filgrastim and should be discontinued in patients with ARDS (1-6).

Serious allergic reactions, including anaphylaxis, can occur in patients receiving filgrastim. The majority of reported events occurred upon initial exposure. Allergic reactions, including anaphylaxis, can recur within days after the discontinuation of initial anti-allergic treatment. Permanently discontinue therapy in patients with serious allergic reactions. Do not administer filgrastim to patients with a history of serious allergic reactions to pegfilgrastim or filgrastim (1-6).

Severe and sometimes fatal sickle cell crises can occur in patients with sickle cell disorders receiving filgrastim (1-6).

Summary

Colony stimulating factors are medications used to stimulate the production of neutrophils, a type of white blood cells important in fighting off infections. Granix (tbo-filgrastim), Neupogen (filgrastim) and Neupogen biosimilars are granulocyte colony-stimulating factors (G-CSF) that act on hematopoietic cells by binding to specific cell surface receptors, thereby stimulating proliferation, differentiation, commitment, and end cell functional activation. Zarxio (filgrastim-sndz), Releuko (filgrastim-awyo), Nivestym (filgrastim-aafi), and Nypozi (filgrastim-txid) are biosimilars to Neupogen and approved for most indications of Neupogen (1-6).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Neupogen and its biosimilars while maintaining optimal therapeutic outcomes.

References

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Preferred products: Nivestym, Zarxio

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