ZARXIO® (filgrastim-sndz)
Clinical, Administration, and Pricing Overview
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Table of Contents

• Indications Shared With NEUPOGEN® (filgrastim)
• Biosimilar Requirements
• Overview of ZARXIO® (filgrastim-sndz)
• The PIONEER Study
• ZARXIO Prefilled Syringe
• Dosage and Administration
• Storage, Handling, and Preparation
• Dilution for Intravenous Administration
• ZARXIO Unit Pricing
• Important Safety Information

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ZARXIO® (filgrastim-sndz) Shares the Following 5 Indications With NEUPOGEN® (filgrastim)\(^1,2\)

- **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.

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Biosimilar Requirements and ZARXIO® (filgrastim-sndz)

<table>
<thead>
<tr>
<th>Requirement</th>
<th>ZARXIO fulfillment of requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DEMONSTRATE HIGH SIMILARITY</strong></td>
<td></td>
</tr>
<tr>
<td>Analytical data</td>
<td>• Physicochemical and functional analytical data demonstrated that ZARXIO is highly similar to NEUPOGEN® (filgrastim)&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td>Animal studies&lt;sup&gt;*&lt;/sup&gt;</td>
<td>• Five animal studies confirmed that the pharmacologic and toxicological profiles of ZARXIO and NEUPOGEN® are similar&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Clinical studies</td>
<td>• Study to evaluate pharmacodynamics, pharmacokinetics, and safety&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
<tr>
<td>Mechanism of action</td>
<td>• The mechanism of action of filgrastim is mediated by selective binding to the G-CSF receptor and is similar across all labeled indications&lt;sup&gt;8,13&lt;/sup&gt;</td>
</tr>
<tr>
<td>Route of administration, dosage form, and strength</td>
<td>• ZARXIO has the same route of administration, dosage form, and strengths as NEUPOGEN&lt;sup&gt;8,14&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>*The use of EU-approved NEUPOGEN<sup>®</sup> as comparator for the non-clinical development of ZARXIO is considered justified by the high level of similarity between EU-approved and US-licensed. NEUPOGEN<sup>®</sup>.</sup>

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Overview of ZARXIO® (filgrastim-sndz)

- ZARXIO is a biosimilar of the reference biologic NEUPOGEN® (filgrastim)\(^1\)-\(^3\)
  - Filgrastim is a granulocyte colony-stimulating factor (G-CSF) analog used to stimulate the proliferation and differentiation of neutrophils\(^4\)
- Received FDA approval on March 6, 2015\(^3\)
- ZARXIO and NEUPOGEN® product attributes\(^4,5\)
  - Identical dosing schedules and routes of administration
  - Identical dosage strengths
- Direct administration of less than 0.3 mL is not recommended due to potential for dosing errors\(^4\)

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The PIONEER Study: Design
Randomized, double-blind, comparative study of efficacy and safety (24 weeks) between ZARXIO® (filgrastim-sndz) and NEUPOGEN® (filgrastim) in 218 breast cancer patients treated with myelosuppressive chemotherapy¹,²*

Eligibility criteria¹,²:

• Women ≥18 years with histologically proven breast cancer (eligible for neoadjuvant or adjuvant TAC, given for 6 cycles†)

• ECOG Performance Status (PS) ≤2

• Adequate bone marrow function (ANC ≥1.5 x 10⁹/L, platelet count ≥100 x 10⁹/L, hemoglobin ≥10 g/dL)

ANC=absolute neutrophil count; ECOG=Eastern Cooperative Oncology Group.¹

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The PIONEER Study:
Baseline Characteristics for Patients Treated With ZARXIO® (filgrastim-sndz) or NEUPOGEN® (filgrastim) in Cycle1,2

<table>
<thead>
<tr>
<th>Parameter</th>
<th>ZARXIO (n=107)</th>
<th>NEUPOGEN® (n=107)</th>
<th>Total (n=214)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean ± SD)</td>
<td>49.5 ± 11.52</td>
<td>48.4 ± 11.02</td>
<td>48.9 ± 11.26</td>
</tr>
<tr>
<td>Time since initial diagnosis in months (median [min, max])</td>
<td>1.0 (0,171*)</td>
<td>1.0 (0,16)</td>
<td>1.0 (0,171*)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parameter</th>
<th>ZARXIO (n=107)</th>
<th>NEUPOGEN® (n=107)</th>
<th>Total (n=214)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical stage (n [%])</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>7 (6.5)</td>
<td>8 (7.5)</td>
<td>15 (7.0)</td>
</tr>
<tr>
<td>II</td>
<td>57 (53.3)</td>
<td>53 (49.5)</td>
<td>110 (51.4)</td>
</tr>
<tr>
<td>III</td>
<td>43 (40.2)</td>
<td>46 (43.0)</td>
<td>89 (41.6)</td>
</tr>
<tr>
<td>IV</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parameter</th>
<th>ZARXIO (n=107)</th>
<th>NEUPOGEN® (n=107)</th>
<th>Total (n=214)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjuvant chemotherapy (n [%])</td>
<td>63 (58.9)</td>
<td>61 (57.0)</td>
<td>124 (57.9)</td>
</tr>
<tr>
<td>Neoadjuvant chemotherapy (n [%])</td>
<td>44 (41.1)</td>
<td>46 (43.0)</td>
<td>90 (42.1)</td>
</tr>
</tbody>
</table>

