Stimufend®
pegfilgrastim-fpgk

PRODUCT MONOGRAPH FOR STIMUFEND

An FDA-approved biosimilar to Neulasta® (pegfilgrastim)

INDICATION

STIMUFEND® (pegfilgrastim-fpgk) 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.

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

IMPORTANT SAFETY INFORMATION

Contraindication

- STIMUFEND is contraindicated in patients with a history of serious allergic reactions to pegfilgrastim products or filgrastim products
- Reactions have included anaphylaxis

Please see Important Safety Information on pages 28 and 29 and full Prescribing Information.

FDA, US Food and Drug Administration.

FRESENIUS KABI
caring for life

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Please see Important Safety Information on pages 28 and 29 and full Prescribing Information.

STIMUFEND® (pegfilgrastim-fpgk), made by Fresenius Kabi, is an FDA-approved biosimilar to Neulasta® (pegfilgrastim)*

- The totality of evidence demonstrates that STIMUFEND is highly similar to Neulasta and supports biosimilarity and the use of STIMUFEND to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies who are receiving myelosuppressive anti-cancer drugs[1,2]
- STIMUFEND is not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation[1]
- The dose, strength, formulation, and route of administration for the STIMUFEND pre-filled syringe are the same as those of Neulasta[1,2]
- STIMUFEND is highly similar to Neulasta, with no structural or functional clinically meaningful differences[3,4]
  - STIMUFEND demonstrated PK/PD equivalence to Neulasta in healthy subjects[3]
  - STIMUFEND immunogenicity—in terms of treatment-induced ADA positive rates—was non-inferior to Neulasta in healthy subjects[4]
  - STIMUFEND showed safety and tolerability comparable to Neulasta in healthy subjects[3,4]
- STIMUFEND is backed by Fresenius Kabi's strong record of manufacturing reliability and award-winning supply and support services

Fresenius Kabi offers ongoing support to patients prescribed STIMUFEND, including copay assistance and help with out-of-pocket costs. See page 24 for details

Important Safety Information (cont'd)

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

ADA, antidrug antibody; PD, pharmacodynamics; PK, pharmacokinetics.

*A biosimilar is a biological medicine that is highly similar to another biological medicine already approved, known as a reference product. The FDA requires that there are no clinically meaningful differences in terms of efficacy, safety, or exposure between a biosimilar and the reference product.[4]

Please see Important Safety Information on pages 28 and 29 and full Prescribing Information.

Stimufend® pegfilgrastim-fpgk

Febrile neutropenia poses complex clinical and economic challenges

Neutropenia can result in a reduced dose, delay, or discontinuation of chemotherapy[5]

Every year in the United States, it is estimated that more than 60,000 patients with cancer are hospitalized for neutropenia[6]

- Patients undergoing chemotherapy who develop febrile neutropenia face significant medical costs[5]
- **$24,700** is the mean cost of hospitalization stay for adults (with an average length of stay of 9.6 days)[6]
- **~1 in 14 patients*** will die from febrile neutropenia[6]

Treating life-threatening, chemotherapy-induced neutropenia increases the clinical burden on both healthcare professionals and patients[5]

Important Safety Information (cont'd)

Acute Respiratory Distress Syndrome (ARDS)

- ARDS can occur in patients receiving pegfilgrastim products
- Evaluate patients who develop fever and lung infiltrates or respiratory distress after receiving STIMUFEND® (pegfilgrastim-fpgk)
- Discontinue STIMUFEND in patients with ARDS

*Patients hospitalized for febrile neutropenia.

Please see Important Safety Information on pages 28 and 29 and full Prescribing Information.

Use of a long-acting G-CSF biosimilar may offset the increased costs of hospitalization[7-9]

The introduction of more long-acting G-CSF biosimilars may drive down treatment costs, thereby increasing availability and access for patients[7-11]

- Congressional Budget Office estimates show the sales-weighted market average discount on biosimilars is **20% to 25%** relative to reference products[11]
- Cost savings from converting to biosimilar pegfilgrastim could be as high as **$1487 per patient** (at a 35% discount) per chemotherapy cycle[12]

Primary prophylaxis with a G-CSF can reduce the incidence of febrile neutropenia[7,13]

Patients with cancer who received primary prophylaxis with a G-CSF were less likely to develop infection as manifested by febrile neutropenia[13]

Biosimilars may offer affordable therapies to a large number of patients and encourage innovation in healthcare[14]

- As highly similar versions of biologic drugs already approved, biosimilars may make state-of-the-art therapies affordable and accessible to an increasing number of patients

G-CSF, granulocyte colony-stimulating factor.

Please see Important Safety Information on pages 28 and 29 and full Prescribing Information.

Stimufend® pegfilgrastim-fpgk

Guideline recommendations for prophylaxis with a G-CSF

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommend prophylaxis with G-CSF when a chemotherapy regimen carries a high risk (>20%) of febrile neutropenia.[15,16] The most recent updates of the American Society of Clinical Oncology (ASCO) and European Organization for Research and Treatment of Cancer (EORTC) guidelines have also adopted the 20% threshold for considering routine prophylactic myeloid growth factor support.[15]

For patients receiving a chemotherapy regimen that carries an intermediate risk (10%–20%) of developing febrile neutropenia, the NCCN Guidelines® recommend individualized consideration of prophylactic G-CSF use based on the presence of patient-specific risk factors. Patients with one or more risk factors should be considered for prophylactic G-CSF, while patients with no risk factors should be observed.[15]

> ***"An FDA-approved biosimilar is an appropriate substitute for filgrastim and pegfilgrastim."***
>
> — NCCN Guidelines®

National Comprehensive Cancer Network® (NCCN®) makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

The American Society of Clinical Oncology recommends primary prophylaxis with G-CSF in patients with a ≥20% risk of FN, based on patient-, disease-, and treatment-related factors.[17]

Please see Important Safety Information on pages 28 and 29 and full Prescribing Information.

