STIMUFEND- pegfilgrastim-fpgk injection, solution
NORTHSTAR RX LLC

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use STIMUFEND safely and effectively. See full prescribing information for STIMUFEND.

STIMUFEND® (pegfilgrastim-fpgk) injection, for subcutaneous use
Initial U.S. Approval: 2022
STIMUFEND (pegfilgrastim-fpgk) is biosimilar* to NEULASTA (pegfilgrastim)

RECENT MAJOR CHANGES

Indications and Usage, Patients with Hematopoietic Subsyndrome of Acute Radiation Syndrome (1.2)	9/2023
Dosage and Administration, Patients with Hematopoietic Subsyndrome of Acute Radiation Syndrome (2.2)	9/2023

INDICATIONS AND USAGE

Stimufend is a leukocyte growth factor indicated to

- decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia. (1.1)
- Increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Subsyndrome of Acute Radiation Syndrome). (1.2)

Limitations of Use
Stimufend is not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation.

DOSAGE AND ADMINISTRATION

- Patients with cancer receiving myelosuppressive chemotherapy
  - 6 mg administered subcutaneously once per chemotherapy cycle. (2.1)
  - Do not administer between 14 days before and 24 hours after administration of cytotoxic chemotherapy. (2.1)
  - Use weight-based dosing for pediatric patients weighing less than 45 kg; refer to Table 1. (2.3)
- Patients acutely exposed to myelosuppressive doses of radiation
  - Two doses, 6 mg each, administered subcutaneously one week apart. Administer the first dose as soon as possible after suspected or confirmed exposure to myelosuppressive doses of radiation, and a second dose one week after. (2.2)
  - Use weight-based dosing for pediatric patients weighing less than 45 kg; refer to Table 1. (2.3)

DOSAGE FORMS AND STRENGTHS

Injection: 6 mg/0.6 mL solution in a single-dose pre-filled syringe for manual use only. (3)

CONTRAINDICATIONS

Patients with a history of serious allergic reactions to human granulocyte colony-stimulating factors such as pegfilgrastim products or filgrastim products. (4)

WARNINGS AND PRECAUTIONS

- Fatal splenic rupture: Evaluate patients who report left upper abdominal or shoulder pain for an enlarged spleen or splenic rupture. (5.1)
- Acute respiratory distress syndrome (ARDS): Evaluate patients who develop fever, lung infiltrates, or respiratory distress. Discontinue Stimufend in patients with ARDS. (5.2)
- Serious allergic reactions, including anaphylaxis: Permanently discontinue Stimufend in patients with serious allergic reactions. (5.3)
- Fatal sickle cell crises: Discontinue Stimufend if sickle cell crisis occurs. (5.4)
- Glomerulonephritis: Evaluate and consider dose- reduction or interruption of Stimufend if causality is likely. (5.5)
- Thrombocytopenia: Monitor platelet counts. (5.7)

- Myelodysplastic Syndrome (MDS) and Acute Myeloid Leukemia (AML): Monitor patients with breast and lung cancer using Stimufend in conjunction with chemotherapy and/or radiotherapy for signs and symptoms of MDS/AML. (5.10)

ADVERSE REACTIONS

Most common adverse reactions (≥ 5% difference in incidence compared to placebo) are bone pain and pain in extremity. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Northstar Rx LLC at 1-800-206-7821 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

* Biosimilar means that the biological product is approved based on data demonstrating that it is highly similar to an FDA-approved biological product, known as a reference product, and that there are no clinically meaningful differences between the biosimilar product and the reference product. Biosimilarity of Stimufend has been demonstrated for the condition(s) of use (e.g. indication(s), dosing regimen(s), strength(s), dosage form(s), and route(s) of administration described in its Full Prescribing Information.

Revised: 8/2025

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Patients with Cancer Receiving Myelosuppressive Chemotherapy

Stimufend is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia *[see Clinical Studies (14.1)]*.

Limitations of Use

Stimufend is not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation.

1.2 Patients with Hematopoietic Subsyndrome of Acute Radiation Syndrome

Stimufend is indicated to increase survival in patients acutely exposed to myelosuppressive doses of radiation *[see Dosage and Administration (2.2) and Clinical Studies (14.2)].*

2 DOSAGE AND ADMINISTRATION

2.1 Patients with Cancer Receiving Myelosuppressive Chemotherapy

The recommended dosage of Stimufend is a single subcutaneous injection of 6 mg administered once per chemotherapy cycle. For dosing in pediatric patients weighing less than 45 kg, refer to Table 1. Do not administer Stimufend between 14 days before and 24 hours after administration of cytotoxic chemotherapy.

2.2 Patients with Hematopoietic Subsyndrome of Acute Radiation Syndrome

The recommended dose of Stimufend is two doses, 6 mg each, administered subcutaneously one week apart. For dosing in pediatric patients weighing less than 45 kg, refer to Table 1. Administer the first dose as soon as possible after suspected or confirmed exposure to radiation levels greater than 2 gray (Gy). Administer the second dose one week after the first dose.

Obtain a baseline complete blood count (CBC). Do not delay administration of Stimufend if a CBC is not readily available. Estimate a patient's absorbed radiation dose (i.e., level of radiation exposure) based on information from public health authorities, biodosimetry if available, or clinical findings such as time to onset of vomiting or lymphocyte depletion kinetics.

2.3 Administration

Stimufend is administered subcutaneously via a single-dose prefilled syringe for manual use.

Prior to use, remove the carton from the refrigerator and allow the Stimufend prefilled syringe to reach room temperature for a minimum of 30 minutes. Discard any prefilled syringe left at room temperature for greater than 72 hours.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not administer Stimufend if discoloration or particulates are observed.

The needle cap on the pre-filled syringes contains dry natural rubber (derived from latex); persons with latex allergies should not administer these products.

Pediatric Patients weighing less than 45 kg

The Stimufend pre-filled syringe is not designed to allow for direct administration of doses less than 0.6 mL (6 mg). The syringe does not bear graduation marks, which are necessary to accurately measure doses of Stimufend less than 0.6 mL (6 mg) for direct administration to patients. Thus, the direct administration to patients requiring dosing of less than 0.6 mL (6 mg) is not recommended due to the potential for dosing errors. Refer to Table 1.

Table 1. Dosing of Stimufend for Pediatric Patients Weighing Less Than 45 kg

Body Weight	Stimufend Dose	Volume to Administer
Less than 10 kg*	See below*	See below*
10 - 20 kg	1.5 mg	0.15 mL
21 - 30 kg	2.5 mg	0.25 mL
31 - 44 kg	4 mg	0.4 mL

*For pediatric patients weighing less than 10 kg, administer 0.1 mg/kg (0.01 mL/kg) of Stimufend.

3 DOSAGE FORMS AND STRENGTHS

Stimufend is a clear, colorless, preservative-free solution available as:

- Injection: 6 mg/0.6 mL in a single-dose pre-filled syringe for manual use only.