*One patient was enrolled in the study with contralateral breast cancer diagnosed 1 month prior to enrollment; the initial diagnosis was 171 months before randomization.

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The PIONEER Study: Confirmed Biosimilarity of ZARXIO® (filgrastim-sndz) to NEUPOGEN® (filgrastim)¹

Primary Endpoint for equivalence (in Cycle 1)

### Mean Duration of Severe Neutropenia (DSN)²,³^

<table>
<thead>
<tr>
<th></th>
<th>ZARXIO</th>
<th>NEUPOGEN®</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>101</td>
<td>103</td>
</tr>
<tr>
<td>Cycle 1 Mean DSN (SD)</td>
<td>1.17 days (1.11)</td>
<td>1.20 days (1.02)</td>
</tr>
</tbody>
</table>

DSN Difference for NEUPOGEN® minus ZARXIO (90% CI)⁴

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>-1 day</td>
<td>+1 day</td>
</tr>
</tbody>
</table>

⁴Defined as the number of consecutive days with severe neutropenia (ANC less than 0.5 x 10⁹/L) in Cycle 1.²
³ANCOVA with treatment, disease status and baseline ANC level.³

Biosimilarity demonstrated through the totality of evidence.⁴

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The PIONEER Study: Secondary Endpoints

Secondary endpoints (in Cycle 1)$^{1,2}$:

- Incidence of febrile neutropenia (FN)$^{1,2}$ (n [%])
- Time to ANC recovery$^{4}$ (days) (mean ± SD)
- Depth of ANC nadir$^{6}$ ($\times 10^9$) (mean ± SD)
- Number of days of fever$^{11}$ (days) (median, range)
- Frequency of infections (n [%])
- Incidence of hospitalizations due to FN (n)

<table>
<thead>
<tr>
<th>ZARXIO</th>
<th>NEUPOGEN®</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=101</td>
<td>N=103</td>
</tr>
<tr>
<td>4 (4.0%)</td>
<td>2 (1.9%)</td>
</tr>
<tr>
<td>1.8 ± 0.97</td>
<td>1.7 ± 0.81</td>
</tr>
<tr>
<td>0.734 ± 1.1388</td>
<td>0.757 ± 1.3131</td>
</tr>
<tr>
<td>0 (0-2)</td>
<td>0 (0-2)</td>
</tr>
<tr>
<td>2 (2.0%)</td>
<td>2 (1.9%)</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

*Secondary endpoints were not adjusted for multiplicity.$^{1}$

$^{1}$Defined as oral temperature ≥38.3°C while having an ANC <0.5 x 10^9/L (both measured on the same day)$^{1,2}$

$^{2}$ANC recovery was defined as the time in days from ANC nadir until the patient’s ANC increases to ≥2 x 10^9/L after the nadir in Cycle 1.$^{1,2}$

$^{3}$Defined as the patient’s lowest ANC in Cycle 1.$^{1,2}$

$^{4}$Defined as oral temperature ≥38.3°C.$^{1,2}$

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The PIONEER Study: ANC Profiles of ZARXIO® (filgrastim-sndz) and NEUPOGEN® (filgrastim)\textsuperscript{1}

Secondary Endpoint: Depth of ANC nadir in Cycle 1\textsuperscript{*}

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The PIONEER Study: Cardinal Adverse Events (Between-Group Comparison)¹

<table>
<thead>
<tr>
<th>Grouped term</th>
<th>ZARXIO (N=107)</th>
<th>NEUPOGEN® (filgrastim) (N=107)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Musculoskeletal pain*</td>
<td>27 (25%)</td>
<td>31 (29%)</td>
</tr>
<tr>
<td>Injection site reaction†</td>
<td>2 (2%)</td>
<td>1 (1%)</td>
</tr>
</tbody>
</table>

*Includes arthralgia, back pain, bone pain, musculoskeletal chest pain, musculoskeletal pain, myalgia, pain, pain in extremity, or spinal pain.
†Includes injection site erythema, extravasation, hematoma, pain, or pruritus.