Select chemotherapy agents in regimens associated with a high risk (>20%) for febrile neutropenia[15,18]:

• Paclitaxel	• Cisplatin	• Oxaliplatin
• Docetaxel	• Etoposide	• Irinotecan
• Gemcitabine	• Fluorouracil	
• Doxorubicin	• Leucovorin	

Important Safety Information (cont'd)

Serious Allergic Reactions

- Serious allergic reactions, including anaphylaxis, can occur in patients receiving pegfilgrastim products
- The majority of reported events occurred upon initial exposure and can recur within days after the discontinuation of initial anti-allergic treatment
- Permanently discontinue STIMUFEND® (pegfilgrastim-fpgk) in patients with serious allergic reactions

Please see Important Safety Information on pages 28 and 29 and full Prescribing Information.

Stimufend® pegfilgrastim-fpgk

3.1: Indications

STIMUFEND® (pegfilgrastim-fpgk) is approved for the following indication of Neulasta® (pegfilgrastim)[1]

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

3.2: Dosing and administration

The dose, strength, and administration for the STIMUFEND pre-filled syringe are the same as those of Neulasta[1]

- The recommended dosage of STIMUFEND is a single subcutaneous injection of 6 mg administered once per chemotherapy cycle
- Do not administer STIMUFEND between 14 days before and 24 hours after administration of cytotoxic chemotherapy

Important Safety Information (cont'd)

Use in Patients with Sickle Cell Disorders

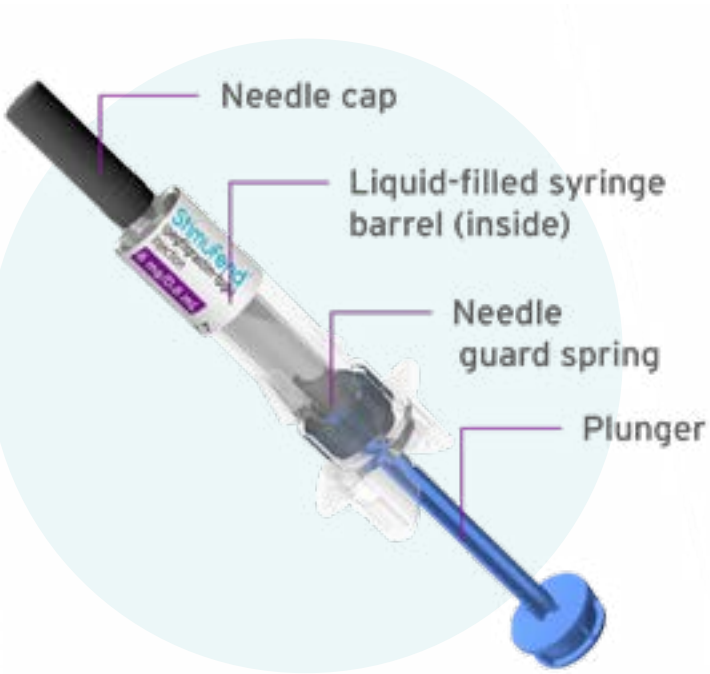
- In patients with sickle cell trait or disease, severe and sometimes fatal sickle cell crises can occur in patients receiving pegfilgrastim products
- Discontinue STIMUFEND if sickle cell crisis occurs

Please see Important Safety Information on pages 28 and 29 and full Prescribing Information.

3.2: Dosing and administration (cont'd)

The STIMUFEND® (pegfilgrastim-fpgk) pre-filled syringe is a fully passive safety device with automatic activation, designed for both home and clinical use

- STIMUFEND is administered subcutaneously via a single-dose pre-filled syringe for manual use*†
  - Prior to use, remove the carton from the refrigerator and allow the STIMUFEND pre-filled syringe to reach room temperature for a minimum of 30 minutes
  - Discard any pre-filled syringe left at room temperature (68 °F to 77 °F [20 °C to 25 °C]) for more than 72 hours



3.3: Dosage forms and strengths

Injection: 6 mg/0.6 mL clear, colorless, preservative-free solution in a single-dose pre-filled syringe.

3.4: Storage

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

*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 handle the needle cap of the syringe.

Please see Important Safety Information on pages 28 and 29 and full Prescribing Information.

Stimufend® pegfilgrastim-fpgk

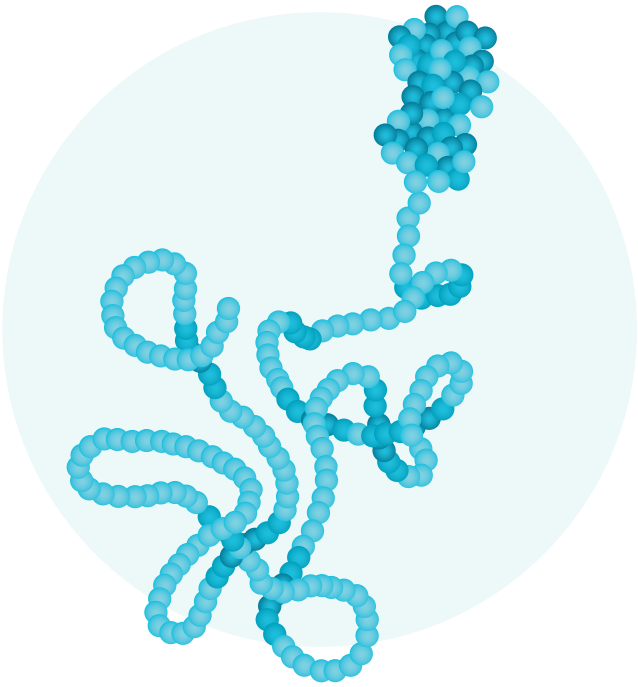
The product profile for STIMUFEND® (pegfilgrastim-fpgk) is similar to that of Neulasta® (pegfilgrastim)[1,2]

