Skip to main content

Zarxio (Filgrastim-sndz Injection)

Zuletzt aktualisiert: 30. November 2017

The following serious adverse reactions are discussed in greater detail in other sections of the labeling:

-]**WARNINGS AND PRECAUTIONS** Splenic Rupture [see
-]**WARNINGS AND PRECAUTIONS** Acute Respiratory Distress Syndrome [see
-]**WARNINGS AND PRECAUTIONS** Serious Allergic Reactions [see
-]**WARNINGS AND PRECAUTIONS** Sickle Cell Disorders [see
-]**WARNINGS AND PRECAUTIONS** Alveolar Hemorrhage and Hemoptysis [see
-]**WARNINGS AND PRECAUTIONS** Capillary Leak Syndrome [see
-]**WARNINGS AND PRECAUTIONS** Thrombocytopenia [see
-]**WARNINGS AND PRECAUTIONS** Leukocytosis [see
-]**WARNINGS AND PRECAUTIONS** Cutaneous Vasculitis [see

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

Adverse Reactions in Patients with Cancer Receiving Myelosuppressive Chemotherapy

The following adverse reaction data in Table 2 are from three randomized, placebo-controlled studies in patients with:

- small cell lung cancer receiving standard dose chemotherapy with cyclophosphamide, doxorubicin, and etoposide (Study 1)
- small cell lung cancer receiving ifosfamide, doxorubicin, and etoposide (Study 2), and
- non-Hodgkin's lymphoma (NHL) receiving doxorubicin, cyclophosphamide, vindesine, bleomycin, methylprednisolone, and methotrexate (“ACVBP”) or mitoxantrone, ifosfamide, mitoguazone, teniposide, methotrexate, folinic acid, methylprednisolone, and methotrexate (“VIM3”) (Study 3).

A total of 451 patients were randomized to receive subcutaneous filgrastim 230 mcg/m² (Study 1), 240 mcg/m² (Study 2) or 4 or 5 mcg/kg/day (Study 3) (n = 294) or placebo (n = 157). The patients in these studies were median age 61 (range 29 to 78) years and 64% were male. The ethnicity was 95% Caucasian, 4% African American, and1% Asian.

Table 2: Adverse Reactions in Patients with Cancer Receiving Myelosuppressive Chemotherapy (With ? 5% Higher Incidence in Filgrastim Compared to Placebo)

Placebo (N = 157)	Filgrastim (N = 294)	System Organ Class Preferred Term
		Blood and lymphatic system disorders
29%	38%	Thrombocytopenia
		Gastrointestinal disorders
32%	43%	Nausea
		General disorders and administration site conditions
29%	48%	Pyrexia
6%	13%	Chest pain
6%	12%	Pain
10%	20%	Fatigue
		Musculoskeletal and connective tissue disorders
8%	15%	Back pain
2%	9%	Arthralgia
6%	11%	Bone pain
3%	7%	Pain in extremity*
		Nervous system disorders
3%	14%	Dizziness
		Respiratory, thoracic and mediastinal disorders

8%	14%	Cough
8%	13%	Dyspnea
		Skin and subcutaneous tissue disorders
5%	14%	Rash
		Investigations
1%	6%	Blood lactate dehydrogenase increased
1%	6%	Blood alkaline phosphatase increased
		*Percent difference (Filgrastim – Placebo) was 4%.

Adverse events with ? 5% higher incidence in filgrastim patients compared to placebo and associated with the sequelae of the underlying malignancy or cytotoxic chemotherapy delivered included anemia, constipation, diarrhea, oral pain, vomiting, asthenia, malaise, edema peripheral, hemoglobin decreased, decreased appetite, oropharyngeal pain, and alopecia.

Adverse Reactions in Patients with Acute Myeloid Leukemia

Adverse reaction data below are from a randomized, double-blind, placebo-controlled study in patients with AML (Study 4) who received an induction chemotherapy regimen of intravenous daunorubicin days 1, 2, and 3; cytosine arabinoside days 1 to 7; and etoposide days 1 to 5 and up to 3 additional courses of therapy (induction 2, and consolidation 1, 2) of intravenous daunorubicin, cytosine arabinoside, and etoposide. The safety population included 518 patients randomized to receive either 5 mcg/kg/day filgrastim (n = 257) or placebo (n = 261). The median age was 54 (range 16 to 89) years and 54% were male.

-Adverse reactions with ? 2% higher incidence in filgrastim patients compared to placebo included epistaxis, back pain, pain in extremity, erythema, and rash maculo papular.

Adverse events with ? 2% higher incidence in filgrastim patients compared to placebo and associated with the sequelae of the underlying malignancy or cytotoxic chemotherapy included diarrhea, constipation, and transfusion reaction.