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The overall safety profile of ZARXIO was similar across all 6 cycles with continuous treatment.²

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ZARXIO® (filgrastim-sndz) Prefilled Syringe

• ZARXIO is available in prefilled syringes, in the same 2 dosage strengths as NEUPOGEN® (filgrastim): 300 mcg/0.5 mL and 480 mcg/0.8 mL

• Identical dosing schedule and route of administration to NEUPOGEN®

• ZARXIO is available with a BD UltraSafe Passive® Needle Guard that provides one-handed passive activation

• ZARXIO is administered by subcutaneous injection, short intravenous infusion (15 to 30 minutes), or continuous intravenous infusion

• You should not inject a dose of ZARXIO less than 0.3 mL (180 mcg) from a ZARXIO prefilled syringe. A dose less than 0.3 mL cannot be accurately measured using the ZARXIO prefilled syringe

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UltraSafe Passive is a registered trademark of Safety Syringes, Inc.
ZARXIO® (filgrastim-sndz) Prefilled Syringe\(^1\) (cont’d)

Features BD UltraSafe Passive\(^{®}\) Needle Guard
- One-handed passive activation\(^2\)
- Automatically covers the exposed needle

Available in pack of:

- 10 prefilled syringes
  - NDC: 61314-304-10
- 1 prefilled syringe
  - NDC: 61314-304-01

Features BD UltraSafe Passive\(^{®}\) Needle Guard
- One-handed passive activation\(^2\)
- Automatically covers the exposed needle

Available in pack of:

- 10 prefilled syringes
  - NDC: 61314-312-10
- 1 prefilled syringe
  - NDC: 61314-312-01

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Dosage and Administration

• Patients with cancer receiving myelosuppressive chemotherapy or induction and/or consolidation chemotherapy for AML
  – Recommended starting dose is 5 mcg/kg/day subcutaneous injection, short intravenous infusion (15 to 30 minutes), or continuous intravenous infusion
  – See full Prescribing Information for recommended dosage adjustments and timing of administration

• Patients with cancer undergoing bone marrow transplantation
  – 10 mcg/kg/day given as an intravenous infusion no longer than 24 hours
  – See full Prescribing Information for recommended dosage adjustments and timing of administration

• Administer ZARXIO at least 24 hours after cytotoxic chemotherapy
• Monitor complete blood count (CBC) and platelet count frequently

Please see Important Safety Information on slides 24-27 and accompanying full Prescribing Information.

Dosage and Administration\(^1\) (cont’d)

• Patients undergoing autologous peripheral blood progenitor cell collection and therapy
  – 10 mcg/kg/day subcutaneous injection
  – Administer for at least 4 days before first leukapheresis procedure and continue until last leukapheresis

• Patients with congenital neutropenia
  – Recommended starting dosage is 6 mcg/kg subcutaneous injection twice daily

• Patients with cyclic or idiopathic neutropenia
  – Recommended starting dosage is 5 mcg/kg subcutaneous injection daily

• Direct administration of less than 0.3 mL is not recommended due to potential for dosing errors

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Nursing Mothers

• It is not known whether filgrastim products are excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised if ZARXIO® (filgrastim-sndz) is administered to women who are breastfeeding.

Pediatric Use

• Direct administration of a volume less than 0.3 mL is not recommended due to the potential for dosing errors.
  - ZARXIO prefilled syringe with BD UltraSafe Passive® Needle Guard may not accurately measure volumes less than 0.3 mL due to the needle spring mechanism design.

• The pharmacokinetics of filgrastim in pediatric patients after chemotherapy are similar to those in adults receiving the same weight-normalized doses, suggesting no age-related differences.
  - Filgrastim was well tolerated in pediatric patients with one report of palpable splenomegaly and one report of hepatosplenomegaly.
  - Musculoskeletal pain was the only consistently reported adverse event, which is no different from the experience in the adult population.