		Neulasta	STIMUFEND
Indications & usage	• Decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs	✓	✓
	• Hematopoietic subsyndrome of acute radiation syndrome	✓	
Dosage & administration	• 6 mg/0.6 mL subcutaneous injection • 6 mg administered once per chemotherapy cycle for patients with cancer receiving myelosuppressive chemotherapy	✓	✓
Dosage forms & strengths	• Pre-filled syringe 6 mg/0.6 mL	✓	✓
	• On-body injector 6 mg/0.6 mL	✓	
Needle guard	• Manual needle guard	✓	
	• Passive needle guard		✓
Needle gauge	• 27-gauge needle	✓	✓
Needle cap	• Presence of latex	✓	✓
Storage conditions	• 48-hour storage at room temperature	✓	
	• 72-hour storage at room temperature		✓
	• 36-month shelf life	✓	✓

Please see Important Safety Information on pages 28 and 29 and full Prescribing Information.

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.[1]



Important Safety Information (cont'd)

Glomerulonephritis

- Has occurred in patients receiving pegfilgrastim products
- Diagnoses based on azotemia, hematuria, proteinuria, and renal biopsy
- Generally, events resolved after dose-reduction or discontinuation of pegfilgrastim products
- If suspected, evaluate for cause and if cause is likely, consider dose-reduction or interruption of STIMUFEND® (pegfilgrastim-fpgk)

Please see Important Safety Information on pages 28 and 29 and full Prescribing Information.

Stimufend® pegfilgrastim-fpgk

Biosimilars are highly similar to an approved biological reference product[19]

There must be no clinically meaningful differences in safety, purity, and potency

*If required by the FDA.

- Reference products must prove a new molecule has significant clinical benefit
- Biosimilars must demonstrate the molecule is highly similar to the reference product
  - Re-establishment of efficacy is not required
- For biosimilars, analytics are the cornerstone of biosimilar development, providing the greatest sensitivity for detecting differences between the biosimilar and the reference product

STIMUFEND® (pegfilgrastim-fpgk) has proven structural, functional, and clinical similarity to Neulasta® (pegfilgrastim)[3,4]

Important Safety Information (cont'd)

Leukocytosis

- Increased white blood cell counts of 100 x 10^9/L have been observed
- Monitoring of complete blood count (CBC) during STIMUFEND therapy is recommended

Please see Important Safety Information on pages 28 and 29 and full Prescribing Information.

STIMUFEND® (pegfilgrastim-fpgk) is FDA-approved based on the totality of evidence supporting its biosimilarity to Neulasta® (pegfilgrastim)

Additional clinical studies
Not required by the FDA

Clinical pharmacology

- PK/PD trial confirmed bioequivalence to Neulasta; also demonstrated comparable safety, tolerability, and immunogenicity profiles[3]
- Immunogenicity trial: STIMUFEND was non-inferior to Neulasta for the rate of confirmed treatment-induced ADA-positivity; also demonstrated comparable safety and tolerability[4]

Animal studies
Not required by the FDA

Analytical studies[25]
An extensive range of state-of-the-art methods showed analytical similarity between STIMUFEND and Neulasta

- Similar or identical physicochemical properties included protein structure, primary, secondary, and tertiary structures, post-translational modifications, purity levels, G-CSF receptor binding, and potency

Based on the analytical, PK/PD, safety, and immunogenicity studies, the FDA determined that there was a high degree of biosimilarity between STIMUFEND and Neulasta. Animal studies and additional clinical studies were not required by the FDA

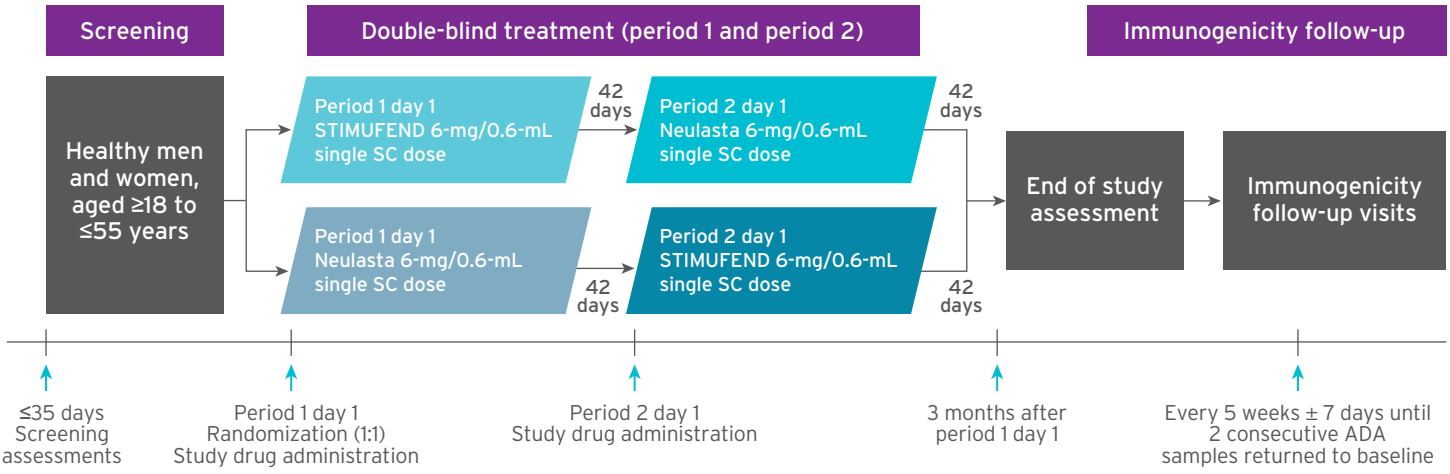
Please see Important Safety Information on pages 28 and 29 and full Prescribing Information.

