Nivestym™ (filgrastim-aafi) – New biosimilar approval

- On July 20, 2018, Pfizer announced the FDA approval of Nivestym (filgrastim-aafi), biosimilar to Amgen's Neupogen® (filgrastim).
    - Nivestym is the second FDA-approved biosimilar to Neupogen. The first biosimilar approved was Zarxio® (filgrastim-sndz).
    - Filgrastim is also available as the branded biological agent Granix® (tbo-filgrastim). Granix was approved before the FDA had an established biosimilar pathway, and therefore cannot be considered a biosimilar to Neupogen.

- Nivestym, Zarxio, and Neupogen share the following indications:
    - To decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever.
    - For reduing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML).
    - To reduce the duration of neutropenia and neutropenia-related clinical sequelae, eg, febrile neutropenia, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation (BMT).
    - For the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.
    - To reduce the incidence and duration of sequelae of neutropenia (eg, fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia.

- Neupogen has the additional indication to increase survival in patients acutely exposed to myelosuppressive doses of radiation (hematopoietic syndrome of acute radiation syndrome).

- Granix is only indicated to reduce the duration of severe neutropenia in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

- A biosimilar product is a biological agent that is considered highly similar to an already approved biological drug, known as the reference product. Biological products are generally derived from a living organism and can come from many sources, including humans, animals, microorganisms or yeast.

- A biosimilar product must show 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.
    - In addition, the biosimilar product may be approved for the indication(s) and condition(s) that have been FDA-approved for the reference product, and must have the same mechanism(s) of action, route(s) of administration, dosage form(s) and strength(s) as the reference product.
    - The facilities where the biosimilars are manufactured must also meet the FDA's standards.

- The approval of Nivestym is based on review of a comprehensive data package and totality of evidence demonstrating a high degree of similarity to its reference product, Neupogen.

Continued . . .

- Nivestym has been approved as a biosimilar to Neupogen, ***not*** as an interchangeable product.

- Similar to Neupogen and Zarxio, Nivestym is contraindicated in patients with a history of serious allergic reactions to human granulocyte colony-stimulating factors such as filgrastim products or pegfilgrastim products.

- Warnings and precautions of Nivestym include fatal splenic rupture, acute respiratory distress syndrome, serious allergic reactions, sickle cell disorders, glomerulonephritis, alveolar hemorrhage and hemoptysis, capillary leak syndrome, patients with severe chronic neutropenia, thrombocytopenia, leukocytosis, cutaneous vasculitis, potential effect on malignant cells, simultaneous use with chemotherapy and radiation therapy not recommended, and nuclear imaging.

- In patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs, the most common adverse reactions (≥ 5% difference in incidence compared to placebo) were pyrexia, pain, rash, cough, and dyspnea.

- In patients with AML, the most common adverse reactions (≥ 2% difference in incidence) were pain, epistaxis, and rash.

- In patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by BMT, the most common adverse reaction (≥ 5% difference in incidence) was rash.

- In patients undergoing peripheral blood progenitor cell mobilization and collection, the most common adverse reactions (≥ 5% incidence) were bone pain, pyrexia, and headache.

- In patients with severe chronic neutropenia, the most common adverse reactions (≥ 5% difference in incidence) were pain, anemia, epistaxis, diarrhea, hypoesthesia, and alopecia.

- The recommended dosage of Nivestym varies by indication and patient weight, and may be administered by subcutaneous (SC) injection or intravenous (IV) infusion.

    — Direct administration of less than 0.3 ml (180 mcg) using Nivestym prefilled syringe is not recommended due to potential for dosing errors.
    — Refer to the Nivestym drug label for additional dosing details.

- Pfizer's launch plans for Nivestym are pending. Nivestym will be available as 300 mcg/mL and 480 mcg/1.6 mL single-dose vials, and as 300 mcg/0.5 mL and 480 mcg/0.8 mL single-dose prefilled syringes with a BD UltraSafe Plus™ Passive Needle Guard.