An FDA-approved biosimilar to Neulasta® (pegfilgrastim)[1*†]

INJECTION
Nyvepria®
pegfilgrastim-apgf
Pfizer

NYVEPRIA® (pegfilgrastim-apgf)

Product Monograph

BUILDING ONTO THE CLINICAL EXPERIENCE OF PEGFILGRASTIM

*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.
†NYVEPRIA does not have a designation of interchangeability with Neulasta.

SELECTED SAFETY INFORMATION

Contraindications

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

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Please see Important Safety Information and Indication on pages 25-27 and full Prescribing Information, Patient Information, and Instructions for Use, also available at NyvepriaHCP.com.

Indication

NYVEPRIA® (pegfilgrastim-apgf) is FDA approved for the eligible indication of Neulasta® (pegfilgrastim)[1]

INDICATION

NYVEPRIA 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

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

Please see Important Safety Information and Indication on pages 25-27 and full Prescribing Information, Patient Information, and Instructions for Use, also available at NyvepriaHCP.com.

SELECTED SAFETY INFORMATION

Warnings and Precautions

Splenic Rupture

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

(continued on next page)

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An FDA-approved biosimilar to Neulasta® (pegfilgrastim)[1]

With the largest portfolio of oncology biosimilars—including NYVEPRIA® (pegfilgrastim-apgf)—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 Indication on pages 25-27 and full Prescribing Information, Patient Information, and Instructions for Use, also available at NyvepriaHCP.com.

SELECTED SAFETY INFORMATION

Warnings and Precautions (continued)

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 NYVEPRIA
- Discontinue NYVEPRIA in patients with ARDS

(continued on next page)

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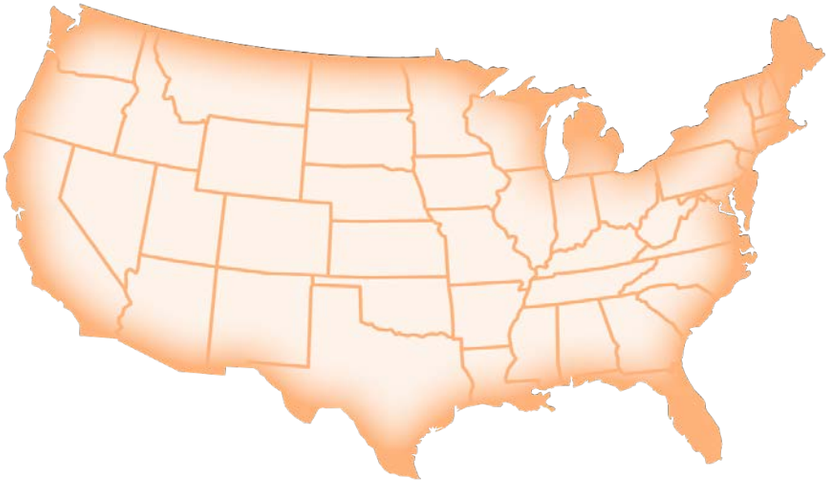
NYVEPRIA® (pegfilgrastim-apgf) coverage

Learn about access in your area

Coverage for NYVEPRIA 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 Indication on pages 25-27 and full Prescribing Information, Patient Information, and Instructions for Use, also available at NyvepriaHCP.com.

SELECTED SAFETY INFORMATION

Warnings and Precautions (continued)

Serious Allergic Reactions

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

(continued on next page)

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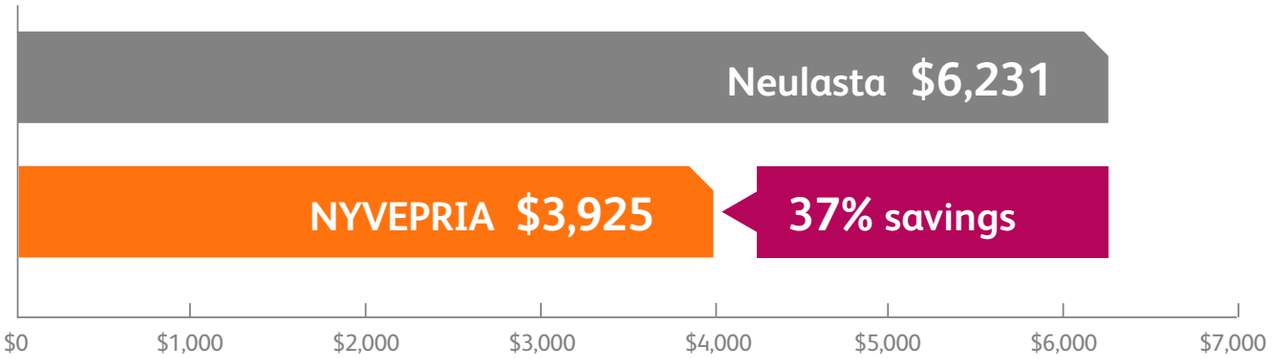
Potential cost savings with NYVEPRIA® (pegfilgrastim-apgf)