Stimufend® pegfilgrastim-fpgk

Double-blind, 2-treatment, crossover study to assess PK/PD in healthy volunteers[3]

STIMUFEND® (pegfilgrastim-fpgk) was assessed in healthy subjects in a double-blind, randomized, 2-sequence, 2-period, 2-treatment, crossover Phase I study (NCT03251248).

Study design



- Primary objective: PK/PD bioequivalence of STIMUFEND to Neulasta® (pegfilgrastim)
  - Primary PK endpoints were AUC from time zero to the last sampling time, AUC from time zero extrapolated to infinity, and C_{max}
  - Primary PD endpoints were E_{max} and AUC from time zero (pre-dose) to time to last quantifiable concentration for ANC
- Secondary objectives: Safety, tolerability, and immunogenicity of STIMUFEND to Neulasta

Healthy subjects are the most homogenous population for a sensitive assessment of PK similarity, thereby avoiding potential confounding factors, including underlying and/or concomitant disease, being heavily medicated, and/or being treated with myelosuppressive agents[19,20]

Please see Important Safety Information on pages 28 and 29 and full Prescribing Information.

PK/PD parameters confirmed bioequivalence to Neulasta® (pegfilgrastim)[3]

For all primary PK/PD parameters, the 90% repeated confidence intervals of the geometric means ratio of STIMUFEND® (pegfilgrastim-fpgk) to Neulasta were entirely within the predefined equivalence range (80%-125%), confirming bioequivalence.

Primary PK/PD evaluation

Parameter	Treatment	n	Geometric LS mean	Ratio of geometric LS mean	90% repeated CI of ratio
PK					
$AUC_{0-\infty}$ (ng•h/mL) (N=240)	STIMUFEND	239	6130	104.39	96.59-112.82
	Neulasta	238	5880		
AUC_{0-last} (ng•h/mL) (N=239)	STIMUFEND	236	6180	105.29	97.29-113.96
	Neulasta	235	5870		
C_{max} (ng/mL) (N=240)	STIMUFEND	240	158	105.69	97.13-114.99
	Neulasta	240	149		
PD					
E_{max} (10^9/L) (N=240)	STIMUFEND	240	36.76	100.55	98.74-102.39
	Neulasta	240	36.56		
$AUEC_{0-t}$ (10^9/L) (N=239)	STIMUFEND	233	5550	98.75	97.30-100.23
	Neulasta	233	5620		

Important Safety Information (cont'd)

Thrombocytopenia

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

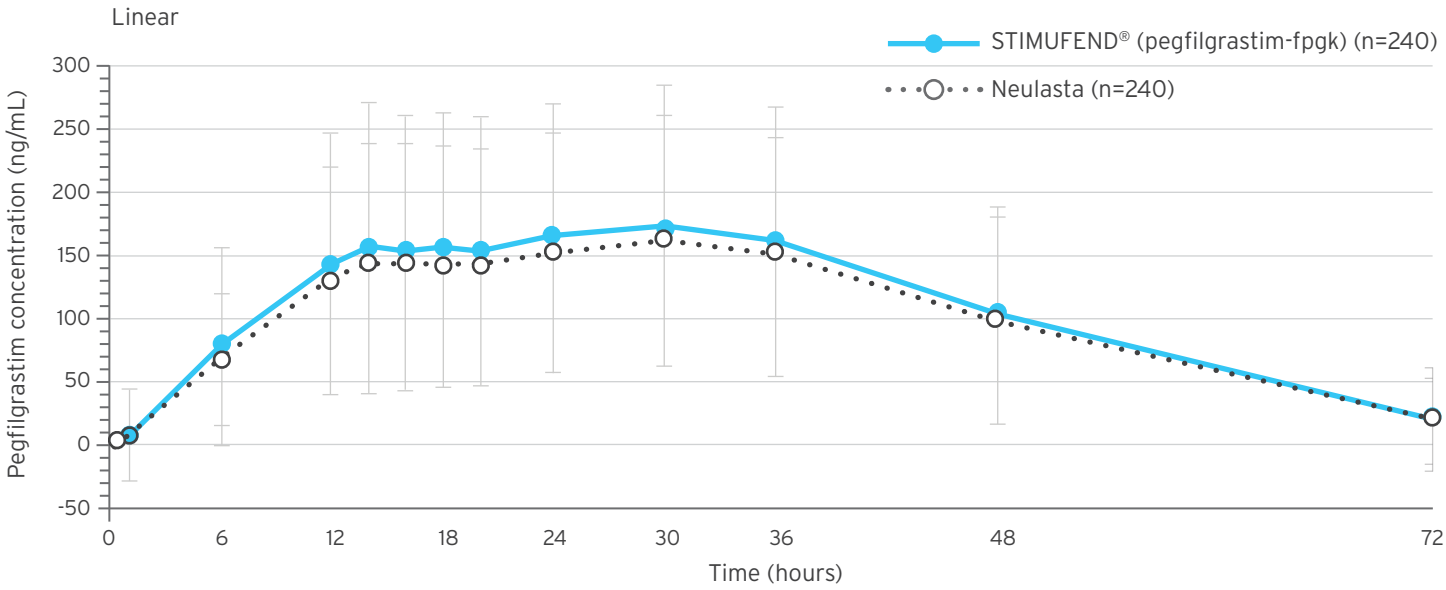
ANC, absolute neutrophil count; AUC, area under the curve; AUEC, area under the effect curve; CI, confidence interval; C_{max}, maximum concentration; E_{max}, maximum observed effect; LS, least squares; SC, subcutaneous.

Please see Important Safety Information on pages 28 and 29 and full Prescribing Information.

