RATIONALE FOR INCLUSION IN PA PROGRAM

Background
Neutropenia is a hematological disorder characterized by an abnormally low number of neutrophils. A person with severe neutropenia has an absolute neutrophil count that is less than 500 mm$^2$ and has a high risk of infection. Neutrophils usually make up 40-60 percent of circulating white blood cells and serve as the primary defense against infections by destroying bacteria in the blood. When chemotherapy agents attack cancer cells in the body, neutrophils and other cells are also attacked. This results in a decrease in healthy white blood cells, making it harder for the body to fight infections. Patients receiving chemotherapy are at risk of becoming neutropenic and can become susceptible to infections that may become life-threatening (1).

Granix is a short-acting human granulocyte colony-stimulating growth factor (G-CSF) produced by recombinant DNA technology. G-CSF is a naturally occurring hormone that is produced by the body to stimulate the bone marrow to produce neutrophils, a type of white blood cell that helps the immune system fight infection. A recombinant form of G-CSF is used to treat certain cancer patients with neutropenia in order to stimulate the bone marrow to produce more white blood cells. Granix binds to G-CSF receptors and stimulates proliferation of neutrophils and increase neutrophil counts and activity (1-2).

Regulatory Status
FDA-approved indication: Granix is a leukocyte growth factor indicated for reduction in the duration of severe neutropenia in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia (2).

Off-label Uses:
Hepatitis C Treatment Related Neutropenia (3-4)

Cancer Patients Receiving Myelosuppressive Chemotherapy
Granix can be used to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anticancer drugs associated with a significant incidence of severe neutropenia with fever (5-6).
Patients with Acute Myeloid Leukemia Receiving Induction or Consolidation Chemotherapy
Granix can be used for reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of adults with AML (5-6).

Patients Undergoing Peripheral Blood Progenitor Cell Collection and Therapy
Granix can be used for the mobilization of hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis (7-9).

Cancer Patients Receiving Bone Marrow Transplant
Granix can be used to reduce the duration of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia, in patients with non-myeloid malignancies undergoing myeloablative chemotherapy followed by marrow transplantation (8).

Patients with Severe Chronic Neutropenia
Granix can be used 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 (5-6).

Neutropenia secondary to anti-rejection medications post-transplant (8). A study by Hornedo determined the role of granulocyte colony stimulating factor (G-CSF) following transplantation in the post-transplant period. Patients receiving G-CSF reached 500 and 1,000 neutrophils significantly faster (P=0.001) than patients with no G-CSF. G-CSF accelerates the time to neutrophil engraftment. This translated into a significantly (P<0.05) shorter hospitalization time for patients receiving G-CSF (9). In kidney and liver transplant recipients, granulocyte colony-stimulating factor has been used successfully to reverse ganciclovir-induced neutropenia or cytomegalovirus-induced neutropenia (9).

Daily dosing with Granix should continue until the expected neutrophil nadir is passed and the neutrophil count has recovered to the normal range. Monitor complete blood count (CBC) prior to chemotherapy and twice per week until recovery. Granix, in clinical studies, was administered at 5 mcg/kg subcutaneously once daily beginning one day after chemotherapy for at least five days and continued to a maximum of 14 days or until an ANC of ≥10,000 x 10^6/L after nadir was
Splenic rupture, including fatal cases, can occur following administration of human granulocyte colony-stimulating factors. In patients who report upper abdominal or shoulder pain after receiving Granix, discontinue Granix and evaluate for an enlarged spleen or splenic rupture (2).

Acute respiratory distress syndrome (ARDS) can occur in patients receiving human granulocyte colony-stimulating factors. Evaluate patients who develop fever and lung infiltrates or respiratory distress after receiving Granix, for ARDS. Discontinue Granix in patients with ARDS (2).

Severe and sometimes fatal sickle cell crises can occur in patients with sickle cell disease receiving human granulocyte colony-stimulating factors. Consider the potential risks and benefits prior to the administration of human granulocyte colony-stimulating factors in patients with sickle cell disease. Discontinue Granix in patients undergoing a sickle cell crisis (2).

The safety and effectiveness of Granix in pediatric patients have not been established (2).

**Summary**

Granix is a leukocyte growth factor indicated for reduction in the duration of severe neutropenia in patients with non-myeloid malignancies receiving myelosuppressive anticancer drugs associated with a clinically significant incidence of febrile neutropenia. Splenic rupture, including fatal cases, can occur following administration of human granulocyte colony-stimulating factors. Acute respiratory distress syndrome (ARDS) and severe and sometimes fatal sickle cell crises can occur in patients receiving human granulocyte colony-stimulating factors. The safety and effectiveness of Granix in pediatric patients have not been established (2).

Prior approval is required to ensure the safe, clinically appropriate and cost effective use of Granix while maintaining optimal therapeutic outcomes.

**References**