4 CONTRAINDICATIONS

Stimufend is contraindicated in patients with a history of serious allergic reactions to pegfilgrastim products or filgrastim products. Reactions have included anaphylaxis *[see Warnings and Precautions (5.3)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Splenic Rupture

Splenic rupture, including fatal cases, can occur following the administration of pegfilgrastim products. Evaluate for an enlarged spleen or splenic rupture in patients who report left upper abdominal or shoulder pain after receiving Stimufend.

5.2 Acute Respiratory Distress Syndrome

Acute respiratory distress syndrome (ARDS) can occur in patients receiving pegfilgrastim products. Evaluate patients who develop fever and lung infiltrates or respiratory distress after receiving Stimufend for ARDS. Discontinue Stimufend in patients with ARDS.

5.3 Serious Allergic Reactions

Serious allergic reactions, including anaphylaxis, can occur in patients receiving pegfilgrastim products. The majority of reported events occurred upon initial exposure. Allergic reactions, including anaphylaxis, can recur within days after the discontinuation of initial anti-allergic treatment. Permanently discontinue Stimufend in patients with serious allergic reactions. Do not administer Stimufend to patients with a history of serious allergic reactions to pegfilgrastim products or filgrastim products.

5.4 Use in Patients with Sickle Cell Disorders

Severe and sometimes fatal sickle cell crises can occur in patients with sickle cell disorders receiving pegfilgrastim products. Discontinue Stimufend if sickle cell crisis occurs.

5.5 Glomerulonephritis

Glomerulonephritis has occurred in patients receiving pegfilgrastim 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 pegfilgrastim products. If glomerulonephritis is suspected, evaluate for cause. If causality is likely, consider dose- reduction or interruption of Stimufend.

5.6 Leukocytosis

White blood cell (WBC) counts of 100×10^9/L or greater have been observed in patients receiving pegfilgrastim products. Monitoring of complete blood count (CBC) during Stimufend therapy is recommended.

5.7 Thrombocytopenia

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

5.8 Capillary Leak Syndrome

Capillary leak syndrome has been reported after G-CSF administration, including pegfilgrastim 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 standard symptomatic treatment, which may include a need for intensive care.

5.9 Potential for Tumor Growth Stimulatory Effects on Malignant Cells

The granulocyte colony-stimulating factor (G-CSF) receptor through which pegfilgrastim products and filgrastim products act has been found on tumor cell lines. The possibility that pegfilgrastim products act as a growth factor for any tumor type, including myeloid malignancies and myelodysplasia, diseases for which pegfilgrastim products are not approved, cannot be excluded.

5.10 Myelodysplastic Syndrome (MDS) and Acute Myeloid Leukemia (AML) in Patients with Breast and Lung Cancer

MDS and AML have been associated with the use of pegfilgrastim products 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.

5.11 Aortitis

Aortitis has been reported in patients receiving pegfilgrastim 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 Stimufend if aortitis is suspected.

5.12 Nuclear Imaging

Increased hematopoietic activity of the bone marrow in response to growth factor therapy has been associated with transient positive bone imaging changes. This should be considered when interpreting bone imaging results.

6 ADVERSE REACTIONS

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

- Splenic Rupture *[see Warnings and Precautions (5.1)]*
- Acute Respiratory Distress Syndrome *[see Warnings and Precautions (5.2)]*
- Serious Allergic Reactions *[see Warnings and Precautions (5.3)]*
- Use in Patients with Sickle Cell Disorders *[see Warnings and Precautions (5.4)]*

- Glomerulonephritis *[see Warnings and Precautions (5.5)]*
- Leukocytosis *[see Warnings and Precautions (5.6)]*
- Thrombocytopenia *[see Warnings and Precautions (5.7)]*
- Capillary Leak Syndrome *[see Warnings and Precautions (5.8)]*
- Potential for Tumor Growth Stimulatory Effects on Malignant Cells *[see Warnings and Precautions (5.9)]*
- Myelodysplastic syndrome *[see Warnings and Precautions (5.10)]*
- Acute myeloid leukemia *[see Warnings and Precautions (5.10)]*
- Aortitis *[see Warnings and Precautions (5.11)]*

6.1 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.

Pegfilgrastim clinical trials safety data are based upon 932 patients receiving pegfilgrastim in seven randomized clinical trials. The population was 21 to 88 years of age and 92% female. The ethnicity was 75% Caucasian, 18% Hispanic, 5% Black, and 1% Asian. Patients with breast (n = 823), lung and thoracic tumors (n = 53) and lymphoma (n = 56) received pegfilgrastim after nonmyeloablative cytotoxic chemotherapy. Most patients received a single 100 mcg/kg (n = 259) or a single 6 mg (n = 546) dose per chemotherapy cycle over 4 cycles.

The following adverse reaction data in Table 2 are from a randomized, double-blind, placebo-controlled study in patients with metastatic or non-metastatic breast cancer receiving docetaxel 100 mg/m^2 every 21 days (Study 3). A total of 928 patients were randomized to receive either 6 mg pegfilgrastim (n = 467) or placebo (n = 461). The patients were 21 to 88 years of age and 99% female. The ethnicity was 66% Caucasian, 31% Hispanic, 2% Black, and < 1% Asian, Native American, or other.

The most common adverse reactions occurring in ≥ 5% of patients and with a between-group difference of ≥ 5% higher in the pegfilgrastim arm in placebo-controlled clinical trials are bone pain and pain in extremity.

Table 2. Adverse Reactions with ≥ 5% Higher Incidence in Pegfilgrastim Patients Compared to Placebo in Study 3

Body System Adverse Reaction	**Placebo (N = 461)**	**Pegfilgrastim 6 mg SC on Day 2 (N = 467)**
Musculoskeletal and connective tissue disorders		
Bone pain	26%	31%
Pain in extremity	4%	9%

Leukocytosis

In clinical studies, leukocytosis (WBC counts > 100 x 10^9/L) was observed in less than 1% of 932 patients with non-myeloid malignancies receiving pegfilgrastim. No

complications attributable to leukocytosis were reported in clinical studies.

6.2 Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors, including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies in the studies described below with the incidence of antibodies in other studies or to other pegfilgrastim products may be misleading.

Binding antibodies to pegfilgrastim were detected using a BIAcore assay. The approximate limit of detection for this assay is 500 ng/mL. Pre-existing binding antibodies were detected in approximately 6% (51/849) of patients with metastatic breast cancer. Four of 521 pegfilgrastim-treated subjects who were negative at baseline developed binding antibodies to pegfilgrastim following treatment. None of these 4 patients had evidence of neutralizing antibodies detected using a cell-based bioassay.

6.3 Postmarketing Experience

The following adverse reactions have been identified during post approval use of pegfilgrastim 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.