Stimufend® pegfilgrastim-fpgk

PK/PD parameters confirmed bioequivalence to Neulasta® (pegfilgrastim)[3] (cont'd)

PK parameters confirmed bioequivalence from post-dose



Arithmetic mean (SD) serum concentration—time profiles after a single dose of pegfilgrastim in healthy subjects

Important Safety Information (cont'd)

Capillary Leak Syndrome (CLS)

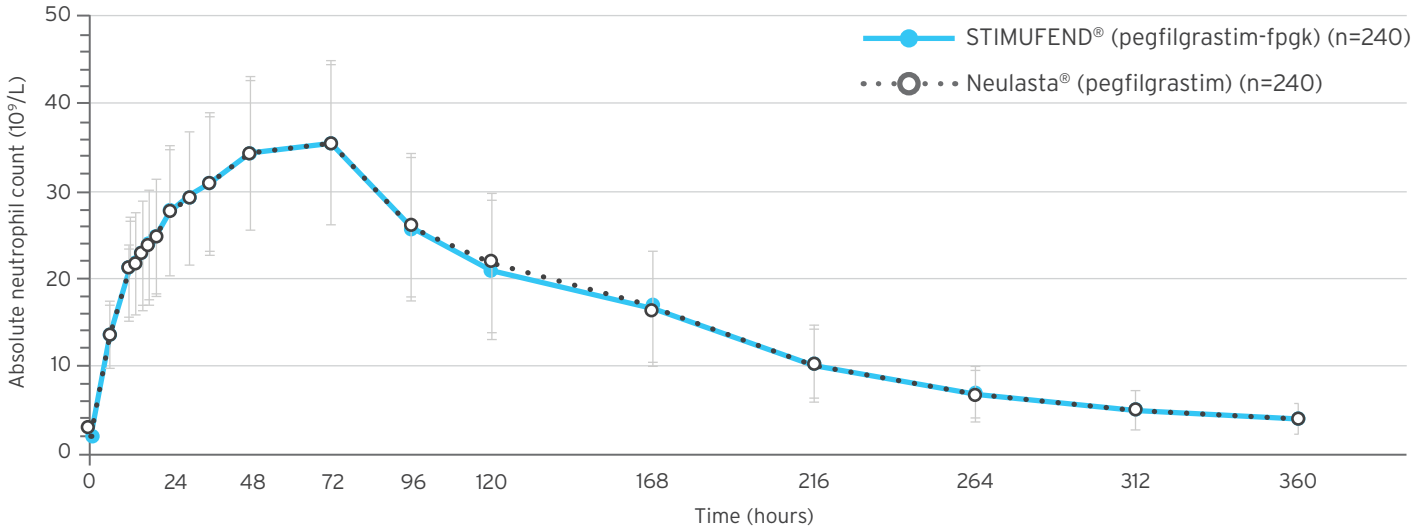
- CLS has been reported after G-CSF administration, including pegfilgrastim products
- Characterized by hypotension, hypoalbuminemia, edema and hemoconcentration
- Episodes vary in frequency, severity and may be life-threatening if treatment is delayed
- Patients with symptoms should be closely monitored and receive standard symptomatic treatment, which may include a need for intensive care

Potential for Tumor Growth Stimulatory Effects on Malignant Cells

- G-CSF receptor 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

Please see Important Safety Information on pages 28 and 29 and full Prescribing Information.

PD parameters confirmed bioequivalence over 16 days post-dose



Arithmetic mean (SD) observed ANC-time profiles after a single dose of pegfilgrastim in healthy subjects

PK/PD are the most sensitive clinical study/assay in which to assess for differences, should they exist[21]

SD, standard deviation.

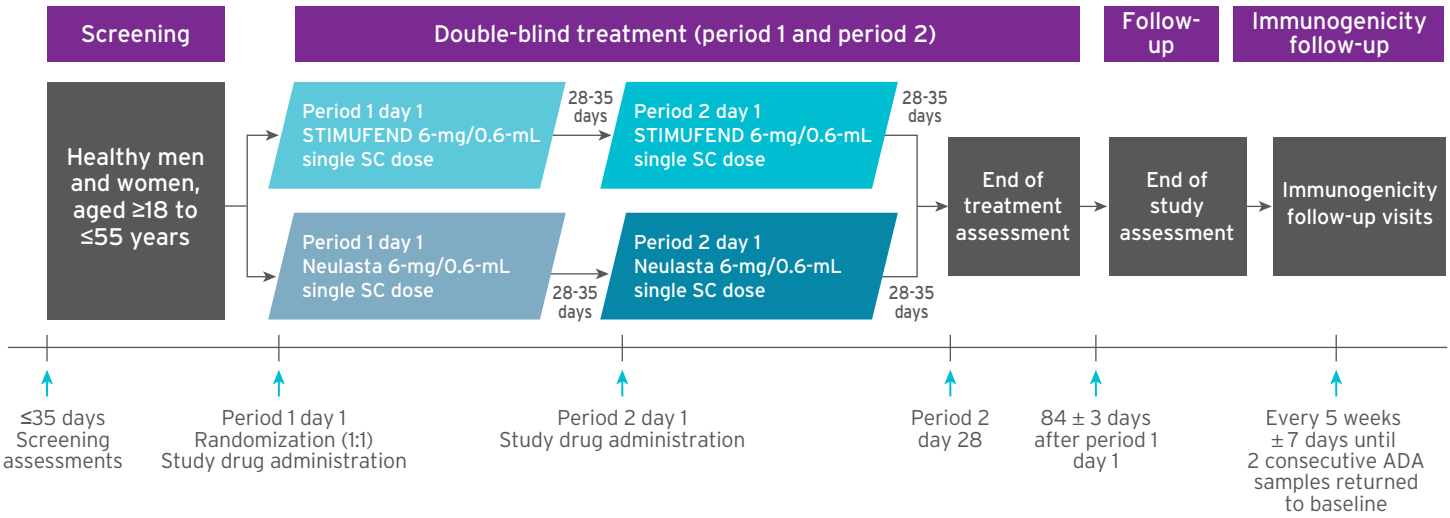
Please see Important Safety Information on pages 28 and 29 and full Prescribing Information.

