The first FDA-approved biosimilar to Neupogen® (filgrastim) available in both prefilled syringes and single-dose vials[1*†]

INJECTION
Nivestym®
filgrastim-aafi
Pfizer

NIVESTYM® (filgrastim-aafi)

Product Monograph

BUILDING ONTO THE CLINICAL EXPERIENCE OF FILGRASTIM

*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 and the reference product.

†NIVESTYM does not have a designation of interchangeability with Neupogen.

SELECTED SAFETY INFORMATION

CONTRAINDICATIONS

NIVESTYM® is contraindicated in patients with a history of serious allergic reactions to human granulocyte-colony stimulating factors (G-CSF), such as filgrastim products or pegfilgrastim products.

WARNINGS AND PRECAUTIONS

Splenic Rupture

Splenic rupture, including fatal cases, has been reported following the administration of filgrastim products. Evaluate patients who report left upper abdominal or shoulder pain for an enlarged spleen or splenic rupture.

(continued on next page)

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Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

Indications

NIVESTYM® (filgrastim-aafi) is FDA approved for all eligible indications of Neupogen® (filgrastim) in the following patient populations[1]

Patients with cancer receiving myelosuppressive chemotherapy

- NIVESTYM is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever

Patients with acute myeloid leukemia (AML) receiving induction or consolidation chemotherapy

- NIVESTYM is indicated for reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with AML

Patients with cancer undergoing bone marrow transplantation (BMT)

- NIVESTYM is indicated to reduce the duration of neutropenia and neutropenia-related clinical sequelae, eg, febrile neutropenia, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by BMT

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Acute Respiratory Distress Syndrome

Acute respiratory distress syndrome (ARDS) has been reported in patients receiving filgrastim products. Evaluate patients who develop fever and lung infiltrates or respiratory distress for ARDS. Discontinue NIVESTYM® in patients with ARDS.

(continued on next page)

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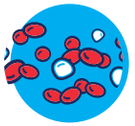
Indications

NIVESTYM® (filgrastim-aafi) is FDA approved for all eligible indications of Neupogen® (filgrastim) in the following patient populations[1]

Patients undergoing autologous peripheral blood progenitor cell (PBPC) collection and therapy

- NIVESTYM is indicated for the mobilization of autologous hematopoietic progenitor cells into the peripheral blood collection by leukapheresis



Patients with severe chronic neutropenia (SCN)

- NIVESTYM is indicated for chronic administration to reduce the incidence and duration of sequelae of severe neutropenia (eg, fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Serious Allergic Reactions

Serious allergic reactions, including anaphylaxis, have been reported in patients receiving filgrastim products. The majority of reported events occurred upon initial exposure. Provide symptomatic treatment for allergic reactions. Allergic reactions, including anaphylaxis, in patients receiving filgrastim products can recur within days after the discontinuation of initial anti-allergic treatment. Permanently discontinue NIVESTYM® in patients with serious allergic reactions. NIVESTYM® is contraindicated in patients with a history of serious allergic reactions to human G-CSF such as filgrastim or pegfilgrastim.

(continued on next page)

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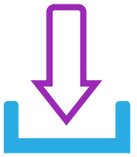
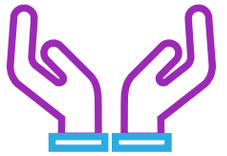
The first FDA-approved biosimilar to Neupogen® (filgrastim) available in both prefilled syringes and single-dose vials[1]

With the largest portfolio of oncology biosimilars—including NIVESTYM—Pfizer is committed to expanding options for patient care[2]

Favorable coverage[3]



Potential savings[3]



Support for you and your patients

Pfizer has over 30 years of biologic experience, and more than a decade in the global biosimilars market.[3,4]

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Sickle Cell Disorders

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

Glomerulonephritis

Glomerulonephritis has occurred in patients receiving filgrastim products. The diagnoses were based upon azotemia, hematuria (microscopic and macroscopic), proteinuria, and renal biopsy. Generally, events of glomerulonephritis resolved after dose reduction or discontinuation of filgrastim products. If glomerulonephritis is suspected, evaluate for cause. If causality is likely, consider dose-reduction or interruption of NIVESTYM®.

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NIVESTYM coverage

Learn about access in your area

Coverage for NIVESTYM varies by location. Your Pfizer Sales Representative can share plan-specific commercial and Medicare coverage rates in your region.

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Alveolar Hemorrhage and Hemoptysis

Alveolar hemorrhage manifesting as pulmonary infiltrates and hemoptysis requiring hospitalization has been reported in healthy donors treated with filgrastim products for peripheral blood progenitor cell (PBPC) mobilization. Hemoptysis resolved with discontinuation of filgrastim products. The use of NIVESTYM® for PBPC mobilization in healthy donors is not an approved indication.

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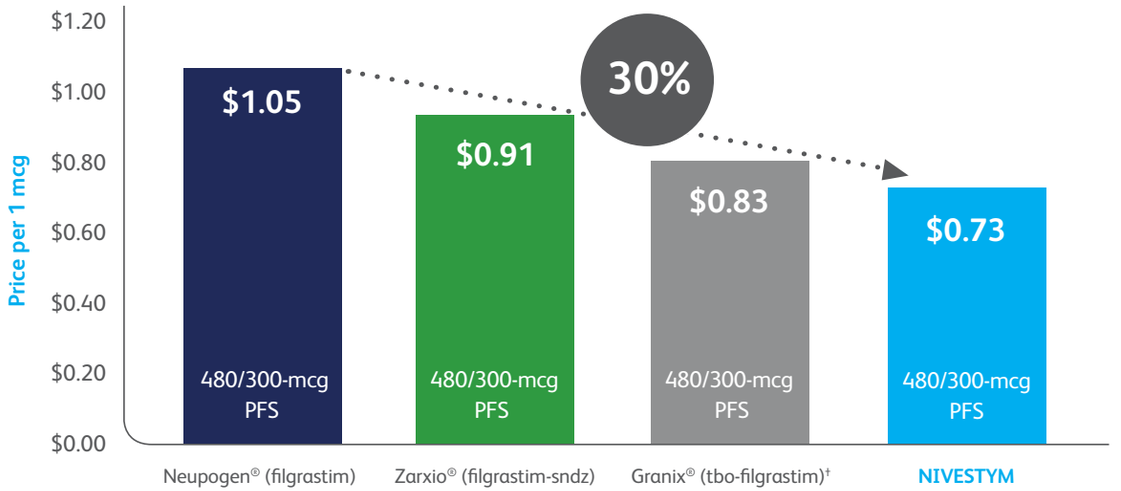
Potential cost savings with NIVESTYM

NIVESTYM offers the lowest WAC price of any short-acting G-CSF, regardless of packaging[3]*

WAC comparison



*The WAC price is not inclusive of rebates or other applicable discounts. There are no head-to-head studies between NIVESTYM, Zarxio, and Granix, and no clinical comparisons can be made between the products.

†Granix is approved for 1 indication.[5] Please refer to the full Prescribing Information for each product for full indication(s).

G-CSF=granulocyte-colony stimulating factor; PFS=prefilled syringe; WAC=wholesale acquisition cost.

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Capillary Leak Syndrome

Capillary leak syndrome (CLS) has been reported after G-CSF administration, including filgrastim products, and is characterized by hypotension, hypoalbuminemia, edema, and hemoconcentration. Episodes vary in frequency and severity and may be life-threatening if treatment is delayed. Patients who develop symptoms of CLS should be closely monitored and receive standard symptomatic treatment, which may include the need for intensive care.

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Pfizer Oncology Together™ Co-Pay Savings Program for Injectables

Eligible patients may pay as little as **$0** per Tx

Eligible,* commercially insured patients† may pay as little as $0 per NIVESTYM treatment.‡ Limits, terms, and conditions apply.

- This program covers up to **$10,000 per calendar year**§
- There are **no income requirements** for patients to qualify
- Patients enrolled in state- or federally funded prescription insurance programs are not eligible for this program
- For information on enrollment, claims submissions, and reimbursement, visit **PfizerOncologyTogether.com** to download the Co-Pay Savings Program Brochure

***Terms and Conditions:** By using this program, you acknowledge that you currently meet the eligibility criteria and will comply with the terms and conditions below:

- The Pfizer Oncology Together Co-Pay Savings Program for Injectables for NIVESTYM® is not valid for patients who are enrolled in a state or federally funded insurance program, including but not limited to Medicare, Medicaid, TRICARE, Veterans Affairs health care, a state prescription drug assistance program, or the Government Health Insurance Plan available in Puerto Rico (formerly known as "La Reforma de Salud").
- Program offer is not valid for cash-paying patients.
- With this program, eligible patients may pay as little as $0 co-pay per NIVESTYM treatment, subject to a maximum benefit of $10,000

Click to view full Terms

†For patients to be eligible for the Injectables Co-Pay Program for NIVESTYM, they must have commercial insurance that covers NIVESTYM and they cannot be enrolled in a state or federally funded insurance program. Whether a co-pay expense is eligible for the Injectables Co-Pay Program for NIVESTYM benefit will be determined at the time the benefit is paid. Co-pay expenses must be in connection with a separately paid claim for NIVESTYM administered in the outpatient setting.

‡The Injectables Co-Pay Program for NIVESTYM will pay the co-pay for NIVESTYM up to the annual assistance limit of $10,000 per calendar year per patient.

§The Injectables Co-Pay Program for NIVESTYM provides assistance for eligible, commercially insured patients prescribed NIVESTYM for co-pays or coinsurance incurred for NIVESTYM up to $10,000 per calendar year. It does not cover or provide support for supplies, services, procedures, or any other physician-related services associated with NIVESTYM treatment.

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Myelodysplastic Syndrome (MDS) and Acute Myeloid Leukemia (AML)

Patients With Severe Chronic Neutropenia (SCN)

Confirm the diagnosis of SCN before initiating NIVESTYM® therapy. MDS and AML have been reported to occur in the natural history of congenital neutropenia without cytokine therapy. Cytogenetic abnormalities, transformation to MDS, and AML have also been observed in patients treated with filgrastim products for SCN. Based on available data including a post-marketing surveillance study, the risk of developing MDS and AML appears to be confined to the subset of patients with congenital neutropenia. Abnormal cytogenetics and MDS have been associated with the eventual development of myeloid leukemia.