- Splenic rupture and splenomegaly (enlarged spleen) *[see Warnings and Precautions (5.1)]*
- Acute respiratory distress syndrome (ARDS) *[see Warnings and Precautions (5.2)]*
- Allergic reactions/hypersensitivity, including anaphylaxis, skin rash, urticaria, generalized erythema, and flushing *[see Warnings and Precautions (5.3)]*
- Sickle cell crisis *[see Warnings and Precautions (5.4)]*
- Glomerulonephritis *[see Warnings and Precautions (5.5)]*
- Leukocytosis *[see Warnings and Precautions (5.6)]*
- Thrombocytopenia *[see Warnings and Precautions (5.7)]*
- Capillary Leak Syndrome *[see Warnings and Precautions (5.8)]*
- Injection site reactions
- Sweet's syndrome (acute febrile neutrophilic dermatosis), cutaneous vasculitis
- Myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML) in patients with breast and lung cancer receiving chemotherapy and/or radiotherapy *[see Warnings and Precautions (5.10)]*
- Aortitis *[see Warnings and Precautions (5.11)]*
- Alveolar hemorrhage

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Although available data with Stimufend or pegfilgrastim product use in pregnant women

are insufficient to establish whether there is a drug associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes, there are available data from published studies in pregnant women exposed to filgrastim products. These studies have not established an association of filgrastim product use during pregnancy with major birth defects, miscarriage, or adverse maternal or fetal outcomes.

In animal studies, no evidence of reproductive/developmental toxicity occurred in the offspring of pregnant rats that received cumulative doses of pegfilgrastim approximately 10 times the recommended human dose (based on body surface area). In pregnant rabbits, increased embryolethality and spontaneous abortions occurred at 4 times the maximum recommended human dose simultaneously with signs of maternal toxicity *(see Data).*

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes.

In the U.S. general population, the estimated background risks of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Data

Animal Data

Pregnant rabbits were dosed with pegfilgrastim subcutaneously every other day during the period of organogenesis. At cumulative doses ranging from the approximate human dose to approximately 4 times the recommended human dose (based on body surface area), the treated rabbits exhibited decreased maternal food consumption, maternal weight loss, as well as reduced fetal body weights and delayed ossification of the fetal skull; however, no structural anomalies were observed in the offspring from either study. Increased incidences of post-implantation losses and spontaneous abortions (more than half the pregnancies) were observed at cumulative doses approximately 4 times the recommended human dose, which were not seen when pregnant rabbits were exposed to the recommended human dose.

Three studies were conducted in pregnant rats dosed with pegfilgrastim at cumulative doses up to approximately 10 times the recommended human dose at the following stages of gestation: during the period of organogenesis, from mating through the first half of pregnancy, and from the first trimester through delivery and lactation. No evidence of fetal loss or structural malformations was observed in any study. Cumulative doses equivalent to approximately 3 and 10 times the recommended human dose resulted in transient evidence of wavy ribs in fetuses of treated mothers (detected at the end of gestation but no longer present in pups evaluated at the end of lactation).

8.2 Lactation

Risk Summary

There are no data on the presence of pegfilgrastim products in human milk, the effects on the breastfed child, or the effects on milk production. Other filgrastim products are secreted poorly into breast milk, and filgrastim products are not absorbed orally by neonates. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Stimufend and any potential adverse effects on the breastfed child from Stimufend or from the underlying maternal condition.

8.4 Pediatric Use

The safety and effectiveness of Stimufend have been established in pediatric patients. No overall differences in safety were identified between adult and pediatric patients based on postmarketing surveillance and review of the scientific literature.

Use of Stimufend in pediatric patients for chemotherapy-induced neutropenia is based on Stimufend's approval as a biosimilar to pegfilgrastim and evidence from adequate and well-controlled studies of pegfilgrastim in adults with additional pharmacokinetic and safety data of pegfilgrastim in pediatric patients with sarcoma *[see Clinical Pharmacology (12.3) and Clinical Studies (14.1)]*.

The use of Stimufend to increase survival in pediatric patients acutely exposed to myelosuppressive doses of radiation is based on Stimufend's approval as a biosimilar to pegfilgrastim, evidence from efficacy studies of pegfilgrastim conducted in animals, and clinical data supporting the use of pegfilgrastim in patients with cancer receiving myelosuppressive chemotherapy. Efficacy studies of pegfilgrastim products could not be conducted in humans with acute radiation syndrome for ethical and feasibility reasons. Results from population modeling and simulation indicate that two weight-based doses of pegfilgrastim (Table 1) administered one week apart provide pediatric patients weighing less than 45 kg with exposures comparable to that of adults receiving two 6 mg doses one week apart *[see Dosage and Administration (2.3), Clinical Pharmacology (12.3) and Clinical Studies (14.2)].*

8.5 Geriatric Use

Of the 932 patients with cancer who received pegfilgrastim in clinical studies, 139 (15%) were aged 65 and over, and 18 (2%) were aged 75 and over. No overall differences in safety or effectiveness were observed between patients aged 65 and older and younger patients.

10 OVERDOSAGE

Overdosage of pegfilgrastim may result in leukocytosis and bone pain. Events of edema, dyspnea, and pleural effusion have been reported in a single patient who administered pegfilgrastim on 8 consecutive days in error. In the event of overdose, the patient should be monitored for adverse reactions *[see Adverse Reactions (6)]*.

11 DESCRIPTION

Pegfilgrastim-fpgk is a covalent conjugate of recombinant methionyl human G-CSF and monomethoxypolyethylene glycol. Recombinant methionyl human G-CSF is a water-soluble 175 amino acid protein with a molecular weight of approximately 19 kilodaltons (kD). Recombinant methionyl human G-CSF is obtained from the bacterial fermentation of a strain of *E coli* transformed with a genetically engineered plasmid containing the human G-CSF gene. To produce pegfilgrastim-fpgk, a 20 kD monomethoxypolyethylene glycol molecule is covalently bound to the N-terminal methionyl residue of recombinant methionyl human G-CSF. The average molecular weight of pegfilgrastim-fpgk is approximately 39 kD.

Stimufend (pegfilgrastim-fpgk) injection is supplied in 0.6 mL pre-filled syringes for

manual subcutaneous injection. The pre-filled syringe does not bear graduation marks and is designed to deliver the entire contents of the syringe (6 mg/0.6 mL).

The delivered 0.6 mL dose from the prefilled syringe contains 6 mg pegfilgrastim-fpgk (based on protein weight) in a sterile, clear, colorless, preservative-free solution (pH 4.0) containing acetate (0.35 mg), polysorbate 20 (0.02 mg), sodium (0.02 mg), and sorbitol (30 mg) in Water for Injection, USP.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Pegfilgrastim products are colony-stimulating factors that act on hematopoietic cells by binding to specific cell surface receptors, thereby stimulating proliferation, differentiation, commitment, and end cell functional activation.