Stimufend® pegfilgrastim-fpgk

Double-blind, randomized, parallel-group study to assess immunogenicity in healthy volunteers[4]

The immunogenicity and safety profiles of STIMUFEND® (pegfilgrastim-fpgk) were demonstrated in healthy subjects in a double-blind, randomized, parallel-group, Phase I study (NCT03251339).

Study design



- Primary objective: Immunogenicity of STIMUFEND and Neulasta® (pegfilgrastim)
  - Primary endpoints were confirmed treatment-induced ADA-positive status and confirmed NAb status to pegfilgrastim, from pre-dose until the end of study assessment
- Secondary objectives: Safety and tolerability of STIMUFEND and Neulasta

Healthy subjects are the most homogenous population for a sensitive assessment of immunogenicity, and their immune system is unaffected by chemotherapy[19,20]

Important Safety Information (cont'd)

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

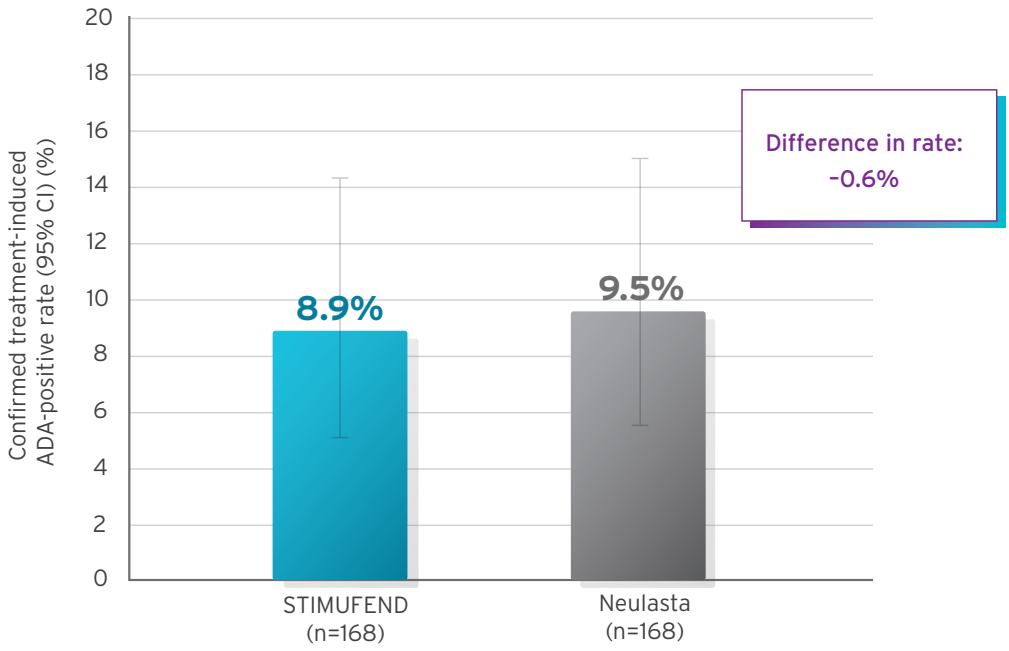
- MDS and AML have been associated with the use of pegfilgrastim products in conjunction with chemotherapy and/or radiotherapy in patients with breast and lung cancer. Monitor patients for signs and symptoms of MDS/AML in these settings

Please see Important Safety Information on pages 28 and 29 and full Prescribing Information.

Immunogenicity similar to that of Neulasta® (pegfilgrastim)[4]

STIMUFEND® (pegfilgrastim-fpgk) demonstrated noninferiority to Neulasta, with confirmed immunogenicity rates of 8.9% and 9.5%, respectively.

Immunogenicity with confirmed treatment-induced ADA-positive rates after first dose of 2 single doses



In this study, noninferiority of STIMUFEND to Neulasta was demonstrated by the rate of confirmed treatment-induced ADA-positive status

There were no differences between treatment groups in ADA characteristics (onset, titer, and specificity). No filgrastim-specific neutralizing antibodies were detected in either treatment group

NAb, neutralizing antibody.

Please see Important Safety Information on pages 28 and 29 and full Prescribing Information.

Stimufend® pegfilgrastim-fpgk

Safety and tolerability were comparable between STIMUFEND® (pegfilgrastim-fpgk) and Neulasta® (pegfilgrastim)

Phase 1 PK/PD trial safety[3]

	STIMUFEND (n=270) n (%)	Neulasta (n=266) n (%)
Any TEAE	252 (93.3)	258 (97.0)
Any study drug-related TEAE	249 (92.2)	249 (93.6)
Any serious TEAE	1 (0.4)	2 (0.8)
Any study drug-related serious AE	0	1 (0.4)*
Any grade 3 or higher† TEAE	27 (10.0)	25 (9.4)
Any study drug-related grade 3 or higher† TEAE	26 (9.6)	24 (9.0)
Death	0	0
Any TEAE leading to discontinuation of study drug	8 (3.0)	6 (2.3)

- Adverse events with STIMUFEND were consistent with the administration of Neulasta
- TEAEs were generally mild to moderate in severity and were self-limiting
- Clinically significant splenomegaly‡ (Grade 1 or 2): STIMUFEND (n=3); all resolved spontaneously with no further study drug administered

Please see full Prescribing Information.

*Pericarditis.
†National Cancer Institute–Common Terminology Criteria for Adverse Events grade, Version 4.03.
‡Rare cases of splenic rupture have been reported following administration of filgrastim or pegfilgrastim; therefore, the spleen was monitored throughout the study.[3]

Please see Important Safety Information on pages 28 and 29 and full Prescribing Information.