(continued on next page)

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*__Terms and Conditions:__ By using this program, you acknowledge that you currently meet the eligibility criteria and will comply with the terms and conditions below:

- The Pfizer Oncology Together Co-Pay Savings Program for Injectables for NIVESTYM® is not valid for patients who are enrolled in a state or federally funded insurance program, including but not limited to Medicare, Medicaid, TRICARE, Veterans Affairs health care, a state prescription drug assistance program, or the Government Health Insurance Plan available in Puerto Rico (formerly known as "La Reforma de Salud").
- Program offer is not valid for cash-paying patients.
- With this program, eligible patients may pay as little as $0 co-pay per NIVESTYM treatment, subject to a maximum benefit of $10,000 per calendar year for out-of-pocket expenses for NIVESTYM including co-pays or coinsurances.
- The amount of any benefit is the difference between your co-pay and $0.
- After the maximum of $10,000 you will be responsible for the remaining monthly out-of-pocket costs.
- Patient must have private insurance with coverage of NIVESTYM.
- This offer is not valid when the entire cost of your prescription drug is eligible to be reimbursed by your private insurance plans or other private health or pharmacy benefit programs.
- You must deduct the value of this assistance from any reimbursement request submitted to your private insurance plan, either directly by you or on your behalf.
- You are responsible for reporting use of the program to any private insurer, health plan, or other third party who pays for or reimburses any part of the prescription filled using the program, as may be required.
- You should not use the program if your insurer or health plan prohibits use of manufacturer co-pay assistance programs.
- This program is not valid where prohibited by law.
- This program cannot be combined with any other savings, free trial or similar offer for the specified prescription.
- **Co-pay card will be accepted only at participating pharmacies.**
- **This program is not health insurance.**
- This program is good only in the U.S. and Puerto Rico.
- This program is limited to 1 per person during this offering period and is not transferable.
- No other purchase is necessary.
- Data related to your redemption of the program assistance may be collected, analyzed, and shared with Pfizer, for market research and other purposes related to assessing Pfizer's programs. Data shared with Pfizer will be aggregated and de-identified; it will be combined with data related to other assistance redemptions and will not identify you.
- Pfizer reserves the right to rescind, revoke or amend this program without notice.
- This program may not be available to patients in all states.
- For more information about Pfizer, visit www.pfizer.com.
- For more information about the Pfizer Oncology Together Co-Pay Savings Program for Injectables, visit pfizeroncologytogether.com, call 1-877-744-5675, or write to
  Pfizer Oncology Together Co-Pay Savings Program for Injectables
  P.O. Box 220366
  Charlotte, NC 28222
- Program terms and offer will expire at the end of each calendar year. Before the calendar year ends, you will receive information and eligibility requirements for continued participation.

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Confirm the diagnosis of SCN before initiating NIVESTYM® therapy. MDS and AML have been reported to occur in the natural history of congenital neutropenia without cytokine therapy. Cytogenetic abnormalities, transformation to MDS, and AML have also been observed in patients treated with filgrastim products for SCN. Based on available data including a post-marketing surveillance study, the risk of developing MDS and AML appears to be confined to the subset of patients with congenital neutropenia. Abnormal cytogenetics and MDS have been associated with the eventual development of myeloid leukemia.

(continued on next page)

Navigating access and reimbursement. Together.

Pfizer Oncology together™

Patient Support. Financial Assistance. Together.

If patients need access or reimbursement support, Pfizer Oncology Together is here to help.

Benefits Verification
We can help determine a patient's coverage and out-of-pocket costs.

Prior Authorization (PA) Assistance
We can coordinate with a patient's insurer to determine the PA requirements. After a PA request is submitted, we can follow up with the payer until a final outcome is determined.

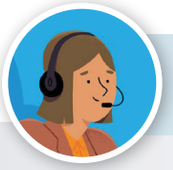
Appeals Assistance
We can review the reasons for a denied claim and provide information on payer requirements. After an appeal is submitted, we can follow up with the payer until a final outcome is determined.

Product Distribution
NIVESTYM is available through most major wholesalers.

Billing and Coding Assistance for IV Products
For your patient claim submissions, we provide easy access to sample forms and template letters, along with billing and coding information for physician's office and hospital outpatient settings of care.

Dedicated Local Support
A Pfizer Oncology Account Specialist can provide detailed information on Pfizer Oncology medications and access resources. In addition, they can help you and your office staff contact a Pfizer Field Reimbursement Manager (FRM) in your area.

FRMs are trained to help address specific access issues—in person or over the phone. They can help educate your staff on our access and reimbursement resources and help address challenging or urgent Pfizer Oncology patient cases you have sent to Pfizer Oncology Together.



FOR LIVE, PERSONALIZED SUPPORT
Call **1-877-744-5675** (Monday–Friday 8 AM–8 PM ET)

VISIT
PfizerOncologyTogether.com

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Myelodysplastic Syndrome (MDS) and Acute Myeloid Leukemia (AML) (continued)

Patients With Severe Chronic Neutropenia (SCN) (continued)

The effect of filgrastim products on the development of abnormal cytogenetics and the effect of continued filgrastim product administration in patients with abnormal cytogenetics or MDS are unknown. Monitor patients for signs and symptoms of MDS/AML in these settings. If a patient with SCN develops abnormal cytogenetics or myelodysplasia, the risks and benefits of continuing NIVESTYM® should be carefully considered.

(continued on next page)

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Pfizer is committed to supporting you and your patients

For commercially insured patients

Co-Pay Savings Program for Injectables

Finding financial support options. Together.

Limits, terms, and conditions apply.
Please see page 7 for terms and conditions.

Eligible patients may pay as little as **$0** per Tx

PfizerBiosimilarsResource.com

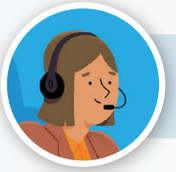
Downloadable tools are available to help support you when implementing Pfizer biosimilars into your practice.

ThisIsLivingWithCancer.com

A free app designed to help manage life with cancer

Help your patients and their caregivers stay connected and get organized by telling them about **LivingWith™**.

The **LivingWith** app is available to anyone living with cancer and their loved ones, and is not specific to NIVESTYM.



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SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Myelodysplastic Syndrome (MDS) and Acute Myeloid Leukemia (AML) (continued)

Patients with Breast and Lung Cancer

MDS and AML have been associated with the use of filgrastim 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.

Thrombocytopenia

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

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Click to view full ISI

The first FDA-approved biosimilar to Neupogen® (filgrastim) available in both prefilled syringes and single-dose vials[1]

NIVESTYM is a biosimilar to Neupogen[1]

Approved for all eligible indications of Neupogen[1]

Same dosing and administration schedule as Neupogen[1]

Useful ordering and coding information

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Leukocytosis

Patients With Cancer Receiving Myelosuppressive Chemotherapy:

White blood cell counts of 100,000/mm^3 or greater were observed in approximately 2% of patients who received filgrastim at dosages above 5 mcg/kg/day. In patients with cancer receiving NIVESTYM® as an adjunct to myelosuppressive chemotherapy, to avoid the potential risks of excessive leukocytosis, it is recommended that NIVESTYM® therapy be discontinued if the absolute neutrophil count (ANC) surpasses 10,000/mm^3 after the chemotherapy-induced ANC nadir has occurred. Monitor CBCs at least twice weekly during therapy.

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NIVESTYM has the same dosing and administration schedule as Neupogen® (filgrastim)[1]

Recommended starting dosage in patients

Indication	Dosing
Patients with cancer receiving myelosuppressive chemotherapy or induction and/or consolidation chemotherapy for AML	• **5 mcg/kg/day** administered as a single daily injection by subcutaneous (SC) injection, by short intravenous (IV) infusion (15 to 30 minutes), or by continuous IV infusion
Patients with cancer receiving BMT	• **10 mcg/kg/day** given as an IV infusion no longer than 24 hours
Patients undergoing autologous PBPC collection and therapy	• **10 mcg/kg/day** given by SC injection
Patients with SCN	• **6 mcg/kg** as a twice-daily SC injection for patients with congenital neutropenia • **5 mcg/kg** as a single daily SC injection for patients with idiopathic or cyclic neutropenia

Please see full Prescribing Information for important dosing adjustments and considerations for each indication.

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Leukocytosis (continued)

Patients With Cancer Receiving Myelosuppressive Chemotherapy (continued):

Dosages of NIVESTYM® that increase the ANC beyond 10,000/mm^3 may not result in any additional clinical benefit. In patients with cancer receiving myelosuppressive chemotherapy, discontinuation of filgrastim therapy usually resulted in a 50% decrease in circulating neutrophils within 1 to 2 days, with a return to pretreatment levels in 1 to 7 days.

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Introduction
Dosing and Administration
Ordering and Product Information
Product Presentation

NIVESTYM is the first FDA-approved Neupogen® (filgrastim) biosimilar available in both PFS and single-dose vials[1]

Ordering NIVESTYM—What you need to know[1,3,6]

Unit of Sale	300 mcg/0.5 mL PFS	300 mcg/0.5 mL PFS	480 mcg/0.8 mL PFS	480 mcg/0.8 mL PFS	300 mcg/mL SDV	480 mcg/1.6 mL SDV
Unit of Sale NDC	0069-0291-01	0069-0291-10	0069-0292-01	0069-0292-10	0069-0293-10	0069-0294-10
Unit of Sale Quantity	1 syringe	1 (10 syringes)	1 syringe	1 (10 syringes)	1 (10 vials)	1 (10 vials)
Unit of Sale List Price*	$219.00	$2,190.00	$350.40	$3,504.00	$2,190.00	$3,504.00
HCPCS Code	Q5110					
Descriptor	Injection, filgrastim-aafi, biosimilar, (NIVESTYM), 1 microgram					

SDV=single-dose vial.
*As of October 2022.

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION
WARNINGS AND PRECAUTIONS (CONTINUED)
Leukocytosis (continued)
Peripheral Blood Progenitor Cell Collection and Therapy:
During the period of administration of NIVESTYM® for PBPC mobilization in patients with cancer, discontinue NIVESTYM® if the leukocyte count rises to >100,000/mm^3.

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Introduction

Dosing and Administration

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NIVESTYM is the first FDA-approved Neupogen® (filgrastim) biosimilar available in both PFS and single-dose vials[1]

Storage and handling

Discard any vial or PFS left at room temperature for more than 24 hours

Store NIVESTYM in the refrigerator at 2 °C to 8 °C (36 °F to 46 °F)

Keep in original carton and protect from light. Avoid freezing. Avoid shaking

See Prescribing Information for detailed storage and handling instructions.

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Cutaneous Vasculitis

Cutaneous vasculitis has been reported in patients treated with filgrastim products. In most cases, the severity of cutaneous vasculitis was moderate or severe. Most of the reports involved patients with SCN receiving long-term filgrastim therapy. Hold NIVESTYM® therapy in patients with cutaneous vasculitis. NIVESTYM® may be started at a reduced dose when the symptoms resolve and the ANC has decreased.

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Among follow-on biologic and biosimilar products, only NIVESTYM offers both presentations of Neupogen® (filgrastim)…

Neupogen presentation	Granix® (tbo-filgrastim)[5]	Zarxio® (filgrastim-sndz)[7]	NIVESTYM[1]
PFS			
Single-dose vials			

The Granix syringe is available with or without a safety needle guard.

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Potential Effect on Malignant Cells

NIVESTYM® is a leukocyte growth factor that primarily stimulates neutrophils. The G-CSF receptor through which NIVESTYM® acts has also been found on tumor cell lines. The possibility that NIVESTYM® acts as a growth factor for any tumor type cannot be excluded. The safety of filgrastim products in chronic myeloid leukemia (CML) and myelodysplasia has not been established.