12.2 Pharmacodynamics

Animal data and clinical data in humans suggest a correlation between pegfilgrastim products' exposure and the duration of severe neutropenia as a predictor of efficacy. Selection of the dosing regimen of Stimufend is based on reducing the duration of severe neutropenia.

12.3 Pharmacokinetics

The pharmacokinetics of pegfilgrastim was studied in 379 patients with cancer. The pharmacokinetics of pegfilgrastim was nonlinear, and clearance decreased with increases in dose. Neutrophil receptor binding is an important component of the clearance of pegfilgrastim, and serum clearance is directly related to the number of neutrophils. In addition to numbers of neutrophils, body weight appeared to be a factor. Patients with higher body weights experienced higher systemic exposure to pegfilgrastim after receiving a dose normalized for body weight. A large variability in the pharmacokinetics of pegfilgrastim was observed. The half-life of pegfilgrastim ranged from 15 to 80 hours after subcutaneous injection.

Specific Populations

No gender-related differences were observed in the pharmacokinetics of pegfilgrastim, and no differences were observed in the pharmacokinetics of geriatric patients (≥ 65 years of age) compared with younger patients (< 65 years of age) *[see Use in Specific Populations (8.5)]*.

Renal Impairment

In a study of 30 subjects with varying degrees of renal dysfunction, including end stage renal disease, renal dysfunction had no effect on the pharmacokinetics of pegfilgrastim.

Pediatric Patients with Cancer Receiving Myelosuppressive Chemotherapy

The pharmacokinetics and safety of pegfilgrastim were studied in 37 pediatric patients with sarcoma in Study 4 *[see Clinical Studies (14.1)]*. The mean (± standard deviation [SD]) systemic exposure ($AUC_{0\text{-}inf}$) of pegfilgrastim after subcutaneous administration at 100 mcg/kg was 47.9 (± 22.5) mcg·hr/mL in the youngest age group (0 to 5 years, n = 11), 22.0 (± 13.1) mcg·hr/mL in the 6 to 11 years age group (n = 10), and 29.3 (±

23.2) mcg•hr/mL in the 12 to 21 years age group (n = 13). The terminal elimination half-lives of the corresponding age groups were 30.1 (± 38.2) hours, 20.2 (± 11.3) hours, and 21.2 (± 16.0) hours, respectively.

Patients Acutely Exposed to Myelosuppressive Doses of Radiation

The pharmacokinetics of pegfilgrastim products is not available in patients acutely exposed to myelosuppressive doses of radiation. Based on limited pharmacokinetic data in irradiated non-human primates, the area under the concentration-time curve (AUC), reflecting the exposure to pegfilgrastim in non-human primates following a 300 mcg/kg dose of pegfilgrastim, appears to be greater than in humans receiving a 6 mg dose. Results from population modeling and simulation indicate that two 6 mg doses of pegfilgrastim administered one week apart in adults result in clinically relevant effects on duration of grade 3 and 4 neutropenia. In addition, weight-based dosing in pediatric patients weighing less than 45 kg *[see Dosage and Administration, Section 2.3, Table 1]* provides exposures comparable to those in adults receiving two 6 mg doses one week apart.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No carcinogenicity or mutagenesis studies have been performed with pegfilgrastim products.

Pegfilgrastim did not affect reproductive performance or fertility in male or female rats at cumulative weekly doses approximately 6 to 9 times higher than the recommended human dose (based on body surface area).

14 CLINICAL STUDIES

14.1 Patients with Cancer Receiving Myelosuppressive Chemotherapy

Pegfilgrastim was evaluated in three randomized, double-blind, controlled studies. Studies 1 and 2 were active-controlled studies that employed doxorubicin 60 mg/m^2 and docetaxel 75 mg/m^2 administered every 21 days for up to 4 cycles for the treatment of metastatic breast cancer. Study 1 investigated the utility of a fixed dose of pegfilgrastim. Study 2 employed a weight-adjusted dose. In the absence of growth factor support, similar chemotherapy regimens have been reported to result in a 100% incidence of severe neutropenia (ANC < 0.5 x 10^9/L) with a mean duration of 5 to 7 days and a 30% to 40% incidence of febrile neutropenia. Based on the correlation between the duration of severe neutropenia and the incidence of febrile neutropenia found in studies with filgrastim, duration of severe neutropenia was chosen as the primary endpoint in both studies, and the efficacy of pegfilgrastim was demonstrated by establishing comparability to filgrastim-treated patients in the mean days of severe neutropenia.

In Study 1, 157 patients were randomized to receive a single subcutaneous injection of pegfilgrastim (6 mg) on day 2 of each chemotherapy cycle or daily subcutaneous filgrastim (5 mcg/kg/day) beginning on day 2 of each chemotherapy cycle. In Study 2, 310 patients were randomized to receive a single subcutaneous injection of pegfilgrastim (100 mcg/kg) on day 2 or daily subcutaneous filgrastim (5 mcg/kg/day) beginning on

day 2 of each chemotherapy cycle.

Both studies met the major efficacy outcome measure of demonstrating that the mean days of severe neutropenia of pegfilgrastim-treated patients did not exceed that of filgrastim-treated patients by more than 1 day in cycle 1 of chemotherapy. The mean days of cycle 1 severe neutropenia in Study 1 were 1.8 days in the pegfilgrastim arm compared to 1.6 days in the filgrastim arm [difference in means 0.2 (95% CI - 0.2, 0.6)] and in Study 2 were 1.7 days in the pegfilgrastim arm compared to 1.6 days in the filgrastim arm [difference in means 0.1 (95% CI - 0.2, 0.4)].

A secondary endpoint in both studies was days of severe neutropenia in cycles 2 through 4 with results similar to those for cycle 1.

Study 3 was a randomized, double-blind, placebo-controlled study that employed docetaxel 100 mg/m^2 administered every 21 days for up to 4 cycles for the treatment of metastatic or non-metastatic breast cancer. In this study, 928 patients were randomized to receive a single subcutaneous injection of pegfilgrastim (6 mg) or placebo on day 2 of each chemotherapy cycle. Study 3 met the major trial outcome measure of demonstrating that the incidence of febrile neutropenia (defined as temperature ≥ 38.2°C and ANC ≤ 0.5 x 10^9/L) was lower for pegfilgrastim-treated patients as compared to placebo-treated patients (1% versus 17%, respectively, $p < 0.001$). The incidence of hospitalizations (1% versus 14%) and IV anti-infective use (2% versus 10%) for the treatment of febrile neutropenia was also lower in the pegfilgrastim-treated patients compared to the placebo-treated patients.