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Pediatric Use\(^1\) (cont’d)

- A phase 3 study of 123 patients (median age, 12 years) was conducted to establish the safety and efficacy of filgrastim in pediatric patients with severe chronic neutropenia (SCN)
  - Additional information is available from a postmarketing surveillance study that included 429 pediatric patients less than 18 years of age with SCN

- Long-term follow-up data from the postmarketing surveillance study suggest that height and weight are not adversely affected in patients who received up to 5 years of filgrastim treatment
  - Limited data from patients who were followed in the phase 3 study for 1.5 years did not suggest alterations in sexual maturation or endocrine function

- Development of cytogenetic abnormalities and transformation to MDS and AML have been seen in pediatric patients with congenital neutropenia receiving chronic filgrastim treatment. The relationship to filgrastim administration is not known

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Geriatric Use¹

• There were 232 patients aged ≥65 years and 22 patients aged ≥75 years among 855 patients enrolled in 3 randomized, placebo-controlled trials of filgrastim-treated patients receiving myelosuppressive chemotherapy
  – No overall differences in safety or effectiveness were observed between these patients and younger patients
  – Clinical studies of filgrastim in other approved indications did not include sufficient numbers of patients aged ≥65 years to determine whether elderly patients respond differently from younger patients


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Storage and Handling¹

- Store refrigerated (2°C-8°C; 36°F-46°F) in original pack to protect from light
  - Avoid shaking; protect from freezing
- If frozen, thaw in the refrigerator before administration. Discard ZARXIO® (filgrastim-sndz) if frozen more than once
- Remove prefilled syringe from refrigerator 30 minutes before use and allow ZARXIO to reach room temperature
  - Discard any prefilled syringe left at room temperature for more than 24 hours
  - Visually inspect ZARXIO for particulate matter and discoloration prior to administration (solution is clear and colorless to slightly yellowish)
  - Do not administer ZARXIO if particulates or discoloration are observed
  - Discard unused portion of ZARXIO in prefilled syringes
  - Do not save unused drug for later administration
- See PI for Important Administration Instructions and How Supplied/Storage and Handling

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Dilution for Intravenous Administration¹

• If required for IV administration, ZARXIO® (filgrastim-sndz) may be diluted in 5% Dextrose Injection, USP to concentrations of 5 mcg/mL-15 mcg/mL
  – ZARXIO diluted to concentrations of 5 mcg/mL-15 mcg/mL should be protected from adsorption to plastic materials by addition of Albumin (Human) to a final concentration of 2 mg/mL
  – When diluted in 5% Dextrose Injection, USP, or 5% Dextrose plus Albumin (Human), ZARXIO is compatible with glass, polyvinylchloride, polyolefin, and polypropylene

• Do not dilute with saline at any time, because the product may precipitate

• Diluted ZARXIO solution can be stored at room temperature for up to 24 hours (this time period includes the duration of the infusion)

• See PI for Important Administration Instructions and How Supplied/Storage and Handling

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# ZARXIO® (filgrastim-sndz) Unit Pricing

<table>
<thead>
<tr>
<th>TYPE OF INJECTABLE</th>
<th>NATIONAL DRUG CODE (NDC) NUMBER</th>
<th>UNIT QUANTITY</th>
<th>UNIT PRICE (WAC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single-dose, preservative-free, prefilled syringes with a BD UltraSafe Passive® Needle Guard, containing 300 mcg/0.5 mL of filgrastim-sndz</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ZARXIO, Injection, Solution, 300 mcg/0.5 mL</td>
<td>61314-304-01</td>
<td>Pack of 1 prefilled syringe</td>
<td>$275.66/syringe</td>
</tr>
<tr>
<td>ZARXIO, Injection, Solution, 300 mcg/0.5 mL</td>
<td>61314-304-10</td>
<td>Pack of 10 prefilled syringes</td>
<td>$275.66/syringe</td>
</tr>
<tr>
<td>Single-dose, preservative-free, prefilled syringes with a BD UltraSafe Passive® Needle Guard, containing 480 mcg/0.8 mL of filgrastim-sndz</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ZARXIO, Injection, Solution, 480 mcg/0.8 mL</td>
<td>61314-312-01</td>
<td>Pack of 1 prefilled syringe</td>
<td>$438.98/syringe</td>
</tr>
<tr>
<td>ZARXIO, Injection, Solution, 480 mcg/0.8 mL</td>
<td>61314-312-10</td>
<td>Pack of 10 prefilled syringes</td>
<td>$438.98/syringe</td>
</tr>
</tbody>
</table>

WAC=Wholesale Acquisition Cost per unit (prefilled syringe).
Source: Analysource, prices effective 4/3/2017. Published WAC amounts are not an indication of what you may pay and are subject to change.

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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.

• 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.

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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.

• 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. If a patient with SCN develops abnormal cytogenetics or myelodysplasia, the risks and benefits of continuing ZARXIO should be carefully considered.

Please see accompanying full Prescribing Information.
IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont’d)

• 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 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.

Please see accompanying full Prescribing Information.
IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

• 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.

• 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

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 accompanying full Prescribing Information.
Please see Important Safety Information on slides 24-27 and accompanying full Prescribing Information.