Adverse Reactions in Patients with Cancer Undergoing Bone Marrow Transplantation

The following adverse reaction data are from one randomized, no treatment-controlled study in patients with acute lymphoblastic leukemia or lymphoblastic lymphoma receiving high-dose chemotherapy (cyclophosphamide or cytarabine, and melphalan) and total body irradiation (Study 5) and one randomized, no treatment controlled study in patients with Hodgkin's disease (HD) and NHL undergoing high-dose chemotherapy and autologous bone marrow transplantation (Study 6). Patients receiving autologous bone marrow transplantation only were included in the analysis. A total of 100 patients received either 30 mcg/kg/day as a 4 hour infusion (Study 5) or 10 mcg/kg/day or 30 mcg/kg/day as a 24 hour infusion (Study 6) filgrastim (n = 72), no treatment control or placebo (n = 28). The median age was 30 (range 15 to 57) years, 57% were male.

Adverse reactions with ? 5% higher incidence in filgrastim patients compared to patients receiving no filgrastim included rash and hypersensitivity.

Adverse reactions in patients receiving intensive chemotherapy followed by autologous BMT with ? 5% higher incidence in filgrastim patients compared to patients receiving no filgrastim included thrombocytopenia, anemia, hypertension, sepsis, bronchitis, and insomnia.

Adverse Reactions in Patients with Cancer Undergoing Autologous Peripheral Blood Progenitor Cell Collection

The adverse reaction data in Table 3 are from a series of 7 trials in patients with cancer undergoing mobilization of autologous peripheral blood progenitor cells for collection by leukapheresis. Patients (n = 166) in all these trials underwent a similar mobilization/collection regimen: filgrastim was administered for 6 to 8 days, in most cases the apheresis procedure occurred on days 5, 6, and 7. The dosage of filgrastim ranged between 5 to 30 mcg/kg/day and was administered subcutaneously by injection or continuous infusion. The median age was 39 (range 15 to 67) years, and 48% were male.

Table 3: Adverse Reactions in Patients with Cancer Undergoing Autologous PBPC in the Mobilization Phase (? 5% Incidence in Filgrastim Patients)

Mobilization Phase (N = 166)	System Organ Class
	Musculoskeletal and connective tissue disorders
30%	Bone pain
	General disorders and administration site conditions
16%	Pyrexia
	Investigations
11%	Blood alkaline phosphatase increased
	Nervous system disorders
10%	Headache

Adverse Reactions in Patients with Severe Chronic Neutropenia

The following adverse reaction data were identified in a randomized, controlled study in patients with SCN receiving filgrastim (Study 7). 123 patients were randomized to a 4 month observation period followed by subcutaneous filgrastim treatment or immediate subcutaneous filgrastim treatment. The median age was 12 years (range 7 months to 76 years) and 46% were male. The dosage of filgrastim was determined by the category of neutropenia.

Initial dosage of filgrastim:

- Idiopathic neutropenia: 3.6 mcg/kg/day
- Cyclic neutropenia: 6 mcg/kg/day
- Congenital neutropenia: 6 mcg/kg/day divided 2 times per day

The dosage was increased incrementally to 12 mcg/kg/day divided 2 times per day if there was no response. Adverse reactions with ? 5% higher incidence in filgrastim patients compared to patients receiving no filgrastim included arthralgia, bone pain, back pain, muscle spasms, musculoskeletal pain, pain in extremity, splenomegaly, anemia, upper respiratory tract infection, and urinary tract infection (upper respiratory tract infection and urinary tract infection were higher in the filgrastim arm, total infection related events were lower in filgrastim treated patients), epistaxis, chest pain, diarrhea, hypoesthesia, and alopecia.

Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity. The incidence of antibody development in patients receiving filgrastim has not been adequately determined. While available data suggest that a small proportion of patients developed binding antibodies to filgrastim, the nature and specificity of these antibodies has not been adequately studied. In clinical studies using filgrastim, the incidence of antibodies binding to filgrastim was 3% (11/333). In these 11 patients, no evidence of a neutralizing response was observed using a cell-based bioassay. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay, and the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, timing of sampling, sample handling, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to filgrastim reported in this section with the incidence of antibodies in other studies or to other filgrastim products may be misleading.

Cytopenias resulting from an antibody response to exogenous growth factors have been reported on rare occasions in patients treated with other recombinant growth factors.

Postmarketing Experience

The following adverse reactions have been identified during post-approval use of filgrastim products. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

-]**WARNINGS AND PRECAUTIONS** splenic rupture and splenomegaly (enlarged spleen) [see
-] **WARNINGS AND PRECAUTIONS**acute respiratory distress syndrome [see
-]**WARNINGS AND PRECAUTIONS** anaphylaxis [see
-]**WARNINGS AND PRECAUTIONS** sickle cell disorders [see
-]**WARNINGS AND PRECAUTIONS** alveolar hemorrhage and hemoptysis [see
-]**WARNINGS AND PRECAUTIONS** capillary leak syndrome [see
-]**WARNINGS AND PRECAUTIONS** leukocytosis [see
-]**WARNINGS AND PRECAUTIONS** cutaneous vasculitis [see
- Sweet's syndrome (acute febrile neutrophilic dermatosis)
- decreased bone density and osteoporosis in pediatric patients receiving chronic treatment with filgrastim products.