Study 4 was a multicenter, randomized, open-label study to evaluate the efficacy, safety, and pharmacokinetics [see Clinical Pharmacology (12.3)] of pegfilgrastim in pediatric and young adult patients with sarcoma. Patients with sarcoma receiving chemotherapy age 0 to 21 years were eligible. Patients were randomized to receive subcutaneous pegfilgrastim as a single-dose of 100 mcg/kg (n = 37) or subcutaneous filgrastim at a dose 5 mcg/kg/day (n = 6) following myelosuppressive chemotherapy. Recovery of neutrophil counts was similar in the pegfilgrastim and filgrastim groups. The most common adverse reaction reported was bone pain.

14.2 Patients with Hematopoietic Subsyndrome of Acute Radiation Syndrome

Efficacy studies of pegfilgrastim products could not be conducted in humans with acute radiation syndrome for ethical and feasibility reasons. Approval of this indication was based on efficacy studies conducted in animals and data supporting pegfilgrastim's effect on severe neutropenia in patients with cancer receiving myelosuppressive chemotherapy *[see Dosage and Administration (2.1)].*

The recommended dose of Stimufend is two doses, 6 mg each, administered one week apart for humans exposed to myelosuppressive doses of radiation. For pediatric patients weighing less than 45 kg, dosing of Stimufend is weight-based and is provided in Table 1 *[see Dosage and Administration (2.3)]*. This dosing regimen is based on population modeling and simulation analyses. The exposure associated with this dosing regimen is expected to provide sufficient pharmacodynamic activity to treat humans exposed to myelosuppressive doses of radiation *[see Clinical Pharmacology (12.3)]*. The safety of pegfilgrastim at a dose of 6 mg has been assessed on the basis of clinical experience in patients with cancer receiving myelosuppressive chemotherapy.

The efficacy of pegfilgrastim for the acute radiation syndrome setting was studied in a

randomized, placebo-controlled non-human primate model of radiation injury. Rhesus macaques were randomized to either a control (n = 23) or treated (n = 23) cohort. On study day 0, animals (n = 6 to 8 per irradiation day) were exposed to total body irradiation (TBI) of 7.50 ± 0.15 Gy delivered at 0.8 ± 0.03 Gy/min, representing a dose that would be lethal in 50% of animals by 60 days of follow-up (LD50/60). Animals were administered subcutaneous injections of a blinded treatment (control article [5% dextrose in water] or pegfilgrastim [300-319 mcg/kg/day]) on study day 1 and on study day 8. The primary endpoint was survival. Animals received medical management consisting of intravenous fluids, antibiotics, blood transfusions, and other support as required.

Pegfilgrastim significantly (at 0.0014 level of significance) increased 60-day survival in irradiated non-human primates: 91% survival (21/23) in the pegfilgrastim group compared to 48% survival (11/23) in the control group.

16 HOW SUPPLIED/STORAGE AND HANDLING

Stimufend single-dose prefilled syringe for manual use

Stimufend (pegfilgrastim-fpgk) injection is a clear, colorless, preservative-free solution supplied in a pre-filled single-dose syringe for manual use containing 6 mg pegfilgrastim-fpgk, supplied with a 27-gauge, 1/2-inch needle with a Safe'n'Sound® passive Needle Guard.

The needle cap of the pre-filled syringe contains natural rubber (a derivative of latex).

Stimufend is provided in a dispensing pack containing one sterile 6 mg/0.6 mL pre-filled syringe (NDC 72603-402-01).

Stimufend pre-filled syringe does not bear graduation marks and is intended only to deliver the entire contents of the syringe (6 mg/0.6 mL) for direct administration. Use of the pre-filled syringe is not recommended for direct administration for pediatric patients weighing less than 45 kg who require doses that are less than the full contents of the syringe.

Store refrigerated between 36°F to 46°F (2°C to 8°C) in the carton to protect from light. Do not shake. Discard syringes stored at room temperature for more than 72 hours. Do not freeze. Discard syringe if frozen.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information and Instructions for Use). Advise patients of the following risks and potential risks with Stimufend:

- Splenic rupture and splenomegaly
- Acute Respiratory Distress Syndrome
- Serious allergic reactions
- Sickle cell crisis
- Glomerulonephritis
- Increased risk of Myelodysplastic Syndrome and/or Acute Myeloid Leukemia in patients with breast and lung cancer who receive Stimufend in conjunction with chemotherapy and/or radiation therapy

- Capillary Leak Syndrome
- Aortitis

Advise patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Subsyndrome of Acute Radiation Syndrome) that efficacy studies of pegfilgrastim products for this indication could not be conducted in humans for ethical and feasibility reasons and that, therefore, approval of this use was based on efficacy studies conducted in animals *[see Clinical Studies (14.2)]*.

Instruct patients who self-administer Stimufend using the single-dose pre-filled syringe of the:
- Importance of following the Instructions for Use (see Instructions for Use).
- Dangers of reusing syringes.
- Importance of following local requirements for proper disposal of used syringes.

Manufactured by:
Fresenius Kabi USA, LLC
Lake Zurich, Illinois 60047
U.S. License No. 2146
Product of Italy

Manufactured for:
Northstar Rx LLC,
Memphis, TN 38141

Patient Information Stimufend®(STIM-yu-fend) (pegfilgrastim-fpgk) injection Single-Dose Prefilled Syringe
What is Stimufend? Stimufend is a man-made form of granulocyte colony-stimulating factor (G-CSF). G-CSF is a substance produced by the body. It stimulates the growth of neutrophils, a type of white blood cell important in the body's fight against infection. Acute Radiation Syndrome: The effectiveness of pegfilgrastim for this use was only studied in animals, because it could not be studied in people.
Do not take Stimufend if you have had a serious allergic reaction to pegfilgrastim products or filgrastim products.
Before you receive Stimufend, tell your healthcare provider about all of your medical conditions, including if you: • have a sickle cell disorder. • have kidney problems. • are allergic to latex. The needle cap on the prefilled syringe contains dry natural rubber (derived from latex). You should not give Stimufend using the prefilled syringe if you have latex allergies. • are pregnant or plan to become pregnant. It is not known if Stimufend will harm your unborn baby. • are breastfeeding or plan to breastfeed. It is not known if Stimufend passes into your breast milk. **Tell your healthcare provider about all of the medicines you take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements.
How will I receive Stimufend?

- **Stimufend is given as an injection under your skin (subcutaneous injection) by a healthcare provider. If your healthcare provider decides that the subcutaneous injections can be given at home by you or your caregiver, follow the detailed "Instructions for Use" that comes with your Stimufend for information on how to prepare and inject a dose of Stimufend.**
- You and your caregiver will be shown how to prepare and inject Stimufend before you use it.
- You should not inject a dose of Stimufend to children weighing less than 45 kg from a Stimufend prefilled syringe. A dose less than 0.6 mL (6 mg) cannot be accurately measured using the Stimufend prefilled syringe.
- If you are receiving Stimufend because you are also receiving chemotherapy, the last dose of Stimufend should be injected at least 14 days before and 24 hours after your dose of chemotherapy.
- If you miss a dose of Stimufend, talk to your healthcare provider about when you should give your next dose.

