Sandoz launches Zarxio™ (filgrastim-sndz), the first biosimilar in the United States

- Launch follows March 6, 2015 FDA approval
- Sandoz One Source™ offers patient support services

Holzkirchen, September 3, 2015 – Sandoz, a Novartis company, announced today that Zarxio™ (filgrastim-sndz) is now available in the United States. Zarxio is the first biosimilar approved by the US Food and Drug Administration (FDA) and the first to launch in the US.

“As the pioneer and global leader in biosimilars, Sandoz has maintained a commitment to bringing high-quality biosimilar medicines to patients and healthcare professionals around the world,” said Richard Francis, Global Head, Sandoz. “With the launch of Zarxio, we look forward to increasing patient, prescriber and payor access to filgrastim in the US by offering a high-quality, more affordable version of this important oncology medicine.”

“While biologics have had a significant impact on how diseases are treated, their cost and co-pays are difficult for many patients and the healthcare budget in general. Biosimilars can help to fill an unmet need by providing expanded options, greater affordability and increased patient access to life-saving therapies,” said Dr. Ralph Boccia, Medical Director of the Center for Cancer and Blood Disorders, and Chief Medical Officer for the International Oncology Network (ION).

Sandoz understands the importance of providing comprehensive patient support services in the oncology setting. With the launch of Zarxio, Sandoz is also proud to offer Sandoz One Source™ a patient services center, providing support that connects the patient to the information and resources they need.

The launch follows the FDA approval of Zarxio on March 6, 2015. The approval, via the new biosimilars pathway established under the Biologics Price Competition and Innovation Act, was based on a comprehensive package of analytical, nonclinical, and clinical data, which confirmed that Zarxio is highly similar with no clinically meaningful differences to the US-licensed reference product. The successful Sandoz pivotal head-to-head PIONEER study was the final piece of data contributing to the totality of evidence used by FDA to approve Zarxio as biosimilar to the reference product. Importantly, the data demonstrating high similarity was sufficient to allow extrapolation of use of Zarxio to five indications of the reference product.

Sandoz has an unwavering commitment to increasing patient access to high-quality, life-enhancing biosimilars. Sandoz is the global market leader and currently markets three biosimilars outside the US. Sandoz has a leading pipeline with several biosimilars across the various stages of development, including five programs in Phase III clinical trials/filing preparation.

For more information on Zarxio, please visit www.zarxio.com.
INDICATIONS

- **Patients with Cancer Receiving Myelosuppressive Chemotherapy:** 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.

- **Patients with Acute Myeloid Leukemia Receiving Induction or Consolidation Chemotherapy:** to reduce the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML).

- **Patients with Cancer Undergoing Bone Marrow Transplantation:** 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 bone marrow transplantation.

- **Patients Undergoing Autologous Peripheral Blood Progenitor Cell Collection and Therapy:** for the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.

- **Patients with Severe Chronic Neutropenia:** 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.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

- **ZARXIO** is contraindicated in patients with a history of serious allergic reactions to human granulocyte colony-stimulating factors such as filgrastim or pegfilgrastim.

WARNINGS AND PRECAUTIONS

- Splenic rupture, including fatal cases, has been reported following the administration of filgrastim products. Patients who report left upper abdominal or shoulder pain should be evaluated.

- Acute respiratory distress syndrome (ARDS) has been reported in patients receiving filgrastim products. Patients who develop fever and lung infiltrates or respiratory distress should be evaluated. Discontinue ZARXIO in patients with ARDS.

- Serious allergic reactions, including anaphylaxis, have been reported in patients receiving filgrastim products. The majority of reported events occurred upon initial exposure. Provide symptomatic treatment for allergic reactions. Allergic reactions, including anaphylaxis, in patients receiving filgrastim products can recur within days after the discontinuation of initial anti-allergic treatment. Permanently discontinue ZARXIO in patients with serious allergic reactions.