When NIVESTYM® is used to mobilize PBPC, tumor cells may be released from the marrow and subsequently collected in the leukapheresis product. The effect of reinfusion of tumor cells has not been well studied, and the limited data available are inconclusive.

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Introduction
Dosing and Administration
Ordering and Product Information
Product Presentation

...and is approved for all eligible indications of Neupogen® (filgrastim)[1,5,7*]

Eligible Neupogen indication[†‡]	Granix[§]	Zarxio	NIVESTYM
Patients with cancer receiving myelosuppressive chemotherapy • NIVESTYM is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever	✓ II	✓	✓
Patients with AML receiving induction or consolidation chemotherapy • NIVESTYM is indicated for reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with AML		✓	✓

***There are no head-to-head studies between NIVESTYM, Zarxio, and Granix, and no clinical comparisons can be made between the products.**

[†]Please refer to the full Prescribing Information for each product for full indication(s).

[‡]Neupogen is also approved with orphan drug exclusivity for use in patients acutely exposed to myelosuppressive doses of radiation (hematopoietic syndrome of acute radiation syndrome).

[§]Granix was approved for 1 indication through the 351(a) Biologics License Application (BLA) process.

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Simultaneous Use With Chemotherapy and Radiation Not Recommended

The safety and efficacy of NIVESTYM® given simultaneously with cytotoxic chemotherapy have not been established. Because of the potential sensitivity of rapidly dividing myeloid cells to cytotoxic chemotherapy, do not use NIVESTYM® in the period of 24 hours before through 24 hours after the administration of cytotoxic chemotherapy.

The safety and efficacy of NIVESTYM® have not been evaluated in patients receiving concurrent radiation therapy. Avoid the simultaneous use of NIVESTYM® with chemotherapy and radiation therapy.

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...and is approved for all eligible indications of Neupogen® (filgrastim)[1,5,7*]

Eligible Neupogen indication[†‡]	Granix[§]	Zarxio	NIVESTYM
Patients with cancer undergoing BMT • NIVESTYM is indicated to reduce the duration of neutropenia and neutropenia-related clinical sequelae, eg, febrile neutropenia, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by BMT		✓	✓
Patients undergoing autologous PBPC collection and therapy • NIVESTYM is indicated for the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis		✓	✓

***There are no head-to-head studies between NIVESTYM, Zarxio, and Granix, and no clinical comparisons can be made between the products.**

[†]Please refer to the full Prescribing Information for each product for full indication(s).

[‡]Neupogen is also approved with orphan drug exclusivity for use in patients acutely exposed to myelosuppressive doses of radiation (hematopoietic syndrome of acute radiation syndrome).

[§]Granix was approved for 1 indication through the 351(a) Biologics License Application (BLA) process.

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

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.

(continued on next page)

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...and is approved for all eligible indications of Neupogen® (filgrastim)[1,5,7]*

Eligible Neupogen indication†‡	Granix§	Zarxio	NIVESTYM
Patients with SCN • NIVESTYM is indicated for chronic administration to reduce the incidence and duration of sequelae of neutropenia (eg, fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital, cyclic, or idiopathic neutropenia		✓	✓

***There are no head-to-head studies between NIVESTYM, Zarxio, and Granix, and no clinical comparisons can be made between the products.**

†Please refer to the full Prescribing Information for each product for full indication(s).

‡Neupogen is also approved with orphan drug exclusivity for use in patients acutely exposed to myelosuppressive doses of radiation (hematopoietic syndrome of acute radiation syndrome).

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Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Aortitis

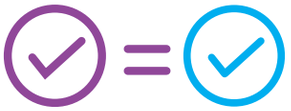
Aortitis has been reported in patients receiving filgrastim products. It may occur as early as the first week after start of therapy. Manifestations may include generalized signs and symptoms such as fever, abdominal pain, malaise, back pain, and increased inflammatory markers (eg, c-reactive protein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

Click to view full ISI

The first FDA-approved biosimilar to Neupogen® (filgrastim) available in both prefilled syringes and single-dose vials[1]

A totality of evidence supports biosimilarity to Neupogen[1,3]

Biosimilarity established based on a totality of evidence[1,8]



Extrapolation allows potential approval for nonstudied indications[8]

No clinically meaningful differences in terms of efficacy or safety[3]

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

ADVERSE REACTIONS

The most common adverse reactions in patients:

- with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs (≥5 % difference in incidence compared to placebo) are anemia, constipation, diarrhea, oral pain, vomiting, asthenia, malaise, peripheral edema, decreased hemoglobin, decreased appetite, oropharyngeal pain, and alopecia
- with AML (≥2 % difference in incidence) are epistaxis, back pain, pain in extremity, erythema, maculopapular rash, diarrhea, constipation, and transfusion reaction
- with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation (BMT) (≥5 % difference in incidence) are rash, hypersensitivity, thrombocytopenia, anemia, hypertension, sepsis, bronchitis, and insomnia

(continued on next page)

Click to view full ISI

The first FDA-approved biosimilar to Neupogen® (filgrastim) available in both prefilled syringes and single-dose vials[1]

NIVESTYM was approved by the FDA based on the totality of evidence demonstrating it is highly similar to Neupogen[1,8]

CLINICAL STUDY	NIVESTYM demonstrated noninferiority immunogenicity in a study of healthy volunteers[3]
CLINICAL PHARMACOLOGY (PD/PK)	NIVESTYM demonstrated similar PD and PK profiles to Neupogen in studies of healthy volunteers[3]
NONCLINICAL	NIVESTYM is similar to Neupogen based on required nonclinical study results[1,3]
ANALYTICAL	NIVESTYM is highly similar in structure and function to Neupogen[1,3]

PD=pharmacodynamic; PK=pharmacokinetic.

Click to view full evidence

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION
ADVERSE REACTIONS (CONTINUED)

The most common adverse reactions in patients (continued):

- undergoing peripheral blood progenitor cell mobilization and collection (≥5% incidence) are bone pain, pyrexia, increased blood alkaline phosphatase, and headache
- with severe chronic neutropenia (≥5% difference in incidence) are arthralgia, bone pain, back pain, muscle spasms, musculoskeletal pain, pain in extremity, splenomegaly, anemia, upper respiratory tract infection, urinary tract infection, epistaxis, chest pain, diarrhea, hypoesthesia, and alopecia

Click to view full ISI

CLINICAL STUDY	**NIVESTYM demonstrated noninferiority immunogenicity in a study of healthy volunteers**[3] • No clinically meaningful differences in immunogenicity risk were observed between NIVESTYM and Neupogen
CLINICAL PHARMACOLOGY (PD/PK)	**NIVESTYM demonstrated similar PD and PK profiles to Neupogen in studies of healthy volunteers**[3] • In clinical studies, primary PD endpoint of ANC was similar across treatment groups • In the studies, primary PK endpoint of serum concentration was similar across treatment groups
NONCLINICAL	**NIVESTYM is similar to Neupogen based on required nonclinical study results**[1,3] • A comparative nonclinical 4-week study in rats demonstrated comparable toxicity between NIVESTYM and Neupogen
ANALYTICAL	**NIVESTYM is highly similar in structure and function to Neupogen**[1,3] • NIVESTYM and Neupogen have a highly similar higher-order structure (protein folding) and have equivalent in vivo potency

ANC=absolute neutrophil count; PD=pharmacodynamic; PK=pharmacokinetic.

CLOSE

ADVERSE REACTIONS (CONTINUED)

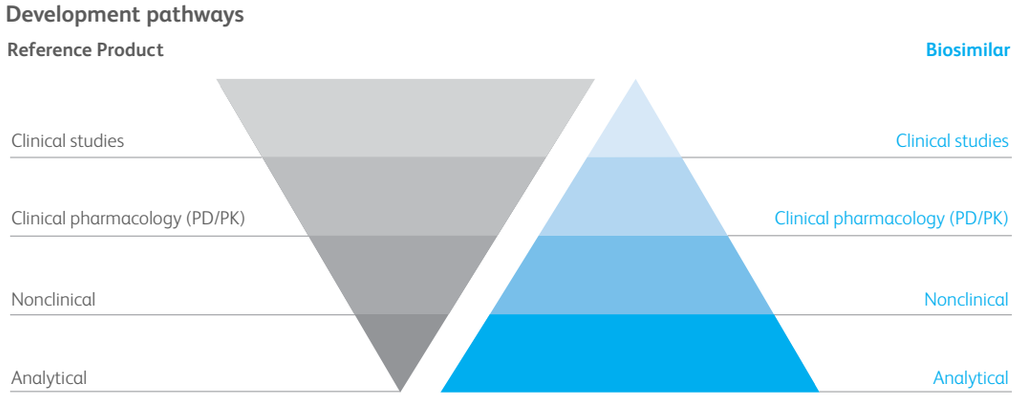
The most common adverse reactions in patients (continued):

- undergoing peripheral blood progenitor cell mobilization and collection (≥5% incidence) are bone pain, pyrexia, increased blood alkaline phosphatase, and headache
- with severe chronic neutropenia (≥5% difference in incidence) are arthralgia, bone pain, back pain, muscle spasms, musculoskeletal pain, pain in extremity, splenomegaly, anemia, upper respiratory tract infection, urinary tract infection, epistaxis, chest pain, diarrhea, hypoesthesia, and alopecia

Biosimilars: Highly similar versions of existing biologic medicines[8]

- According to the FDA, a biosimilar is a medicine highly similar to another biological medicine or reference product already marketed in the United States
  - Biosimilars have no clinically meaningful differences in terms of safety, purity, and potency from their reference products

The FDA evaluates biosimilars based on a totality of evidence approach[8,9]



- The goal of biosimilar development is to demonstrate that there are no clinically meaningful differences based on the totality of evidence[8,9]
- Analytical studies are the foundation of biosimilar development and provide the greatest sensitivity for detecting differences between a biosimilar and its reference product[8,9]

Click to enlarge

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

CONTRAINDICATIONS

NIVESTYM® is contraindicated in patients with a history of serious allergic reactions to human granulocyte-colony stimulating factors (G-CSF), such as filgrastim products or pegfilgrastim products.

WARNINGS AND PRECAUTIONS

Splenic Rupture

Splenic rupture, including fatal cases, has been reported following the administration of filgrastim products. Evaluate patients who report left upper abdominal or shoulder pain for an enlarged spleen or splenic rupture.