What are possible side effects of Stimufend?
Stimufend may cause serious side effects, including:

- **Spleen rupture.** Your spleen may become enlarged and can rupture. A ruptured spleen can cause death. Call your healthcare provider right away if you have pain in the left upper stomach area or your left shoulder.
- **A serious lung problem called Acute Respiratory Distress Syndrome (ARDS).** Call your healthcare provider or get emergency help right away if you have shortness of breath with or without a fever, trouble breathing, or a fast rate of breathing.
- **Serious allergic reactions.** Stimufend can cause serious allergic reactions. These reactions can cause a rash over your whole body, shortness of breath, wheezing, dizziness, swelling around your mouth or eyes, fast heart rate, and sweating. If you have any of these symptoms, stop using Stimufend and call your healthcare provider or get emergency medical help right away.
- **Sickle cell crises.** You may have a serious sickle cell crisis, which could lead to death, if you have a sickle cell disorder and receive Stimufend. Call your healthcare provider right away if you have symptoms of sickle cell crisis such as pain or difficulty breathing.
- **Kidney injury (glomerulonephritis).** Stimufend can cause kidney injury. Call your healthcare provider right away if you develop any of the following symptoms:
  - swelling of your face or ankles
  - blood in your urine or dark colored urine
  - you urinate less than usual
- **Increased white blood cell count (leukocytosis).** Your healthcare provider will check your blood during treatment with Stimufend.
- **Decreased platelet count (thrombocytopenia).** Your healthcare provider will check your blood during treatment with Stimufend. Tell your healthcare provider if you have unusual bleeding or bruising during treatment with Stimufend. This could be a sign of decreased platelet counts, which may reduce the ability of your blood to clot.
- **Capillary Leak Syndrome.** Stimufend can cause fluid to leak from blood vessels into your body's tissues. This condition is called "Capillary Leak Syndrome" (CLS).

CLS can quickly cause you to have symptoms that may become life-threatening. Get emergency medical help right away if you develop any of the following symptoms:
  - swelling or puffiness and are urinating less than usual
  - trouble breathing
  - swelling of your stomach area (abdomen) and feeling of fullness
  - dizziness or feeling faint
  - a general feeling of tiredness
- **Myelodysplastic syndrome and acute myeloid leukemia.** If you have breast cancer or lung cancer, when Stimufend is used with chemotherapy and radiation therapy, or with radiation therapy alone, you may have an increased risk of developing a precancerous blood condition called myelodysplastic syndrome (MDS) or a blood cancer called acute myeloid leukemia (AML). Symptoms may include tiredness, fever, and easy bruising or bleeding. Call your healthcare provider if you develop these symptoms during treatment with Stimufend.
- **Inflammation of the aorta (aortitis).** Inflammation of the aorta (the large blood vessel which transports blood from the heart to the body) has been reported in patients who received pegfilgrastim products. Symptoms may include fever, abdominal pain, feeling tired, and back pain. Call your healthcare provider if you experience these symptoms.

The most common side effects of Stimufend are pain in the bones, arms, and legs. These are not all the possible side effects of Stimufend. Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store Stimufend?

- Store Stimufend in the refrigerator between 36˚F to 46˚F (2˚C to 8°C).
- **Do not** freeze. Throw away (dispose of) Stimufend that has been frozen.
- Keep the prefilled syringe in the original carton to protect from light or physical damage.
- Do not shake the prefilled syringe.
- Take Stimufend out of the refrigerator 30 minutes before use and allow it to reach room temperature before preparing an injection.
- Throw away (dispose of) any Stimufend that has been left at room temperature, 68°F to 77°F (20°C to 25°C), for more than 72 hours.

Keep the Stimufend prefilled syringe out of the reach of children.

General information about the safe and effective use of Stimufend.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use Stimufend for a condition for which it was not prescribed. Do not give Stimufend to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about Stimufend that is written for health professionals.

What are the ingredients in Stimufend?

Active ingredient: pegfilgrastim-fpgk

Inactive ingredients: acetate, polysorbate 20, sodium and sorbitol in Water for Injection, USP.

Manufactured by:

Fresenius Kabi USA, LLC

Lake Zurich, Illinois 60047
U.S. License No. 2146
Product of Italy

Manufactured for:
Northstar Rx LLC,
Memphis, TN 38141
For more information go to www.northstarrxllc.com or call 1-800-206-7821.

This Patient Information has been approved by the U.S. Food and Drug Administration. Revised: August 2025

451860A

Instructions for Use
STIMUFEND® (STIM-yu-fend)
(pegfilgrastim-fpgk)
Injection, for subcutaneous use
Single-Dose Prefilled Syringe

Guide to parts

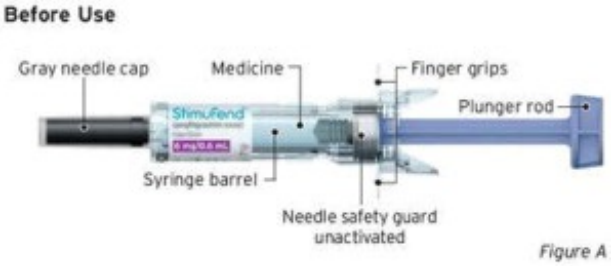


Figure A

After Use (Clear needle guard locked in place)

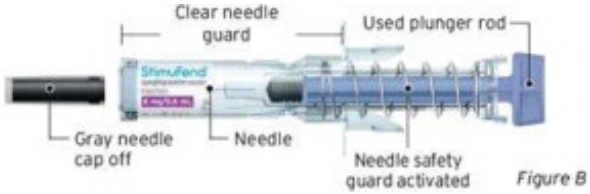


Figure B

Important: The needle is covered by a gray needle cap before use.

Important:
Read the Patient Information for important information you need to know about STIMUFEND before using these Instructions for Use.

Before you use a STIMUFEND prefilled syringe, read this important information.

Storing the prefilled syringe

- Store STIMUFEND in the refrigerator between 36°F to 46°F (2°C to 8°C).
- **Do not** freeze. Throw away (dispose of) STIMUFEND that has been frozen.
- Keep the prefilled syringe in the original carton to protect from light or physical damage.

- Take the prefilled syringe out of the refrigerator 30 minutes before use and allow it to reach room temperature before preparing an injection.
- Throw away (dispose of) any STIMUFEND that has been left at room temperature, 68°F to 77°F (20°C to 25°C), for more than 72 hours.
- Keep the STIMUFEND prefilled syringe out of the reach of children.