- Sickle cell crisis, in some cases fatal, has been reported with the use of filgrastim products in patients with sickle cell trait or sickle cell disease.

- Glomerulonephritis has occurred in patients receiving filgrastim products. The diagnoses were based upon azotemia, hematuria (microscopic and macroscopic), proteinuria, and renal biopsy. Generally, events of glomerulonephritis resolved after dose reduction or
discontinuation of filgrastim. If glomerulonephritis is suspected, evaluate for cause. If causality is likely, consider dose-reduction or interruption of ZARXIO.

- Alveolar hemorrhage manifesting as pulmonary infiltrates and hemoptysis requiring hospitalization have been reported in healthy donors treated with filgrastim undergoing peripheral blood progenitor cell (PBPC) collection mobilization. Hemoptysis resolved with discontinuation of filgrastim. The use of ZARXIO for PBPC mobilization in healthy donors is not an approved indication.

- Capillary leak syndrome (CLS) has been reported after G-CSF administration, including filgrastim products, and is characterized by hypotension, hypoalbuminemia, edema and hemoconcentration. Episodes vary in frequency, severity and may be life-threatening if treatment is delayed. Patients who develop symptoms of capillary leak syndrome should be closely monitored and receive appropriate treatment.

- Confirm the diagnosis of severe chronic neutropenia (SCN) before initiating ZARXIO therapy. Myelodysplastic syndrome (MDS) and acute myelogenous leukemia (AML) have been reported to occur in the natural history of congenital neutropenia without cytokine therapy. Cytogenetic abnormalities, transformation to MDS, and AML have also been observed in patients treated with filgrastim for SCN. Abnormal cytogenetics and MDS have been associated with the eventual development of myeloid leukemia. The effect of filgrastim products on the development of abnormal cytogenetics and the effect of continued filgrastim administration in patients with abnormal cytogenetics or MDS are unknown. If a patient with SCN develops abnormal cytogenetics or myelodysplasia, the risks and benefits of continuing ZARXIO should be carefully considered.

- Thrombocytopenia has been reported in patients receiving filgrastim products. Monitor platelet counts.

- Leukocytosis:
  - Patients with Cancer Receiving Myelosuppressive Chemotherapy: White blood cell counts of 100,000/mm³ or greater were observed in approximately 2% of patients receiving filgrastim at dosages above 5 mcg/kg/day. In patients with cancer receiving ZARXIO as an adjunct to myelosuppressive chemotherapy, to avoid the potential risks of excessive leukocytosis, it is recommended that ZARXIO therapy be discontinued if the ANC surpasses 10,000/mm³ after the chemotherapy-induced ANC nadir has occurred. Monitor CBCs at least twice weekly during therapy.
  - Peripheral Blood Progenitor Cell (PBPC) Collection and Therapy: During the period of administration of ZARXIO for PBPC mobilization in patients with cancer, discontinue ZARXIO if the leukocyte count rises to >100,000/mm³.

- Cutaneous vasculitis has been reported in patients treated with filgrastim products. In most cases, the severity of cutaneous vasculitis was moderate or severe. Most of the reports involved patients with SCN receiving long-term filgrastim therapy. Hold ZARXIO therapy in patients with cutaneous vasculitis. ZARXIO may be started at a reduced dose when the symptoms resolve and the ANC has decreased.

- The possibility that filgrastim acts as a growth factor for any tumor type, including myeloid malignancies and myelodysplasia, diseases for which filgrastim is not approved, cannot be excluded. The safety of filgrastim products in chronic myeloid leukemia (CML) and myelodysplasia has not been established. When ZARXIO is used to mobilize PBPC, tumor cells may be released from the marrow and subsequently collected in the leukapheresis product. Available data is limited and inconclusive.

- The safety and efficacy of filgrastim products given simultaneously with cytotoxic
chemotherapy have not been established. Do not use ZARXIO in the period 24 hours before through 24 hours after the administration of cytotoxic chemotherapy. The safety and efficacy of filgrastim products have not been evaluated in patients receiving concurrent radiation therapy. Avoid the simultaneous use of ZARXIO with chemotherapy and radiation therapy.