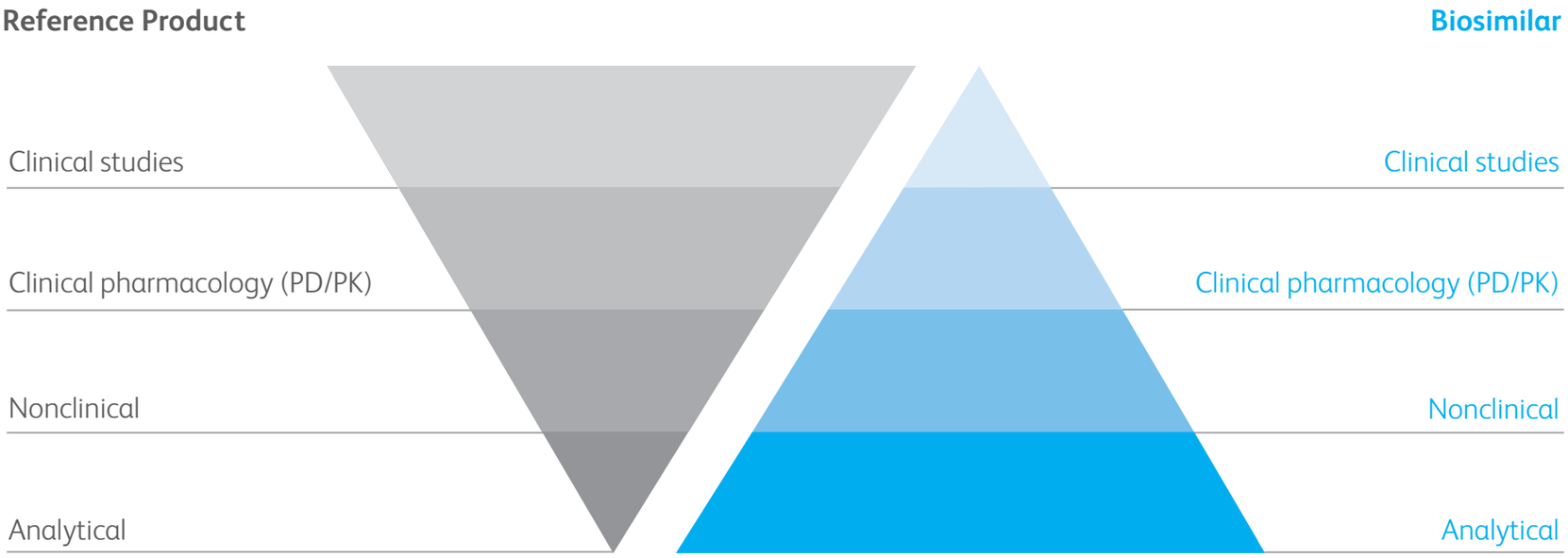
(continued on next page)

Click to view full ISI

- According to the FDA, a biosimilar is a medicine highly similar to another biological medicine or reference product already marketed in the United States
  - Biosimilars have no clinically meaningful differences in terms of safety, purity, and potency from their reference products

The FDA evaluates biosimilars based on a totality of evidence approach[8,9]

Development pathways



- The goal of biosimilar development is to demonstrate that there are no clinically meaningful differences based on the totality of evidence[8,9]
- Analytical studies are the foundation of biosimilar development and provide the greatest sensitivity for detecting differences between a biosimilar and its reference product[8,9]

CLOSE

WARNINGS AND PRECAUTIONS

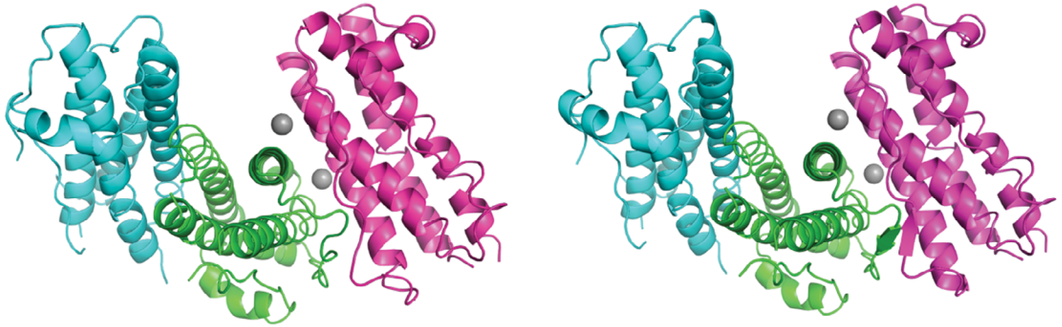
Splenic Rupture

Splenic rupture, including fatal cases, has been reported following the administration of filgrastim products. Evaluate patients who report left upper abdominal or shoulder pain for an enlarged spleen or splenic rupture.

(continued on next page)

NIVESTYM and Neupogen® (filgrastim) have a highly similar higher-order structure (protein folding)[1,3]

X-ray crystallography



NIVESTYM showed no clinically meaningful differences in efficacy and safety vs Neupogen

- NIVESTYM and Neupogen have equivalent in vivo potency
- NIVESTYM showed no clinically meaningful differences in immunogenicity risk vs Neupogen in healthy volunteers
- NIVESTYM showed comparable incidence of adverse events (AEs) of special interest vs Neupogen in healthy volunteers

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION
WARNINGS AND PRECAUTIONS (CONTINUED)
Acute Respiratory Distress Syndrome
Acute respiratory distress syndrome (ARDS) has been reported in patients receiving filgrastim products. Evaluate patients who develop fever and lung infiltrates or respiratory distress for ARDS. Discontinue NIVESTYM® in patients with ARDS.

(continued on next page)

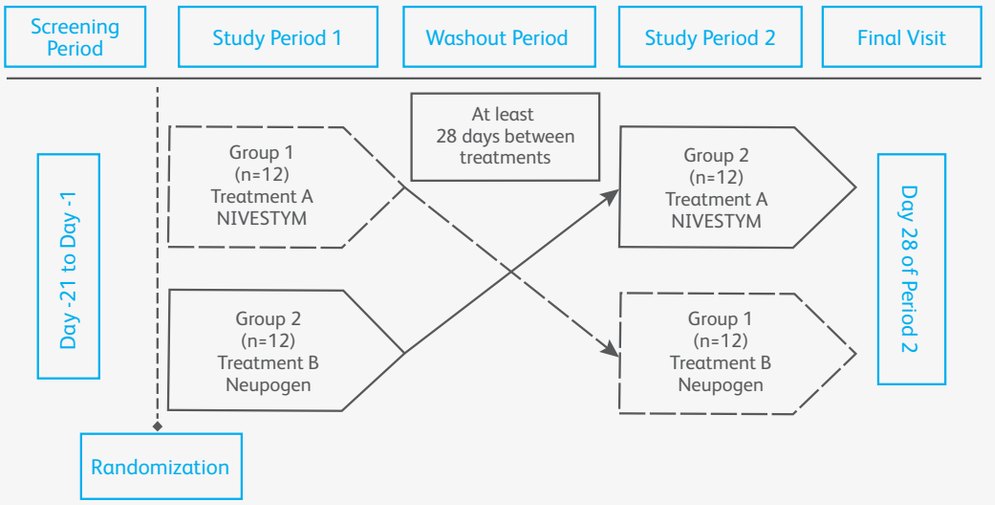
Click to view full ISI

Introduction
Data Summary
FDA Evaluation
Similar Structure
PD/PK Single-Dose Study
PD/PK Multiple-Dose Study
Immunogenicity
Safety Evaluation

Single-dose, crossover study to assess PD/PK similarity in healthy volunteers[3]

A single-center, randomized, open-label, single-dose crossover study designed to evaluate the PD and PK equivalence of a single SC dose of 5 mcg/kg of NIVESTYM and Neupogen® (filgrastim) in healthy volunteers (N=24)

NIVESTYM PD/PK study design



ANC
Serum

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Serious Allergic Reactions

Serious allergic reactions, including anaphylaxis, have been reported in patients receiving filgrastim products. The majority of reported events occurred upon initial exposure. Provide symptomatic treatment for allergic reactions. Allergic reactions, including anaphylaxis, in patients receiving filgrastim products can recur within days after the discontinuation of initial anti-allergic treatment. Permanently discontinue NIVESTYM® in patients with serious allergic reactions. NIVESTYM® is contraindicated in patients with a history of serious allergic reactions to human G-CSF such as filgrastim or pegfilgrastim.

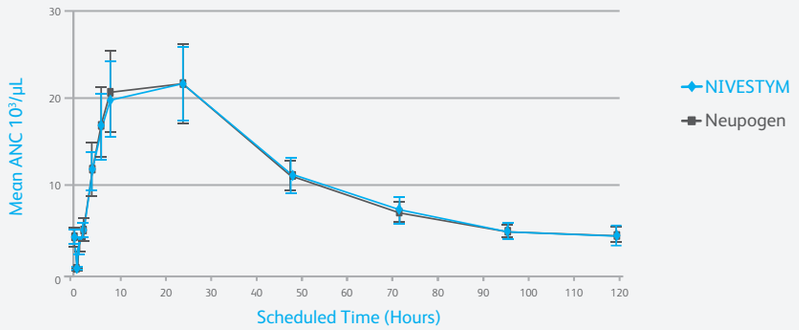
(continued on next page)

Click to view full ISI

NIVESTYM PD analysis established equivalence to Neupogen® (filgrastim) in support of biosimilarity[3]

Primary PD endpoint of ANC was similar across treatments

Mean (±SD) ANC over-time profiles (linear) for NIVESTYM and Neupogen



PD population: n=23 (NIVESTYM); n=23 (Neupogen).

Primary PD evaluation

Parameter statistic	NIVESTYM	Neupogen	GMR	90% CI
$AUEC_{ANC}$ (10^3*hr/µL)	1241.45	1247.31	0.99	(0.95, 1.02)
ANC_{max} (10^3/µL)	21.44	21.86	0.98	(0.93, 1.02)

ANC_{max}=maximum observed ANC; $AUEC_{ANC}$=area under the effect curve for ANC; CI=confidence interval; GMR=geometric mean ratio; SD=standard deviation.

Click to enlarge

ANC

Serum

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Sickle Cell Disorders

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

Glomerulonephritis

Glomerulonephritis has occurred in patients receiving filgrastim products. The diagnoses were based upon azotemia, hematuria (microscopic and macroscopic), proteinuria, and renal biopsy. Generally, events of glomerulonephritis resolved after dose reduction or discontinuation of filgrastim products. If glomerulonephritis is suspected, evaluate for cause. If causality is likely, consider dose-reduction or interruption of NIVESTYM®.