Using the prefilled syringe

- **It is important that you do not try to give the injection unless you or your caregiver has received training from your healthcare provider.**
- Make sure the name STIMUFEND appears on the carton and prefilled syringe label.
- Check the carton and prefilled syringe label to make sure the dose strength is 6 mg/0.6 mL.
- You should not inject a dose of STIMUFEND to children weighing less than 45 kg from a STIMUFEND prefilled syringe. A dose less than 0.6 mL (6 mg) cannot be accurately measured using the STIMUFEND prefilled syringe.
- **Do not** use a prefilled syringe after the expiration date on the label.
- **Do not** shake the prefilled syringe.
- **Do not** remove the gray needle cap from the prefilled syringe until you are ready to inject.
- **Do not** use the prefilled syringe if the carton is open or damaged.
- **Do not** use a prefilled syringe if it has been dropped on a hard surface. The prefilled syringe may be broken even if you cannot see the break. Use a new prefilled syringe.
- The gray needle cap on the prefilled syringe contains dry natural rubber (made from latex). **Tell your healthcare provider if you are allergic to latex. You should not give STIMUFEND using the prefilled syringe if you have latex allergies.**

  The prefilled syringe has a clear needle guard that automatically activates to cover the needle after the injection is given. **Do not** use a prefilled syringe if the clear needle guard has been activated. Use another prefilled syringe that has not been activated and is ready to use.

Call your healthcare provider if you have any questions.

Step 1: Prepare

1.1 Remove the prefilled syringe carton from the refrigerator. Remove the syringe tray from the carton.
On a clean, well-lit surface, place the syringe tray at room temperature for **30** minutes before you give an injection.

- **Do not** use the prefilled syringe if the carton is damaged.
- **Do not** try to warm the prefilled syringe by using a heat source such as hot water or microwave.
- **Do not** leave the prefilled syringe in direct sunlight.
- **Do not** shake the prefilled syringe.

Open the tray by peeling away the cover. Grab the clear needle guard to remove the prefilled syringe from the tray (see Figure C).

For safety reasons:

- **Do not** grab the plunger rod.
- **Do not** grab the gray needle cap.

Figure C

1.2 Inspect the medicine and prefilled syringe.
Make sure the medicine in the prefilled syringe is clear and colorless.

- **Do not** use the prefilled syringe if:
  - The needle safety guard is activated (see Figure D).
  - The medicine is cloudy or discolored, or contains flakes or particles (see Figure E).
  - Any part appears cracked or broken.
  - The prefilled syringe has been dropped.
  - The gray needle cap is missing or not securely attached (see Figure E).
  - The expiration date printed on the label has passed (see Figure E).

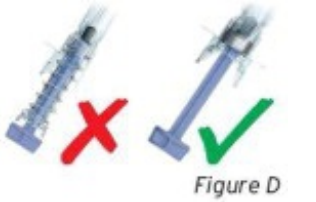


Figure D

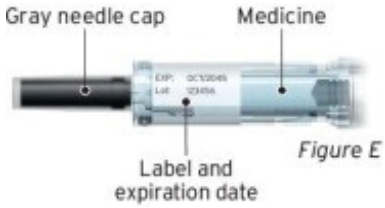


Figure E

In all cases use a new syringe and call your healthcare provider.

1.3 Gather all materials needed for the injection (see Figure F). Wash your hands thoroughly with soap and water.
On a clean, well-lit work surface, place the:

- Prefilled syringe
- Alcohol wipe
- Cotton ball or gauze pad
- Adhesive bandage
- Sharps disposal container

Figure F

Step 2: Get ready

2.1 Prepare and clean the injection site(s).
You can use:

- Stomach area (abdomen) except for a **2**-inch area away from the navel (belly button) (see Figure G)
- Thigh (see Figure G)

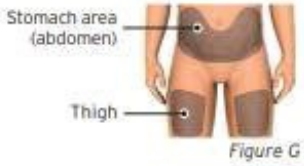


Figure G

- Back area of upper arm (only if someone else is giving you the injection) (see Figure H)
- Upper outer area of the buttocks (only if someone else is giving you the injection) (see Figure H)

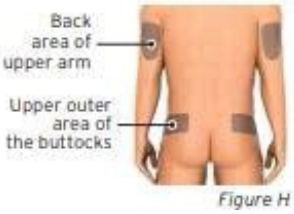


Figure H

Clean the injection site with an alcohol wipe (see Figure I). Let the skin dry.

- **Do not** touch this area again before injecting.
- If you want to use the same injection site, make sure it is not the same spot on the injection site you used for a previous injection.
- **Do not** inject into areas where the skin is tender, bruised, red, or hard. Avoid injecting into areas with scars or stretch marks.

Figure I

2.2 Hold the prefilled syringe by the clear needle guard. Carefully pull the gray needle cap straight off and away from the body (see Figure J).

- **Do not** remove the gray needle cap from the prefilled syringe until you are ready to inject.
- **Do not** twist or bend the gray needle cap.
- **Do not** hold the prefilled syringe by the plunger rod.
- **Do not** put the gray needle cap back onto the prefilled syringe.

Figure J

Important: Throw the gray needle cap into the sharps disposal container (see Figure K).

Figure K

Step 3: Subcutaneous (under the skin) injection

3.1 Pinch the injection site to create a firm surface (see Figure L).
Important: Keep skin pinched while injecting.

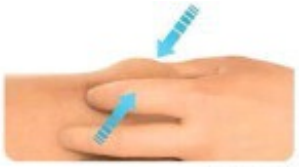


Figure L

3.2 Hold the pinch. Insert the needle into the skin at 45 to 90 degrees (see Figure M).

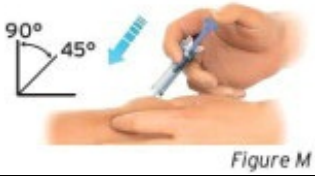


Figure M

3.3 Using slow and constant pressure, push the plunger rod until it reaches the bottom (see Figure N).

- The plunger rod must be pushed down fully to ensure the full dose has been injected (see Figure O).
- **Do not** remove the needle from the skin when the plunger reaches the end and proceed with next step.

Figure N

Figure O

Step 4: Finish

4.1 Slowly release your thumb upward. This will allow the needle to move up into the clear needle guard and cover the entire needle (see Figure P).

- **Do not** try to recap the needle as it could lead to needle stick injury.

Figure P

Important: When you remove the syringe, if it looks like the medicine is still in the syringe barrel, this means you have not received a full dose. Call your healthcare provider right away.

4.2 Discard (throw away) your prefilled syringe.

- Put the used prefilled syringe in a FDA-cleared sharps disposal container right away after use (see Figure Q).
- **Do not** throw away (dispose of) the prefilled syringe in your household trash.
- If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
  - made of a heavy-duty plastic,
  - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
  - upright and stable during use,
  - leak-resistant, and
  - properly labeled to warn of hazardous waste inside the container.

Figure Q

- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal

- **Do not** reuse the prefilled syringe.
- **Do not** recycle the prefilled syringe or sharps disposal container or throw them in the household trash.

Important: Always keep the sharps disposal container out of the reach of children.

4.3 Examine the injection site.

- If there is blood, press a cotton ball or gauze pad on the injection site. **Do not** rub the injection site. Apply an adhesive bandage if needed (see Figure R).