- Increased hematopoietic activity of the bone marrow in response to growth factor therapy has been associated with transient positive bone-imaging changes on nuclear imaging.

**ADVERSE REACTIONS**

Most common adverse reactions in patients:

- With nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs (≥ 5% difference in incidence compared to placebo) are thrombocytopenia, nausea, pyrexia, chest pain, pain, fatigue, back pain, arthralgia, bone pain, pain in extremity, dizziness, cough, dyspnea, rash, blood lactate dehydrogenase increased and blood alkaline phosphatase increased
- With AML (≥ 2% difference in incidence) are epistaxis, back pain, pain in extremity, erythema, and rash maculo-papular
- With nonmyeloid malignancies undergoing myeloablative chemotherapy followed by BMT (≥ 5% difference in incidence) are rash and hypersensitivity
- Undergoing peripheral blood progenitor cell mobilization and collection (≥ 5% incidence) are bone pain, pyrexia, blood alkaline phosphatase increased and headache
- With severe chronic neutropenia (SCN) (≥ 5% difference in incidence) are arthralgia, bone pain, back pain, muscle spasms, musculoskeletal pain, pain in extremity, splenomegaly, anemia, upper respiratory tract infection, urinary tract infection, epistaxis, chest pain, diarrhea, hypoesthesia, and alopecia

Please see full [Prescribing Information](#).

To report SUSPECTED ADVERSE REACTIONS, contact Sandoz Inc. at 1-800-525-8747 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

**Disclaimer**

The foregoing release contains forward-looking statements that can be identified by words such as "launches," "launch," "commitment," "look forward," or similar terms, or by express or implied discussions regarding potential future product approvals, or regarding potential revenues from Zarxio or potential future products. You should not place undue reliance on these statements. Such forward-looking statements are based on the current beliefs and expectations of management regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no guarantee that biosimilar filgrastim will be submitted for sale in any additional markets, or at any particular time. Nor can there be any guarantee that Zarxio or any potential future products will be commercially successful in the future. In particular, management's expectations regarding Zarxio and such potential future products could be affected by, among other things,
unexpected regulatory actions or delays or government regulation generally; unexpected clinical trial results and additional analysis of existing clinical data; competition in general, including potential approval of additional versions of biosimilar filgrastim; government, industry and general public pricing pressures; unexpected litigation outcomes; unexpected safety issues; unexpected manufacturing or quality issues; general economic and industry conditions, and other risks and factors referred to in Novartis AG’s current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

About Sandoz
Sandoz, a Novartis company, is a global leader in generic pharmaceuticals, driving sustainable access to high-quality healthcare. Sandoz employs more than 26,000 people worldwide and supplies a broad range of affordable, primarily off-patent products to patients and customers around the globe. The Sandoz global portfolio comprises approximately 1,100 molecules, which accounted for 2014 sales of USD 9.6 billion. Sandoz holds the global #1 position in biosimilars as well as in generic anti-infectives, ophthalmics and transplantation medicines. In addition, Sandoz holds leading global positions in key therapeutic areas ranging from generic injectables, dermatology and respiratory to cardiovascular, metabolism, central nervous system, pain and gastrointestinal. Sandoz develops, produces and markets finished dosage form (FDF) medicines as well as intermediary products including active pharmaceutical ingredients (APIs) and biotechnological substances. Nearly half of Sandoz’s portfolio is in differentiated products – products that are scientifically more difficult to develop and manufacture than standard generics.

In addition to strong organic growth since consolidating its generics businesses under the Sandoz brand name in 2003, Sandoz has consistently driven growth in selected geographies and differentiated product areas through a series of targeted acquisitions, including Hexal (Germany), EBEWE Pharma (Austria), and Fougera Pharmaceuticals (US).

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