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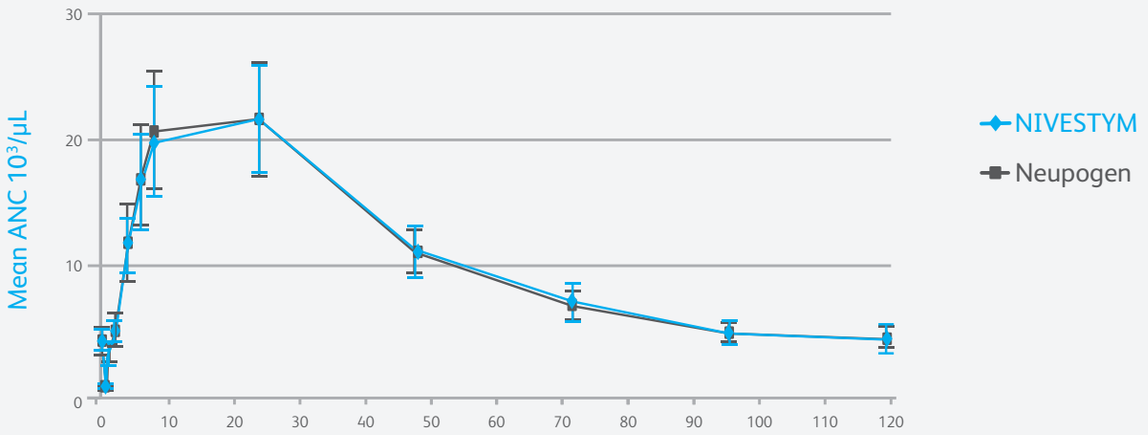
Click to view full ISI

Primary PD endpoint of ANC was similar across treatments

Mean (±SD) ANC over-time profiles (linear) for NIVESTYM and Neupogen



PD population: n=23 (NIVESTYM); n=23 (Neupogen).

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CLOSE

ANC
Serum

SELECTED SAFETY
WARNINGS AND
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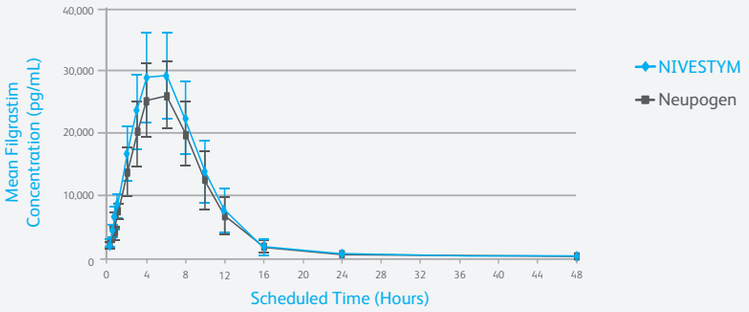
(continued on next page)

NIVESTYM PK analysis established equivalence to Neupogen® (filgrastim) in support of biosimilarity[3]

Primary PK endpoint of serum concentration was similar across treatments

Mean (±SD) serum filgrastim concentration over-time profiles for NIVESTYM and Neupogen



PK population: n=23 (NIVESTYM); n=23 (Neupogen).

Primary PK evaluation

Parameter statistic	NIVESTYM	Neupogen	GMR	90% CI
$AUC_{0-\infty}$ (hr*pg/mL)	244,859.6	215,409.8	1.14	(1.05, 1.23)
C_{max} (pg/mL)	29,630.67	26,628.29	1.11	(1.02, 1.21)

$AUC_{0-\infty}$=area under the serum concentration-time profile from time 0 extrapolated to infinite time;
C_{max}=maximum serum concentration.

Click to enlarge

ANC

Serum

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Alveolar Hemorrhage and Hemoptysis

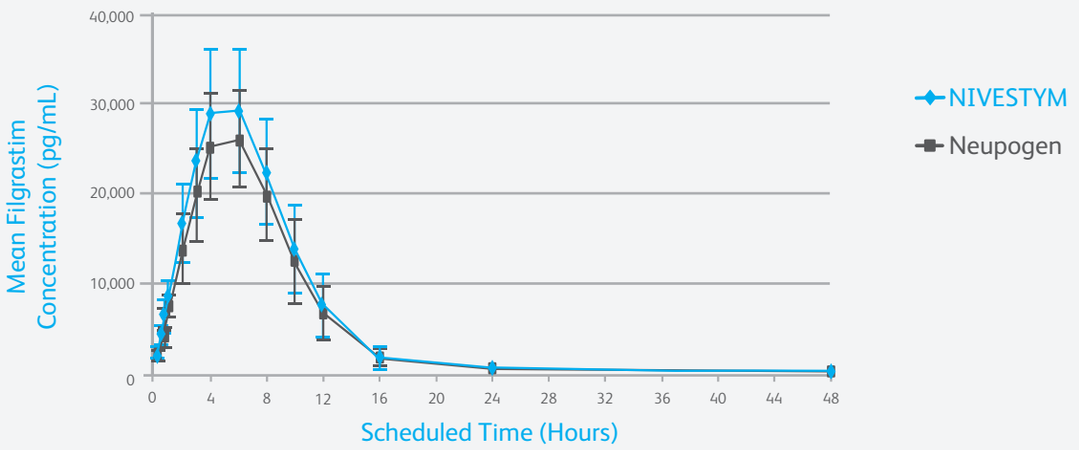
Alveolar hemorrhage manifesting as pulmonary infiltrates and hemoptysis requiring hospitalization has been reported in healthy donors treated with filgrastim products for peripheral blood progenitor cell (PBPC) mobilization. Hemoptysis resolved with discontinuation of filgrastim products. The use of NIVESTYM® for PBPC mobilization in healthy donors is not an approved indication.

Click to view full ISI

(continued on next page)

Primary PK endpoint of serum concentration was similar across treatments

Mean (±SD) serum filgrastim concentration over-time profiles for NIVESTYM and Neupogen



PK population: n=23 (NIVESTYM); n=23 (Neupogen).

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C_{max} (pg/mL)	29,630.67	26,628.29	1.11	(1.02, 1.21)

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CLOSE

SELECTED SAFET
WARNINGS AND
Alveolar Hemorrh
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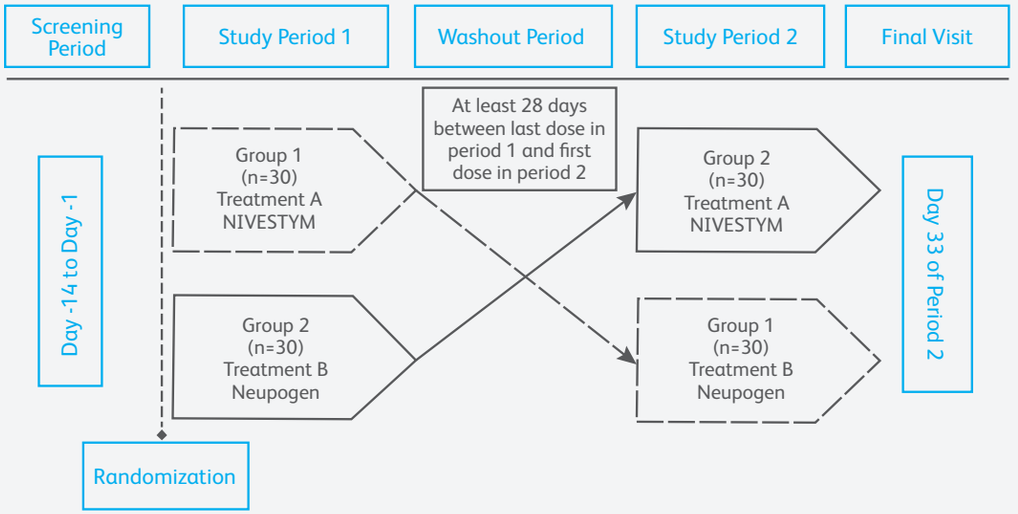
Multiple-dose crossover study to assess PD/PK similarity in healthy volunteers[3]

A single-center, randomized, open-label, multiple-dose crossover study designed to evaluate the PD and PK equivalence following administration of 5 SC doses of 5 mcg/kg of NIVESTYM and Neupogen® (filgrastim) in healthy volunteers (N=60)

NIVESTYM PD/PK study design



Subjects were administered study medication for 5 consecutive days at a dose of 5 mcg/kg/day.

CD34+
Serum

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Capillary Leak Syndrome

Capillary leak syndrome (CLS) has been reported after G-CSF administration, including filgrastim products, and is characterized by hypotension, hypoalbuminemia, edema, and hemoconcentration. Episodes vary in frequency and severity and may be life-threatening if treatment is delayed. Patients who develop symptoms of CLS should be closely monitored and receive standard symptomatic treatment, which may include the need for intensive care.

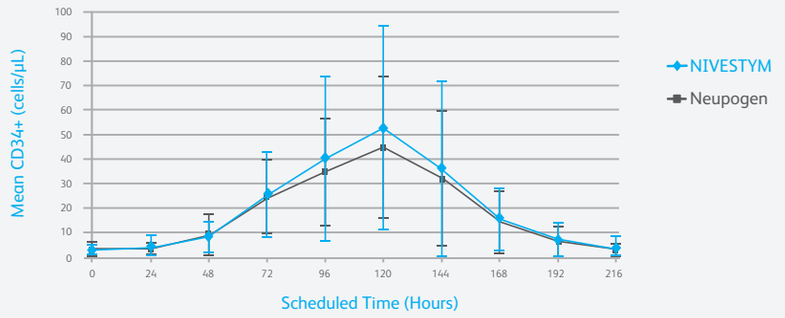
(continued on next page)

Click to view full ISI

NIVESTYM PD analysis established equivalence to Neupogen® (filgrastim) in support of biosimilarity[3]

Primary PD endpoint of CD34+ cells for PD population was similar across treatment groups

Mean (±SD) CD34+ over-time profiles (linear) for NIVESTYM and Neupogen (PD population)



PD population: n=56 (NIVESTYM); n=56 (Neupogen). PD equivalence was concluded if the 90% CIs for both $AUEC_{CD34+}$ and $CD34+_{max}$ were completely contained within the prespecified acceptance limits of 0.80-1.25.

Primary PD evaluation

Parameter statistic	NIVESTYM	Neupogen	GMR	90% CI
$AUEC_{CD34+}$ (cells*hr/µL)	3433.65	3222.22	1.06	(0.98, 1.15)
$CD34+_{max}$ (cells/µL)	43.21	40.74	1.06	(0.95, 1.19)

$AUEC_{CD34+}$=area under the effect curve for CD34+ count; $CD34+_{max}$=maximum observed CD34+ count.