	STIMUFEND® (pegfilgrastim-fpgk) (n=270) n (%)	Neulasta (n=266) n (%)
Most common TEAEs (>5% of subjects)		
Headache	151 (55.9)	150 (56.4)
Musculoskeletal pain	133 (49.3)	114 (42.9)
Bone pain	67 (24.8)	70 (26.3)
Back pain	45 (16.7)	55 (20.7)
Upper respiratory tract infection	32 (11.9)	20 (7.5)
Nausea	30 (11.1)	31 (11.7)
Injection-site pain	28 (10.4)	25 (9.4)
Myalgia	27 (10.0)	23 (8.6)
Neutropenia	24 (8.9)	22 (8.3)
Abdominal pain	23 (8.5)	21 (7.9)
Palpitations	23 (8.5)	14 (5.3)
Injection-site bruising	17 (6.3)	18 (6.8)
Abdominal pain upper	13 (4.8)	19 (7.1)
Leukocytosis	13 (4.8)	149 (5.3)

Important Safety Information (cont'd)

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

TEAE, treatment-emergent adverse event.

Please see Important Safety Information on pages 28 and 29 and full Prescribing Information.

Stimufend® pegfilgrastim-fpgk

Safety and tolerability were comparable between STIMUFEND® (pegfilgrastim-fpgk) and Neulasta® (pegfilgrastim)

Phase 1 immunogenicity trial safety[4]

	STIMUFEND (n=168) n (%)	Neulasta (n=168) n (%)
Any TEAE	167 (99.4)	167 (99.4)
Any study drug-related TEAE	166 (98.8)	158 (94.0)
Any serious TEAE	1 (0.6)	2 (1.2)
Any study drug-related serious AE	1 (0.6)*	1 (0.6)†
Any grade 3 or higher‡ TEAE	1 (0.6)	2 (1.2)
Any study drug-related grade 3‡ or higher TEAE	0	0
Death	0	0
Any TEAE leading to discontinuation of study drug	25 (14.9)	25 (14.9)
AE of special interest	25 (14.9)	30 (17.9)
Splenomegaly	2 (1.2)	0
Drug hypersensitivity	0	2 (1.2)
White blood cells increased§	23 (13.7)	27 (16.1)
Drug eruption	0	1 (0.6)

*Acute febrile neutrophilic dermatosis.
†Spontaneous abortion in partner.
‡National Cancer Institute–Common Terminology Criteria for Adverse Events grade, Version 4.03.
§All events considered related to study drug.

Please see Important Safety Information on pages 28 and 29 and full Prescribing Information.

	STIMUFEND® (pegfilgrastim-fpgk) (n=168) n (%)	Neulasta (n=168) n (%)
Most common TEAEs (>5% of subjects)		
Headache	105 (62.5)	120 (71.4)
Bone pain	113 (67.3)	101 (60.1)
Spinal pain	67 (39.9)	68 (40.5)
Upper respiratory tract infection	32 (19.0)	20 (11.9)
Nausea	32 (19.0)	19 (11.3)
White blood cell count increased[§]	23 (13.7)	27 (16.1)
Myalgia	19 (11.3)	17 (10.1)
Vomiting	18 (10.7)	9 (5.4)
Musculoskeletal chest pain	12 (7.1)	17 (10.1)
Abdominal pain	9 (5.4)	15 (8.9)
Diarrhea	8 (4.8)	15 (8.9)
Oropharyngeal pain	12 (7.1)	14 (8.3)
Injection-site bruising	12 (7.1)	10 (6.0)
Arthralgia	11 (6.5)	11 (6.5)
Dizziness	11 (6.5)	11 (6.5)
Contusion	11 (6.5)	7 (4.2)
Fatigue	7 (4.2)	11 (6.5)
Back pain	8 (4.8)	9 (5.4)

- TEAEs were generally mild to moderate in severity and were self-limiting, and resolved without sequelae
- Splenomegaly[‖] (Grades 1 and 2, respectively): STIMUFEND (n=2); resolved spontaneously and the subjects completed the study

Important Safety Information (cont'd)

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

TEAE, treatment-emergent adverse event.

[‖]Rare cases of splenic rupture have been reported following administration of filgrastim or pegfilgrastim; therefore, the spleen was monitored throughout the study.[4]

Please see Important Safety Information on pages 28 and 29 and full Prescribing Information.

Stimufend® pegfilgrastim-fpgk

Fresenius Kabi provides comprehensive patient support

We are dedicated to providing your patients with ongoing support to help them access Fresenius Kabi medications as prescribed.

KabiCare Program

- ✓ Centralized portal with real-time status from patient enrollment to product fulfillment*
- ✓ Dedicated support to address access challenges, including benefits investigation/verification, prior authorization, and appeals
- ✓ Financial support, including copay assistance with out-of-pocket costs as little as $0 for commercially insured patients prescribed STIMUFEND® (pegfilgrastim-fpgk)†
- ✓ Bridge to Therapy program to avoid treatment delay (eligibility criteria apply†)
- › To enroll patients online, visit CoverMyMeds.com. To download the KabiCare enrollment form, visit KabiCare.us.

Additional patient support available throughout their treatment journey

- Educational resources designed for patients about disease, medication, and health and well-being
- Identifying potential treatment-related transportation and lodging benefits with patient's insurance or provide list of independent foundations‡
- Nurse educators available to answer medication-related questions Monday-Friday, 8AM-8PM ET (excluding holidays) for patients and caregivers§

Contact your STIMUFEND Key Account Manager to connect with a Field Reimbursement Manager, who is available to share the latest updates in payer coverage and to help providers secure access and coverage for patients. They can assist with billing and coding, reimbursement, and KabiCare patient support offerings

Please see Important Safety Information on pages 28 and 29 and full Prescribing Information.

