ZARXIO®
(filgrastim-sndz)

Subcutaneous or Intravenous Injection
300 mcg/0.5 mL | 480 mcg/0.8 mL

- 1st FDA-approved biosimilar[1]
- 1st biosimilar to surpass its reference product in market share[2]

More oncologists CHOOSE ZARXIO as the #1 prescribed filgrastim[2]*

ZARXIO shares the following 5 indications with Neupogen®[3,4]

- Patients with cancer receiving myelosuppressive chemotherapy
- Patients with acute myeloid leukemia receiving induction or consolidation chemotherapy
- Patients with cancer undergoing bone marrow transplantation
- Patients undergoing autologous peripheral blood progenitor cell collection and therapy
- Patients with severe chronic neutropenia

*Based on market share analysis as of September 2020.

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 products.

WARNINGS AND PRECAUTIONS

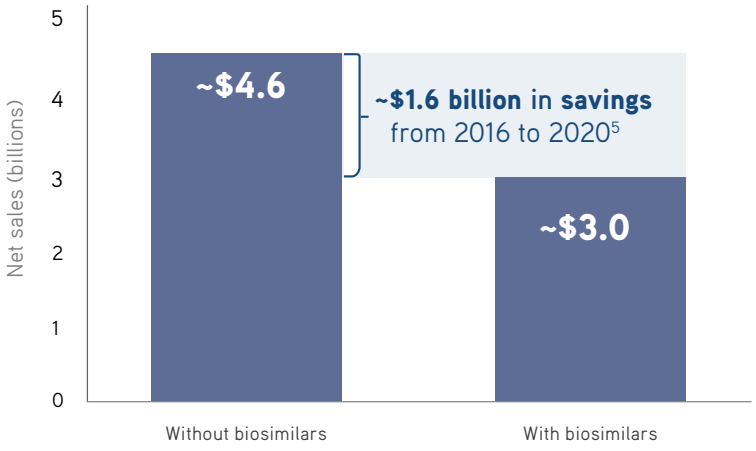
- Splenic rupture, including fatal cases, has been reported following the administration of filgrastim products. Patients who report left upper abdominal or shoulder pain should be evaluated.
- Acute respiratory distress syndrome (ARDS) has been reported in patients receiving filgrastim products. Patients 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. Discontinue ZARXIO if sickle cell crisis occurs.
- 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 products. If glomerulonephritis is suspected, evaluate for cause. If causality is likely, consider dose-reduction or interruption of ZARXIO.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information.

ZARXIO cost savings may liberate healthcare resources and expand patient access

~$1.6 billion savings were driven by biosimilar filgrastim[5*]

Net cost savings with biosimilars in the filgrastim market†



ZARXIO
IS THE **#1**
PRESCRIBED FILGRASTIM
and holds
50%
of the prefilled syringe filgrastim market[2]

*Based on year-to-date (YTD) sales as of December 2020; based on filgrastim net sales of $926 million.
†Estimated refers to the extrapolation of the estimated spend based on the assumption that there are no biosimilars in the market.

Biosimilars allow for expanded patient access and significant savings for patients, helping alleviate the overburdened healthcare system[5,6]

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- Alveolar hemorrhage manifesting as pulmonary infiltrates and hemoptysis requiring hospitalization have been reported in healthy donors treated with filgrastim products 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.
- Myelodysplastic Syndrome (MDS) and Acute Myeloid Leukemia (AML):
  - Patients with Severe Chronic Neutropenia: 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 products 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. Monitor patients for signs and symptoms of MDS/AML in these settings. If a patient with SCN develops abnormal cytogenetics or myelodysplasia, the risks and benefits of continuing ZARXIO should be carefully considered.
  - Patients with Breast and Lung Cancer: MDS and AML have been associated with the use of filgrastim in conjunction with chemotherapy and/or radiotherapy in patients with breast and lung cancer. Monitor patients for signs and symptoms of MDS/AML in these settings.
- Thrombocytopenia has been reported in patients receiving filgrastim products. Monitor platelet counts.