Click to enlarge

CD34+

Serum

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Myelodysplastic Syndrome (MDS) and Acute Myeloid Leukemia (AML)

Patients With Severe Chronic Neutropenia (SCN)

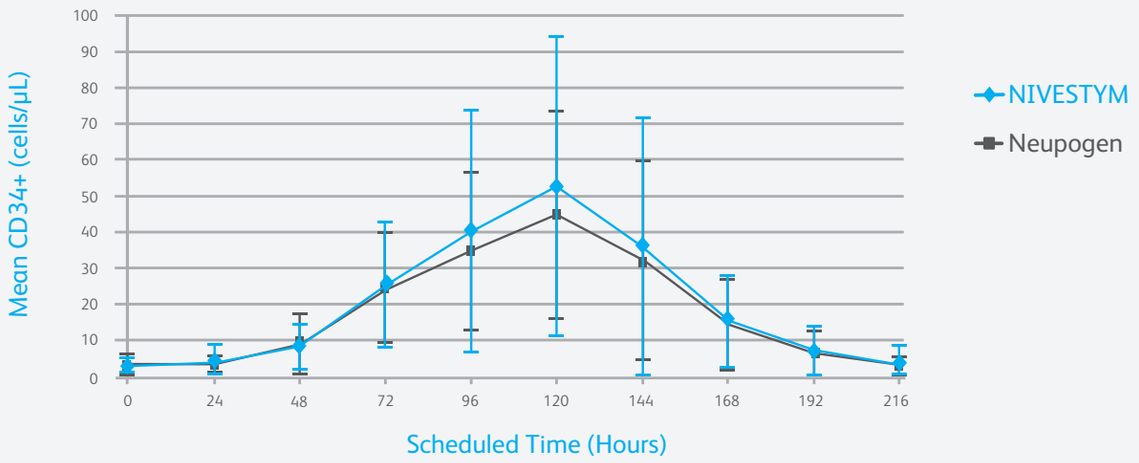
Confirm the diagnosis of SCN before initiating NIVESTYM® therapy. MDS and AML have been reported to occur in the natural history of congenital neutropenia without cytokine therapy. Cytogenetic abnormalities, transformation to MDS, and AML have also been observed in patients treated with filgrastim products for SCN. Based on available data including a post-marketing surveillance study, the risk of developing MDS and AML appears to be confined to the subset of patients with congenital neutropenia. Abnormal cytogenetics and MDS have been associated with the eventual development of myeloid leukemia.

(continued on next page)

Click to view full ISI

Primary PD endpoint of CD34+ cells for PD population was similar across treatment groups

Mean (±SD) CD34+ over-time profiles (linear) for NIVESTYM and Neupogen (PD population)



PD population: n=56 (NIVESTYM); n=56 (Neupogen). PD equivalence was concluded if the 90% CIs for both $AUEC_{CD34+}$ and $CD34+_{max}$ were completely contained within the prespecified acceptance limits of 0.80-1.25.

Primary PD evaluation

Parameter statistic	NIVESTYM	Neupogen	GMR	90% CI
$AUEC_{CD34+}$ (cells*hr/µL)	3433.65	3222.22	1.06	(0.98, 1.15)
$CD34+_{max}$ (cells/µL)	43.21	40.74	1.06	(0.95, 1.19)

$AUEC_{CD34+}$=area under the effect curve for CD34+ count; $CD34+_{max}$=maximum observed CD34+ count.

CLOSE

SELECTED SAFE
WARNINGS AN
Myelodysplastic S
Patients With Severe Chronic Neutropenia (SCN)

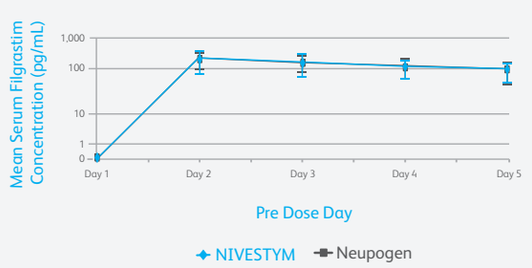
Confirm the diagnosis of SCN before initiating NIVESTYM® therapy. MDS and AML have been reported to occur in the natural history of congenital neutropenia without cytokine therapy. Cytogenetic abnormalities, transformation to MDS, and AML have also been observed in patients treated with filgrastim products for SCN. Based on available data including a post-marketing surveillance study, the risk of developing MDS and AML appears to be confined to the subset of patients with congenital neutropenia. Abnormal cytogenetics and MDS have been associated with the eventual development of myeloid leukemia.

(continued on next page)

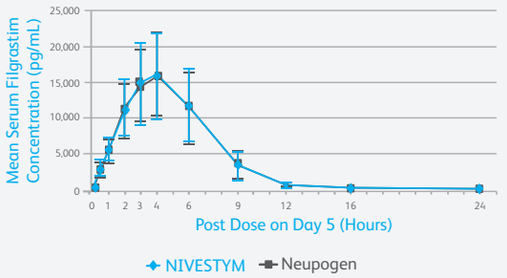
NIVESTYM PK analysis established equivalence to Neupogen® (filgrastim) in support of biosimilarity[3]

Primary PK endpoint of serum predose and postdose concentration was similar across treatments

Mean (±SD) serum predose concentration over-time profiles for NIVESTYM and Neupogen



Mean (±SD) serum postdose concentration over-time profiles for NIVESTYM and Neupogen



PK population: n=56 (NIVESTYM); n=56 (Neupogen).

Primary PK evaluation

Parameter statistic	NIVESTYM	Neupogen	GMR	90% CI
$AUC_{0\text{-}24}$ (hr*pg/mL)	90,885.66	88,840.38	1.02	(0.97, 1.08)
C_{max} (pg/mL)	15,661.75	15,121.66	1.03	(0.95, 1.12)

$AUC_{0\text{-}24}$=area under the serum concentration-time profile from time 0 to 24 hours.

Click to enlarge

CD34+

Serum

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Myelodysplastic Syndrome (MDS) and Acute Myeloid Leukemia (AML) (continued)

Patients With Severe Chronic Neutropenia (SCN) (continued)

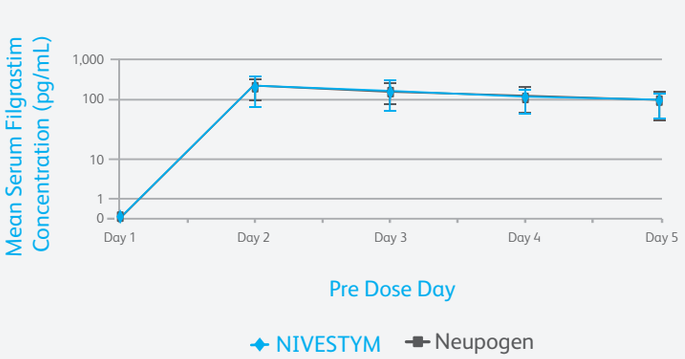
The effect of filgrastim products on the development of abnormal cytogenetics and the effect of continued filgrastim product administration in patients with abnormal cytogenetics or MDS are unknown. Monitor patients for signs and symptoms of MDS/AML in these settings. If a patient with SCN develops abnormal cytogenetics or myelodysplasia, the risks and benefits of continuing NIVESTYM® should be carefully considered.

Click to view full ISI

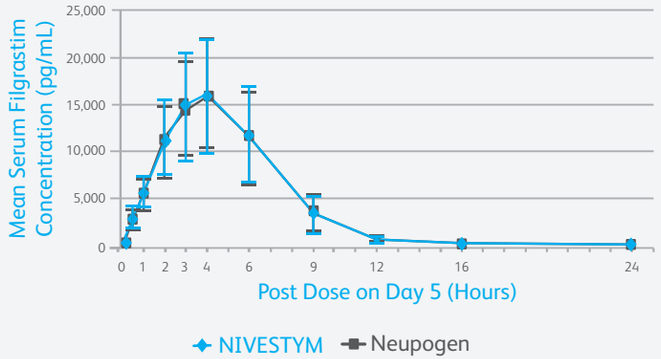
(continued on next page)

Primary PK endpoint of serum predose and postdose concentration was similar across treatments

Mean (±SD) serum predose concentration over-time profiles for NIVESTYM and Neupogen



Mean (±SD) serum postdose concentration over-time profiles for NIVESTYM and Neupogen



PK population: n=56 (NIVESTYM); n=56 (Neupogen).

Primary PK evaluation

Parameter statistic	NIVESTYM	Neupogen	GMR	90% CI
$AUC_{0\text{-}24}$ (hr*pg/mL)	90,885.66	88,840.38	1.02	(0.97, 1.08)
C_{max} (pg/mL)	15,661.75	15,121.66	1.03	(0.95, 1.12)

$AUC_{0\text{-}24}$=area under the serum concentration-time profile from time 0 to 24 hours.

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CD34+
Serum

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WARNINGS AND
Myelodysplastic Sy

Patients With Severe Chronic Neutropenia (SCN) (continued)

continued filgrastim product administration in patients with abnormal cytogenetics or MDS are unknown. Monitor patients for signs and symptoms of MDS/AML in these settings. If a patient with SCN develops abnormal cytogenetics or myelodysplasia, the risks and benefits of continuing NIVESTYM® should be carefully considered.

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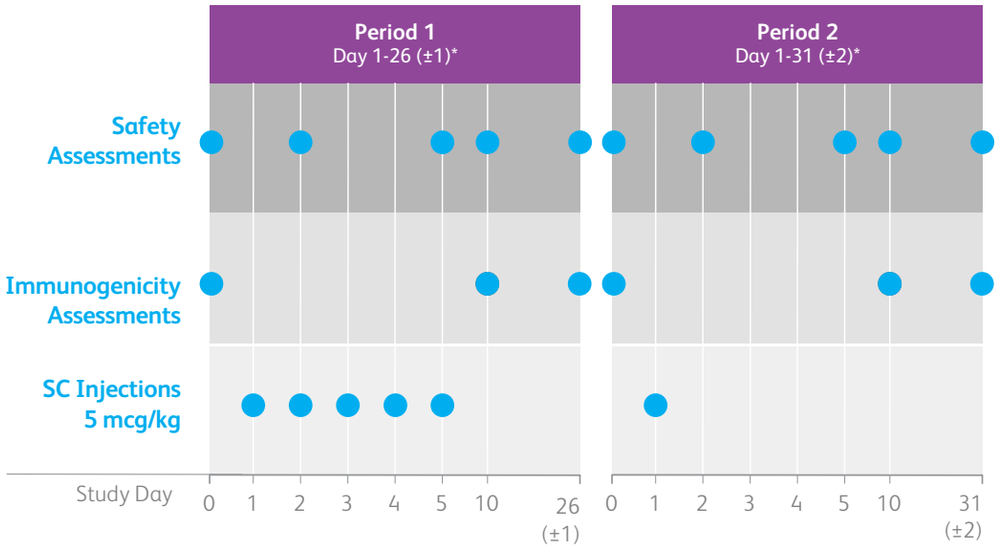
A parallel clinical study assessed the immunogenicity of NIVESTYM vs Neupogen® (filgrastim) in healthy subjects[3]



ADA=antidrug antibody.

*Periods 1 and 2 were separated by an interval of approximately 1 month.

†Analyzed similarly to the primary endpoint except that a noninferiority test was not applied at each postdose assessment during treatment periods 1 and 2.

Primary endpoint

- The proportion of subjects with a negative baseline ADA test result and confirmed postdose positive ADA test result at any time during the study

Secondary endpoint

- The proportion of subjects with a negative baseline ADA test result and a postdose positive neutralizing antibody at any time during the study†

ADAs

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Myelodysplastic Syndrome (MDS) and Acute Myeloid Leukemia (AML) (continued)

Patients with Breast and Lung Cancer

MDS and AML have been associated with the use of filgrastim 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.