KabiCare provides additional support programs to eligible patients†

Commercial or private insurance

Patients with commercial or private insurance may be eligible† for the commercial copay support program that lowers out-of-pocket costs to as little as $0/month for STIMUFEND® (pegfilgrastim-fpgk) with annual maximum.

Government insurance (Medicare/Medicaid)

Patients with government insurance that does not cover STIMUFEND may be eligible for assistance through the Patient Assistance Program (PAP) or through independent nonprofit patient assistance programs that may be able to help afford STIMUFEND copay costs‡

Uninsured/Underinsured‖

Patients who do not have insurance and/or cannot afford STIMUFEND may be eligible for additional assistance through the Patient Assistance Program (PAP). Talk to your patients about the cost savings of a biosimilar, including STIMUFEND

KabiCare
Patient support from Fresenius Kabi

To connect with a Patient Support Guide for assistance, call **1-833-KABICARE (1-833-522-4227)**.

To learn more, please visit **KabiCare.us** or call **1-833-KABICARE (1-833-522-4227)**

Important Safety Information (cont'd)

Most common adverse reactions

- Bone pain
- Pain in extremity

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

*In case of medical benefit; otherwise, real-time status available up to prescription transfer to dispensing pharmacy.
†Eligibility criteria apply. Patients are not eligible for commercial copay assistance or Bridge to Therapy program support if the prescription is eligible to be reimbursed, in whole or in part, by any state or federal healthcare program.
‡Eligibility for resources provided by independent nonprofit patient assistance programs is based on the nonprofits' criteria. Fresenius Kabi has no control over these programs.
§Nurse support provided by KabiCare is not meant to replace discussions with a healthcare provider regarding a patient's care and treatment.
‖Underinsured means that your patient's health insurance plan does not cover STIMUFEND.

Please see Important Safety Information on pages 28 and 29 and full Prescribing Information.

Stimufend® pegfilgrastim-fpgk

Fresenius Kabi has a strong track record of manufacturing reliability, award-winning supply, and support offerings

We support the needs of all decision-makers

We are committed to addressing the needs of the oncology community with[22]:

- Over **25 years of experience** supplying oncology medications in the United States
- One of the largest injectable oncology portfolios in the industry, with **82% of products** filled and finished in the United States
- Over **30 products** used in more than 460 different chemotherapy regimens
- Over **220 chemotherapy regimens** that can be supported entirely by Fresenius Kabi

Winner of the FDA Drug Shortage Assistance Award

Fresenius Kabi strives to make STIMUFEND® (pegfilgrastim-fpgk) consistently available

With **90 centers of science, manufacturing, and research and development** around the globe, Fresenius Kabi can leverage a first-class supply chain to increase access to essential medicines and medical devices for patients. We are continuing to invest almost 1 billion dollars over the next few years in new US plants, to double production capacity, and in supply chain expansion, to build in supply chain redundancies. Our advanced manufacturing processes allow us to scale production to meet market needs.

We also partner closely with the FDA and other stakeholders, including other government agencies, pharmaceutical wholesalers, professional associations, and group purchasing organizations.

Fresenius Kabi has dedicated more than 100 years to increasing the availability and affordability of high-quality medicines

Stimufend® pegfilgrastim-fpgk

INDICATION

STIMUFEND® (pegfilgrastim-fpgk) 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.

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

IMPORTANT SAFETY INFORMATION

Contraindication

- STIMUFEND is contraindicated in patients with a history of serious allergic reactions to pegfilgrastim products or filgrastim products
- Reactions have included anaphylaxis

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

Acute Respiratory Distress Syndrome (ARDS)

- ARDS can occur in patients receiving pegfilgrastim products
- Evaluate patients who develop fever and lung infiltrates or respiratory distress after receiving STIMUFEND
- Discontinue STIMUFEND in patients with ARDS

Serious Allergic Reactions

- Serious allergic reactions, including anaphylaxis, can occur in patients receiving pegfilgrastim products
- The majority of reported events occurred upon initial exposure and can recur within days after the discontinuation of initial anti-allergic treatment
- Permanently discontinue STIMUFEND in patients with serious allergic reactions

Use in Patients with Sickle Cell Disorders

- In patients with sickle cell trait or disease, severe and sometimes fatal sickle cell crises can occur in patients receiving pegfilgrastim products
- Discontinue STIMUFEND if sickle cell crisis occurs

Glomerulonephritis

- Has occurred in patients receiving pegfilgrastim products
- Diagnoses based on azotemia, hematuria, proteinuria, and renal biopsy
- Generally, events resolved after dose-reduction or discontinuation of pegfilgrastim products
- If suspected, evaluate for cause and if cause is likely, consider dose-reduction or interruption of STIMUFEND

Please see Important Safety Information on pages 28 and 29 and full Prescribing Information.

Leukocytosis

- Increased white blood cell counts of 100 x 10^9/L have been observed
- Monitoring of complete blood count (CBC) during STIMUFEND® (pegfilgrastim-fpgk) therapy is recommended

Thrombocytopenia

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

Capillary Leak Syndrome (CLS)

- CLS has been reported after G-CSF administration, including pegfilgrastim products
- Characterized by hypotension, hypoalbuminemia, edema and hemoconcentration
- Episodes vary in frequency, severity and may be life-threatening if treatment is delayed
- Patients with symptoms should be closely monitored and receive standard symptomatic treatment, which may include a need for intensive care

Potential for Tumor Growth Stimulatory Effects on Malignant Cells

- G-CSF receptor 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

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

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

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

Most common adverse reactions

- Bone pain
- Pain in extremity

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

Please see Important Safety Information on pages 28 and 29 and full Prescribing Information.

Stimufend® pegfilgrastim-fpgk

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To learn more about STIMUFEND® (pegfilgrastim-fpgk), visit StimufendHCP.com. To learn about our patient support programs and resources, visit KabiCare.us.

Please see Important Safety Information on pages 28 and 29 and full Prescribing Information.

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