- #1 prescribed short-acting filgrastim with more than **27 million** patient-exposure days in **100 countries**[2,3,7]
- ZARXIO has the most unrestricted combined medical and pharmacy benefit coverage in the SA G-CSF class[8]*
- The Sandoz One Source Commercial Co-Pay Program for ZARXIO supports eligible,† commercially insured patients with their out-of-pocket co-pay costs for ZARXIO

*"Most" defined as a comparison to Neupogen® and Granix® in terms of combined medical and pharmacy benefit status. "Unrestricted" defined as on formulary, managed to PI, and not requiring prior authorization and step edits. Coverage defined as "Drug Covered, Unrestricted" on Commercial and Health Exchange plans, and Pharmacy Benefit Managers on pharmacy benefit and Commercial and Health Exchange plans on medical benefit according to Zitter data as of November 3, 2017.

†Eligibility Requirements: Maximum benefit of $10,000 annually. Prescription must be for an approved indication. This program is not health insurance. This program is for insured patients only; cash-paying or uninsured patients are not eligible. Patients are not eligible if prescription for ZARXIO is paid, in whole or in part, by any state or federally funded programs, including but not limited to Medicare (including Part D, even in the coverage gap) or Medicaid, Medigap, VA, DOD, or TRICARE, or private indemnity plans that do not cover prescription drugs, or HMO insurance plans that reimburse the patient for the entire cost of their prescription drugs, or where prohibited by law. Co-Pay Program may apply to out-of-pocket expenses that occurred within 120 days prior to the date of the enrollment. Patients can participate for a maximum of 12 months. Co-Pay Program may not be combined with any other rebate, coupon, or offer. Co-Pay Program has no cash value. Sandoz reserves the right to rescind, revoke, or amend this offer without further notice.

SA G-CSF=short-acting granulocyte colony-stimulating factor.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- Leukocytosis:
  - Patients with Cancer Receiving Myelosuppressive Chemotherapy: White blood cell counts of 100,000/mm^3 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/mm^3 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/mm^3.
- 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 ZARXIO acts as a growth factor for any tumor type 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 ZARXIO 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 ZARXIO have not been evaluated in patients receiving concurrent radiation therapy. Avoid the simultaneous use of ZARXIO with chemotherapy and radiation therapy.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information.

ZARXIO® (filgrastim-sndz)

Sandoz is committed to bringing biosimilars to more patients around the world

- **Strong investment in manufacturing:** End-to-end technical capabilities ensure the reliable development, manufacture, and supply of industry-leading, quality biosimilars
- **Robust pipeline:** With 8 approved biosimilars in Europe, as well as a strong development pipeline, Sandoz will continue to leverage its global expertise in the US[9]
- **Proven track record:** 1st company to bring biosimilars to patients both in the US and worldwide[1,10]

See the value ZARXIO can bring to your practice. To learn more, visit ZARXIO.com

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- 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.
- Aortitis has been reported in patients receiving filgrastim products. It may occur as early as the first week after start of therapy. Manifestations may include generalized signs and symptoms such as fever, abdominal pain, malaise, back pain, and increased inflammatory markers (e.g., c-reactive protein and white blood cell count). Consider aortitis in patients who develop these signs and symptoms without known etiology. Discontinue ZARXIO if aortitis is suspected.

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

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*.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information.

References: 1. FDA approves first biosimilar product Zarxio [press release]. US Food and Drug Administration; March 6, 2015. http://web.archive.org/web/20180126055225/https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm436648.htm. Accessed January 13, 2021. **2.** Data on file. Zarxio Market Share Data. Sandoz Inc. September 2020. **3.** ZARXIO Prescribing Information. Sandoz Inc. March 2021. **4.** Neupogen® Prescribing Information. Amgen Inc. February 2021. **5.** Data on file. Filgrastim Net Sales Analysis Model. Sandoz Inc. April 2021. **6.** Mulcahy AW, Hlava JP, Case SR. Biosimilar cost savings in the United States: initial experience and future potential. *Rand Health Q.* 2018;7(4):3 doi:10.7249/PE264. **7.** Data on file. Sandoz Biosimilar PSUR Data. Sandoz Inc. February 2021. **8.** Data on file. Zitter Raw Data. October 2017. **9.** Columbus G. Pegfilgrastim biosimilar approved in Europe. OncLive website. https://www.onclive.com/web-exclusives/pegfilgrastim-biosimilar-approved-in-europe. Published November 27, 2018. Accessed September 18, 2019. **10.** Data on file. Periodic Safety Update Report 13 (PSUR 13) for somatropin-containing products, April 1, 2017—September 30, 2017. Sandoz Inc. November 2017.

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