Thrombocytopenia

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

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A parallel clinical study assessed the immunogenicity of NIVESTYM vs Neupogen® (filgrastim) in healthy subjects[3]

Proportion of subjects with negative baseline ADAs and confirmed postdose positive ADAs

	NIVESTYM (n=128) n (%)	Neupogen (n=127) n (%)
Positive ADAs	9 (7.4)	6 (4.9)
Positive neutralizing antibodies	0	0

- The protocol for this comparative immunogenicity study was based on the use of a comparative crossover study design for the previously completed single- and multiple-dose PD/PK studies

ADAs

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION
WARNINGS AND PRECAUTIONS (CONTINUED)
Leukocytosis
Patients With Cancer Receiving Myelosuppressive Chemotherapy:
White blood cell counts of 100,000/mm^3 or greater were observed in approximately 2% of patients who received filgrastim at dosages above 5 mcg/kg/day. In patients with cancer receiving NIVESTYM® as an adjunct to myelosuppressive chemotherapy, to avoid the potential risks of excessive leukocytosis, it is recommended that NIVESTYM® therapy be discontinued if the absolute neutrophil count (ANC) surpasses 10,000/mm^3 after the chemotherapy-induced ANC nadir has occurred. Monitor CBCs at least twice weekly during therapy.

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NIVESTYM showed a similar safety profile to Neupogen® (filgrastim) across AE categories in healthy volunteers[3]

NIVESTYM showed comparable incidence of TEAEs in a randomized immunogenicity study in healthy volunteers

TEAEs reported by at least 5% of subjects in any treatment group

	NIVESTYM (n=128) n (%)	Neupogen (n=127) n (%)
Back pain	37 (28.9)	37 (29.1)
Headache	19 (14.8)	21 (16.5)
Pain in extremity	4 (3.1)	7 (5.5)
Injection site hemorrhage	1 (0.8)	8 (6.3)

TEAE=treatment-emergent AE.

- 3 subjects discontinued the study due to an AE
  - – 2 subjects in the NIVESTYM group (diverticular perforation; back pain)
  - – 1 subject in US-Neupogen group (back pain)

AEs of special interest

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION
WARNINGS AND PRECAUTIONS (CONTINUED)
Leukocytosis (continued)
Patients With Cancer Receiving Myelosuppressive Chemotherapy (continued):
Dosages of NIVESTYM® that increase the ANC beyond 10,000/mm^3 may not result in any additional clinical benefit. In patients with cancer receiving myelosuppressive chemotherapy, discontinuation of filgrastim therapy usually resulted in a 50% decrease in circulating neutrophils within 1 to 2 days, with a return to pretreatment levels in 1 to 7 days.

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NIVESTYM showed a similar safety profile to Neupogen® (filgrastim) across AE categories in healthy volunteers[3]

NIVESTYM showed comparable incidence of TEAEs in a randomized immunogenicity study in healthy volunteers

Summary of TEAEs leading to discontinuation

Number (%) of subjects by system organ class and preferred term	NIVESTYM 5 mcg/kg (n=128)	Neupogen 5 mcg/kg (n=127)	Total (N=255)
With any AE leading to discontinuation from study	2 (1.6)	1 (0.8)	3 (1.2)
Gastrointestinal disorders			
Diverticular perforation	1 (0.8)	0	1 (0.4)
Musculoskeletal and connective tissue disorders			
Back pain	1 (0.8)	1 (0.8)	2 (0.8)

AEs of special interest

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION
WARNINGS AND PRECAUTIONS (CONTINUED)
Leukocytosis (continued)
Peripheral Blood Progenitor Cell Collection and Therapy:
During the period of administration of NIVESTYM® for PBPC mobilization in patients with cancer, discontinue NIVESTYM® if the leukocyte count rises to >100,000/mm^3.

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NIVESTYM showed a similar safety profile to Neupogen® (filgrastim) across AE categories in healthy volunteers[3]

NIVESTYM showed comparable incidence of AEs of special interest in an immunogenicity study in healthy volunteers

Frequency of AEs of special interest

Number of subjects evaluable for AEs	NIVESTYM 5 mcg/kg (n=128)	Neupogen 5 mcg/kg (n=127)	Total (N=255)
Number (%) of subjects by AE of special interest criteria and preferred term	n (%)	n (%)	n (%)
With any AE of special interest	1 (0.8)	0	1 (0.4)
Potential allergic reactions Dermatitis	1 (0.8)	0	1 (0.4)
Splenomegaly	0	0	0
Splenic rupture	0	0	0

- One subject in the NIVESTYM treatment group experienced a nonserious AE of special interest of dermatitis, which is in the category of potential allergic reactions

There were no deaths in this study. Three subjects discontinued the study due to an AE: 2 subjects in the NIVESTYM group (diverticular perforation unrelated to study drug; back pain) and 1 subject in the US-Neupogen group (back pain).

AEs of special interest

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Cutaneous Vasculitis

Cutaneous vasculitis has been reported in patients treated with filgrastim products. In most cases, the severity of cutaneous vasculitis was moderate or severe. Most of the reports involved patients with SCN receiving long-term filgrastim therapy. Hold NIVESTYM® therapy in patients with cutaneous vasculitis. NIVESTYM® may be started at a reduced dose when the symptoms resolve and the ANC has decreased.

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NIVESTYM showed a similar safety profile to Neupogen® (filgrastim) across AE categories in healthy volunteers[3]

NIVESTYM showed comparable incidence of AEs of special interest in an immunogenicity study in healthy volunteers

Frequency of AEs of special interest

Number of subjects evaluable for AEs	NIVESTYM 5 mcg/kg (n=128)	Neupogen 5 mcg/kg (n=127)	Total (N=255)
Splenic rupture	0	0	0
Acute respiratory distress syndrome	0	0	0
Alveolar hemorrhage	0	0	0
Hemoptysis	0	0	0
Leukocytosis	0	0	0
Thrombocytopenia	0	0	0

- One subject in the NIVESTYM treatment group experienced a nonserious AE of special interest of dermatitis, which is in the category of potential allergic reactions

There were no deaths in this study. Three subjects discontinued the study due to an AE: 2 subjects in the NIVESTYM group (diverticular perforation unrelated to study drug; back pain) and 1 subject in the US-Neupogen group (back pain).

AEs of special interest

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Potential Effect on Malignant Cells

NIVESTYM® is a leukocyte growth factor that primarily stimulates neutrophils. The G-CSF receptor through which NIVESTYM® acts has also been found on tumor cell lines. The possibility that NIVESTYM® acts as a growth factor for any tumor type cannot be excluded. The safety of filgrastim products in chronic myeloid leukemia (CML) and myelodysplasia has not been established.

When NIVESTYM® is used to mobilize PBPC, tumor cells may be released from the marrow and subsequently collected in the leukapheresis product. The effect of reinfusion of tumor cells has not been well studied, and the limited data available are inconclusive.

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NIVESTYM showed a similar safety profile to Neupogen® (filgrastim) across AE categories in healthy volunteers[3]

NIVESTYM showed comparable incidence of AEs of special interest in an immunogenicity study in healthy volunteers

Frequency of AEs of special interest

Number of subjects evaluable for AEs	NIVESTYM 5 mcg/kg (n=128)	Neupogen 5 mcg/kg (n=127)	Total (N=255)
Capillary leak syndrome	0	0	0
Cytokine release syndrome	0	0	0
Cutaneous vasculitis	0	0	0
Glomerulonephritis	0	0	0

- One subject in the NIVESTYM treatment group experienced a nonserious AE of special interest of dermatitis, which is in the category of potential allergic reactions

There were no deaths in this study. Three subjects discontinued the study due to an AE: 2 subjects in the NIVESTYM group (diverticular perforation unrelated to study drug; back pain) and 1 subject in the US-Neupogen group (back pain).

AEs of special interest

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Simultaneous Use With Chemotherapy and Radiation Not Recommended

The safety and efficacy of NIVESTYM® given simultaneously with cytotoxic chemotherapy have not been established. Because of the potential sensitivity of rapidly dividing myeloid cells to cytotoxic chemotherapy, do not use NIVESTYM® in the period of 24 hours before through 24 hours after the administration of cytotoxic chemotherapy.

The safety and efficacy of NIVESTYM® have not been evaluated in patients receiving concurrent radiation therapy. Avoid the simultaneous use of NIVESTYM® with chemotherapy and radiation therapy.

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Important Safety Information and Indications

CONTRAINDICATIONS

NIVESTYM® is contraindicated in patients with a history of serious allergic reactions to human granulocyte-colony stimulating factors (G-CSF), such as filgrastim products or pegfilgrastim products.

WARNINGS AND PRECAUTIONS

Splenic Rupture

Splenic rupture, including fatal cases, has been reported following the administration of filgrastim products. Evaluate patients who report left upper abdominal or shoulder pain for an enlarged spleen or splenic rupture.

Acute Respiratory Distress Syndrome

Acute respiratory distress syndrome (ARDS) has been reported in patients receiving filgrastim products. Evaluate patients who develop fever and lung infiltrates or respiratory distress for ARDS. Discontinue NIVESTYM® in patients with ARDS.

Serious Allergic Reactions

Serious allergic reactions, including anaphylaxis, have been reported in patients receiving filgrastim products. The majority of reported events occurred upon initial exposure. Provide symptomatic treatment for allergic reactions. Allergic reactions, including anaphylaxis, in patients receiving filgrastim products can recur within days after the discontinuation of initial anti-allergic treatment. Permanently discontinue NIVESTYM® in patients with serious allergic reactions. NIVESTYM® is contraindicated in patients with a history of serious allergic reactions to human G-CSF such as filgrastim or pegfilgrastim.

Sickle Cell Disorders

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

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

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.

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Important Safety Information and Indications

Glomerulonephritis

Glomerulonephritis has occurred in patients receiving filgrastim products. The diagnoses were based upon azotemia, hematuria (microscopic and macroscopic), proteinuria, and renal biopsy. Generally, events of glomerulonephritis resolved after dose reduction or discontinuation of filgrastim products. If glomerulonephritis is suspected, evaluate for cause. If causality is likely, consider dose-reduction or interruption of NIVESTYM®.

Alveolar Hemorrhage and Hemoptysis

Alveolar hemorrhage manifesting as pulmonary infiltrates and hemoptysis requiring hospitalization has been reported in healthy donors treated with filgrastim products for peripheral blood progenitor cell (PBPC) mobilization. Hemoptysis resolved with discontinuation of filgrastim products. The use of NIVESTYM® for PBPC mobilization in healthy donors is not an approved indication.

Capillary Leak Syndrome

Capillary leak syndrome (CLS) has been reported after G-CSF administration, including filgrastim products, and is characterized by hypotension, hypoalbuminemia, edema, and hemoconcentration. Episodes vary in frequency and severity and may be life-threatening if treatment is delayed. Patients who develop symptoms of CLS should be closely monitored and receive standard symptomatic treatment, which may include the need for intensive care.