Figure R

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

Manufactured by: Fresenius Kabi USA, LLC Lake Zurich, Illinois 60047
U.S. License No. 2146
Manufactured for: Northstar Rx LLC, Memphis, TN 38141
Revised: 8/2025

PACKAGE LABEL – PRINCIPAL DISPLAY – STIMUFEND –One 0.6 mL Single-Dose Prefilled Syringe CARTON PANEL

Stimufend

pegfilgrastim-fpgk

Injection

6 mg/0.6 mL

NDC 72603-402-01

Rx Only

Pegylated Recombinant Methionyl Human Granulocyte Colony-Stimulating Factor (PEG-rmethHuG-

CSF) derived from E Coli

For Subcutaneous Use Only

1 single-dose pre-filled syringe

This product contains Dry Natural Rubber

Sterile Solution-No Preservative

Aisling®

PACKAGE LABEL – PRINCIPAL DISPLAY – STIMUFEND – 0.6 mL Single-Dose Prefilled Syringe BLISTER PACK LABEL

Stimufend

(pegfilgrastim-fpgk)

Injection

6 mg/0.6 mL

Pegylated Recombinant Methionyl Human Granulocyte Colony-Stimulating Factor (PEG-rmethHuG-

CSF) derived from E Coli

For Subcutaneous Use Only

Inactive ingredients: acetate (0.35 mg), polysorbate 20

(0.02 mg), sodium (0.02 mg), sorbitol (30 mg) in Water

for Injection, USP.

Aisling®

1 single-dose pre-filled syringe

Store refrigerated between 36°F to 46°F (2°C to 8°C).

Do not freeze or shake.

Protect from light.

This product contains dry natural rubber.

Sterile Solution-No Preservative

815018A

NDC 72603-402-01

Manufactured by:

Fresenius Kabi USA, LLC

Lake Zurich, Illinois 60047

U.S. License No. 2146

Product of Italy

Manufactured for:

Northstar Rx LLC,

Memphis, TN 38141

PACKAGE LABEL – PRINCIPAL DISPLAY – STIMUFEND – 0.6 mL Single-Dose Prefilled SYRINGE LABEL

Stimufend

(pegfilgrastim-fpgk)

Injection

6 mg/0.6 mL

Manufactured by:

Fresenius Kabi USA, LLC

Lake Zurich, Illinois 60047

U.S. License No. 2146

Manufactured for:

Northstar Rx LLC,

Memphis, TN 38141

404197A

Stimufend®

(pegfilgrastim-fpgk)
Injection

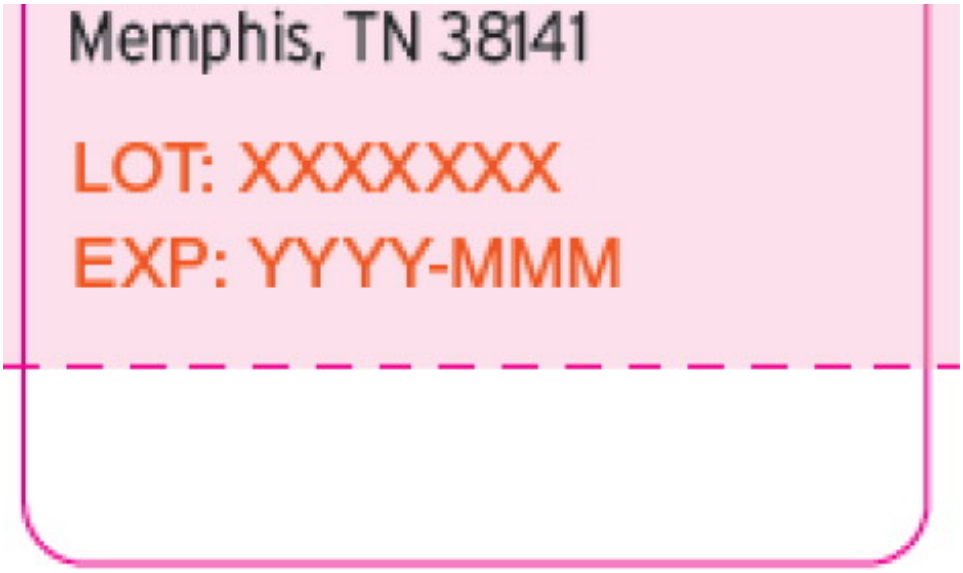
6 mg/0.6 mL

(01)00372603402018

4041197A

Manufactured by:
Fresenius Kabi USA, LLC
Lake Zurich, Illinois 60047
U.S. License No. 2146

Manufactured for:
Northstar Rx LLC,



STIMUFEND

pegflilgrastim-fpgk injection, solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:72603-402
Route of Administration	SUBCUTANEOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
PEGFILGRASTIM (UNII: 3A58010674) (PEGFILGRASTIM - UNII:3A58010674)	PEGFILGRASTIM	6 mg in 0.6 mL

Inactive Ingredients	
Ingredient Name	**Strength**
ACETATE ION (UNII: 569DQM74SC)	
POLYSORBATE 20 (UNII: 7T1F30V5YH)	
SODIUM (UNII: 9NEZ333N27)	
SORBITOL (UNII: 506T60A25R)	
WATER (UNII: 059QF0KO0R)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:72603-402-01	1 in 1 CARTON	12/29/2025	
1		1 in 1 BLISTER PACK		
1		0.6 mL in 1 SYRINGE; Type 3: Prefilled Biologic Delivery Device/System (syringe, patch, etc.)		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA761173	12/29/2025	

Labeler - NORTHSTAR RX LLC (830546433)

Establishment

Name	Address	ID/FEI	Business Operations
Merck Biodevelopment, Martillac		260400248	ANALYSIS(72603-402) , API MANUFACTURE(72603-402)

Establishment

Name	Address	ID/FEI	Business Operations
FUJIFILM Diosynth Biotechnologies UK Ltd.		778997119	ANALYSIS(72603-402) , API MANUFACTURE(72603-402)

Establishment

Name	Address	ID/FEI	Business Operations
Merck Serono S.p.A (MS-Bari)		437803088	MANUFACTURE(72603-402)

Establishment

Name	Address	ID/FEI	Business Operations
Merck Serono S.p.A (MS-Guidonia)		339654002	ANALYSIS(72603-402)

Establishment

Name	Address	ID/FEI	Business Operations
Istituto di Ricerche Biomediche Antoine marxer RBM S.P.A		436298533	ANALYSIS(72603-402)

Establishment

Name	Address	ID/FEI	Business Operations
Fresenius Kabi USA, LLC		964475045	ANALYSIS(72603-402) , MANUFACTURE(72603-402)

Establishment

Name	Address	ID/FEI	Business Operations
Fresenius Kabi Austria GmbH		300206604	PACK(72603-402)