RATIONALE FOR INCLUSION IN PA PROGRAM

Background
Zarxio is a leukocyte growth factor which is biosimilar to Amgen Inc.’s Neupogen (filgrastim), and approved for most indications as Neupogen. Zarxio is granulocyte colony-stimulating factor (G-CSF), which is made using the bacteria Escherichia coli. G-CSF is a substance naturally produced by the body. It stimulates the growth of neutrophils, a type of white blood cell important in the body’s fight against infection. A biosimilar product is a biological product that is approved based on a showing that it is highly similar to an already-approved biological product, known as a reference product. The biosimilar also must show it has no clinically meaningful differences in terms of safety and effectiveness from the reference product. Only minor differences in clinically inactive components are allowable in biosimilar products (1).

Regulatory Status
FDA-approved indications:

1. **Cancer Patients Receiving Myelosuppressive Chemotherapy**
   Zarxio 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).

2. **Patients With Acute Myeloid Leukemia Receiving Induction or Consolidation Chemotherapy**
   Zarxio 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. **Cancer Patients Receiving Bone Marrow Transplant**
   Zarxio 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).

4. **Patients Undergoing Peripheral Blood Progenitor Cell Collection and Therapy**
   Zarxio is indicated for the mobilization of hematopoietic progenitor cells into the peripheral blood for collection by leukopheresis (1).

5. **Patients with Severe Chronic Neutropenia**
Zarxio 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).

Off-label Use
Neutropenia secondary to anti-rejection medications post-transplant. 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 (2). In kidney and liver transplant recipients, granulocyte colony-stimulating factor has been used successfully to reverse ganciclovir-induced neutropenia or cytomegalovirus-induced neutropenia (3).

Splenic rupture, including fatal cases, can occur following the administration of Zarxio. Patients who report left upper abdominal or shoulder pain after receiving Zarxio should be evaluated for an enlarged spleen or splenic rupture (1).

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

Serious allergic reactions, including anaphylaxis, can occur in patients receiving Zarxio. 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 Zarxio to patients with a history of serious allergic reactions to pegfilgrastim or filgrastim (1).

Severe sickle cell crises can occur in patients with sickle cell disorders receiving Zarxio. Severe and sometimes fatal sickle cell crises can occur in patients with sickle cell disorders receiving filgrastim (1).
Summary
Zarxio is a recombinant human granulocyte-macrophage colony stimulating factor (rhu G-CSF) produced by *Escherichia coli* (*E coli*) bacteria. It is FDA approved for use in myelosuppressive chemotherapy, AML receiving chemotherapy, bone marrow transplant, harvesting of peripheral blood stem cells and severe chronic neutropenia. Zarxio is biosimilar to Neupogen (filgrastim) and is approved for the same indications as. A biosimilar product is a biological product that is approved based on a showing that it is highly similar to an already-approved biological product, known as a reference product (1).

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

References