Myelodysplastic Syndrome (MDS) and Acute Myeloid Leukemia (AML)

Patients With Severe Chronic Neutropenia (SCN)

Confirm the diagnosis of SCN before initiating NIVESTYM® therapy. MDS and AML have been reported to occur in the natural history of congenital neutropenia without cytokine therapy. Cytogenetic abnormalities, transformation to MDS, and AML have also been observed in patients treated with filgrastim products for SCN. Based on available data including a post-marketing surveillance study, the risk of developing MDS and AML appears to be confined to the subset of patients with congenital neutropenia. Abnormal cytogenetics and MDS have been associated with the eventual development of myeloid leukemia.

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Aortitis

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

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Important Safety Information and Indications

The effect of filgrastim products on the development of abnormal cytogenetics and the effect of continued filgrastim product administration in patients with abnormal cytogenetics or MDS are unknown. Monitor patients for signs and symptoms of MDS/AML in these settings. If a patient with SCN develops abnormal cytogenetics or myelodysplasia, the risks and benefits of continuing NIVESTYM® should be carefully considered.

Patients with Breast and Lung Cancer

MDS and AML have been associated with the use of filgrastim 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.

Thrombocytopenia

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

Leukocytosis

Patients With Cancer Receiving Myelosuppressive Chemotherapy:

White blood cell counts of 100,000/mm^3 or greater were observed in approximately 2% of patients who received filgrastim at dosages above 5 mcg/kg/day. In patients with cancer receiving NIVESTYM® as an adjunct to myelosuppressive chemotherapy, to avoid the potential risks of excessive leukocytosis, it is recommended that NIVESTYM® therapy be discontinued if the absolute neutrophil count (ANC) surpasses 10,000/mm^3 after the chemotherapy-induced ANC nadir has occurred. Monitor CBCs at least twice weekly during therapy. Dosages of NIVESTYM® that increase the ANC beyond 10,000/mm^3 may not result in any additional clinical benefit. In patients with cancer receiving myelosuppressive chemotherapy, discontinuation of filgrastim therapy usually resulted in a 50% decrease in circulating neutrophils within 1 to 2 days, with a return to pretreatment levels in 1 to 7 days.

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

ADVERSE REACTIONS

The most common adverse reactions in patients:

- with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs (≥5% difference in incidence compared to placebo) are anemia, constipation, diarrhea, oral pain, vomiting, asthenia, malaise, peripheral edema, decreased hemoglobin, decreased appetite, oropharyngeal pain, and alopecia
- with AML (≥2% difference in incidence) are epistaxis, back pain, pain in extremity, erythema, maculopapular rash, diarrhea, constipation, and transfusion reaction
- with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation (BMT) (≥5% difference in incidence) are rash, hypersensitivity, thrombocytopenia, anemia, hypertension, sepsis, bronchitis, and insomnia

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Important Safety Information and Indications

Peripheral Blood Progenitor Cell Collection and Therapy:

During the period of administration of NIVESTYM® for PBPC mobilization in patients with cancer, discontinue NIVESTYM® if the leukocyte count rises to >100,000/mm^3.

Cutaneous Vasculitis

Cutaneous vasculitis has been reported in patients treated with filgrastim products. In most cases, the severity of cutaneous vasculitis was moderate or severe. Most of the reports involved patients with SCN receiving long-term filgrastim therapy. Hold NIVESTYM® therapy in patients with cutaneous vasculitis. NIVESTYM® may be started at a reduced dose when the symptoms resolve and the ANC has decreased.

Potential Effect on Malignant Cells

NIVESTYM® is a leukocyte growth factor that primarily stimulates neutrophils. The G-CSF receptor through which NIVESTYM® acts has also been found on tumor cell lines. The possibility that NIVESTYM® acts as a growth factor for any tumor type cannot be excluded. The safety of filgrastim products in chronic myeloid leukemia (CML) and myelodysplasia has not been established.

When NIVESTYM® is used to mobilize PBPC, tumor cells may be released from the marrow and subsequently collected in the leukapheresis product. The effect of reinfusion of tumor cells has not been well studied, and the limited data available are inconclusive.

Simultaneous Use With Chemotherapy and Radiation Not Recommended

The safety and efficacy of NIVESTYM® given simultaneously with cytotoxic chemotherapy have not been established. Because of the potential sensitivity of rapidly dividing myeloid cells to cytotoxic chemotherapy, do not use NIVESTYM® in the period of 24 hours before through 24 hours after the administration of cytotoxic chemotherapy.

The safety and efficacy of NIVESTYM® have not been evaluated in patients receiving concurrent radiation therapy. Avoid the simultaneous use of NIVESTYM® with chemotherapy and radiation therapy.

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

ADVERSE REACTIONS (CONTINUED)

The most common adverse reactions in patients (continued):

- undergoing peripheral blood progenitor cell mobilization and collection (≥5% incidence) are bone pain, pyrexia, increased blood alkaline phosphatase, and headache
- with severe chronic neutropenia (≥5% difference in incidence) are arthralgia, bone pain, back pain, muscle spasms, musculoskeletal pain, pain in extremity, splenomegaly, anemia, upper respiratory tract infection, urinary tract infection, epistaxis, chest pain, diarrhea, hypoesthesia, and alopecia

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Important Safety Information and Indications

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.

Aortitis

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

ADVERSE REACTIONS

The most common adverse reactions in patients:

- with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs (≥5 % difference in incidence compared to placebo) are anemia, constipation, diarrhea, oral pain, vomiting, asthenia, malaise, peripheral edema, decreased hemoglobin, decreased appetite, oropharyngeal pain, and alopecia
- with AML (≥2 % difference in incidence) are epistaxis, back pain, pain in extremity, erythema, maculopapular rash, diarrhea, constipation, and transfusion reaction
- with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation (BMT) (≥5 % difference in incidence) are rash, hypersensitivity, thrombocytopenia, anemia, hypertension, sepsis, bronchitis, and insomnia
- undergoing peripheral blood progenitor cell mobilization and collection (≥5 % incidence) are bone pain, pyrexia, increased blood alkaline phosphatase, and headache
- with severe chronic neutropenia (≥5 % difference in incidence) are arthralgia, bone pain, back pain, muscle spasms, musculoskeletal pain, pain in extremity, splenomegaly, anemia, upper respiratory tract infection, urinary tract infection, epistaxis, chest pain, diarrhea, hypoesthesia, and alopecia

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

CONTRAINDICATIONS

NIVESTYM® is contraindicated in patients with a history of serious allergic reactions to human granulocyte-colony stimulating factors (G-CSF), such as filgrastim products or pegfilgrastim products.

WARNINGS AND PRECAUTIONS

Splenic Rupture

Splenic rupture, including fatal cases, has been reported following the administration of filgrastim products. Evaluate patients who report left upper abdominal or shoulder pain for an enlarged spleen or splenic rupture.

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Important Safety Information and Indications

INDICATIONS

Patients With Cancer Receiving Myelosuppressive Chemotherapy

- NIVESTYM® is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever

Patients With Acute Myeloid Leukemia Receiving Induction or Consolidation Chemotherapy

- NIVESTYM® is indicated for reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML)

Patients With Cancer Undergoing Bone Marrow Transplantation

- NIVESTYM® is indicated to reduce the duration of neutropenia and neutropenia-related clinical sequelae, eg, febrile neutropenia, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by BMT

Patients Undergoing Autologous Peripheral Blood Progenitor Cell Collection and Therapy

- NIVESTYM® is indicated for the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis

Patients With Severe Chronic Neutropenia

- NIVESTYM® is indicated for chronic administration to reduce the incidence and duration of sequelae of neutropenia (eg, fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia

This product's labeling may have been updated. For the most recent prescribing information, please visit www.pfizer.com.

Please see Important Safety Information and Indications on pages 35-40 and full Prescribing Information, including Patient Information, available at NivestymHCP.com.

SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Acute Respiratory Distress Syndrome

Acute respiratory distress syndrome (ARDS) has been reported in patients receiving filgrastim products. Evaluate patients who develop fever and lung infiltrates or respiratory distress for ARDS. Discontinue NIVESTYM® in patients with ARDS.

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Summary

References

NIVESTYM: Pfizer Oncology's commitment to building onto the clinical experience of filgrastim

Pfizer

With the largest portfolio of oncology biosimilars—including NIVESTYM—Pfizer is committed to expanding options for patient care[2]

Favorable coverage[3]

Potential savings[3]

Support for you and your patients

Approved for all eligible indications of Neupogen® (filgrastim), with an identical dosing and administration schedule[1]

Realize the full potential of biosimilars. Ask about the Pfizer Biosimilars Portfolio

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SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Serious Allergic Reactions

Serious allergic reactions, including anaphylaxis, have been reported in patients receiving filgrastim products. The majority of reported events occurred upon initial exposure. Provide symptomatic treatment for allergic reactions. Allergic reactions, including anaphylaxis, in patients receiving filgrastim products can recur within days after the discontinuation of initial anti-allergic treatment. Permanently discontinue NIVESTYM® in patients with serious allergic reactions. NIVESTYM® is contraindicated in patients with a history of serious allergic reactions to human G-CSF such as filgrastim or pegfilgrastim.

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Summary

References

1. NIVESTYM [prescribing information]. New York, NY: Pfizer Inc.; November 2021.
2. McGowan S, Jesse M, Biehn B. U.S. Biosimilar Report. AmerisourceBergen. November 15, 2021. Accessed October 12, 2022. https://amerisourcebergen.com/-/media/assets/amerisourcebergen/biosimilars-page/sgs-biosimilars-usmarketlandscape-111521-final.pdf.
3. Data on file. Pfizer Inc.; New York, NY.
4. Generics and Biosimilar Initiative Online. Biosimilars approved in Europe. Updated July 1, 2022. Accessed October 12, 2022. https://gabionline.net/biosimilars/general/biosimilars-approved-in-europe.
5. Granix [prescribing information]. North Wales, PA: Teva Pharmaceuticals; November 2019.
6. HCPCS Codes. 2021 HCPCS Codes Level II. Accessed November 23, 2021. https://hcpcs.codes/q-codes/Q5110/.
7. Zarxio [highlights of prescribing information]. Princeton, NJ: Sandoz, Inc.; March 2021.
8. US Food and Drug Administration. Guidance for Industry: Scientific Considerations in Demonstrating Biosimilarity to a Reference Product. Silver Spring, MD: FDA, US Dept of Health and Human Services; April 2015. Accessed October 12, 2022. https://www.fda.gov/downloads/drugs/guidances/ucm291128.pdf.
9. Melosky B, Reardon DA, Nixon AB, Subramanian J, Bair AH, Jacobs I. Bevacizumab biosimilars: scientific justification for extrapolation of indications. *Future Oncol.* 2018;14(24):2507-2520.

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SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Sickle Cell Disorders

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

Glomerulonephritis

Glomerulonephritis has occurred in patients receiving filgrastim products. The diagnoses were based upon azotemia, hematuria (microscopic and macroscopic), proteinuria, and renal biopsy. Generally, events of glomerulonephritis resolved after dose reduction or discontinuation of filgrastim products. If glomerulonephritis is suspected, evaluate for cause. If causality is likely, consider dose-reduction or interruption of NIVESTYM®.

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