Wholesale acquisition cost (WAC) represents a 37% discount vs Neulasta® (pegfilgrastim) per 6-mg prefilled syringe[3]*



An estimated cumulative maximum potential savings over 10 years from implementation of all available biosimilars could reach as much as $150 billion.[5†]

*WAC is a manufacturer's undiscounted or list price to wholesalers/direct purchasers and, therefore, is not inclusive of discounts to payers, providers, distributors, and other purchasing organizations. Data as of October 2022.

†Estimated reduction in direct spending on biologic drugs between 2017 and 2026 (RAND Corporation). Based on an assumption of a biosimilar market share of 50% and biosimilar prices at 50% of the reference product.

Please see Important Safety Information and Indication on pages 25-27 and full Prescribing Information, Patient Information, and Instructions for Use, also available at NyvepriaHCP.com.

SELECTED SAFETY INFORMATION

Warnings and Precautions (continued)

Use in Patients with Sickle Cell Disorders

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

(continued on next page)

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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 NYVEPRIA 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 NYVEPRIA® 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 NYVEPRIA 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 NYVEPRIA, they must have commercial insurance that covers NYVEPRIA 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 NYVEPRIA benefit will be determined at the time the benefit is paid. Co-pay expenses must be in connection with a separately paid claim for NYVEPRIA administered in the outpatient setting.

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

§The Injectables Co-Pay Program for NYVEPRIA provides assistance for eligible, commercially insured patients prescribed NYVEPRIA for co-pays or coinsurance incurred for NYVEPRIA 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 NYVEPRIA treatment.

Please see Important Safety Information and Indication on pages 25-27 and full Prescribing Information, Patient Information, and Instructions for Use, also available at NyvepriaHCP.com.

SELECTED SAFETY INFORMATION

Warnings and Precautions (continued)

Glomerulonephritis

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

(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 NYVEPRIA® 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 NYVEPRIA treatment, subject to a maximum benefit of $10,000 per calendar year for out-of-pocket expenses for NYVEPRIA 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 NYVEPRIA.
- 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.

CLOSE

- Generally, events of glomerulonephritis resolved after dose-reduction or discontinuation of pegfilgrastim products
- If glomerulonephritis is suspected, evaluate for cause. If causality is likely, consider dose-reduction or interruption of NYVEPRIA

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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

NYVEPRIA is available through most major wholesalers.

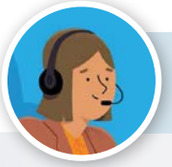
Billing and Coding Assistance for IV Products

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 Indication on pages 25-27 and full Prescribing Information, Patient Information, and Instructions for Use, also available at NyvepriaHCP.com.

SELECTED SAFETY INFORMATION

Warnings and Precautions (continued)

Leukocytosis

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

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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 6 for terms and conditions.

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

ThisIsLivingWithCancer.com

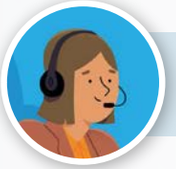
A free app designed to help manage life with cancer

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 NYVEPRIA.

PfizerBiosimilarsResource.com

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



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SELECTED SAFETY INFORMATION

Warnings and Precautions (continued)

Thrombocytopenia

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

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Introduction

Dosing and Administration

Ordering and Product Information

An FDA-approved biosimilar to Neulasta® (pegfilgrastim)[1]

NYVEPRIA® (pegfilgrastim-apgf) is a biosimilar to Neulasta[1]

Approved for the eligible indication of Neulasta[1]

Identical dosing and administration schedule to Neulasta[1]

Useful ordering and coding information

Please see Important Safety Information and Indication on pages 25-27 and full Prescribing Information, Patient Information, and Instructions for Use, also available at NyvepriaHCP.com.

SELECTED SAFETY INFORMATION

Warnings and Precautions (continued)

Capillary Leak Syndrome (CLS)

- CLS has been reported after granulocyte-colony stimulating factor (G-CSF) administration, including pegfilgrastim 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 a need for intensive care

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Dosing and Administration
Ordering and Product Information

NYVEPRIA® (pegfilgrastim-apgf) has an identical dosing and administration schedule to Neulasta® (pegfilgrastim)[1]

DOSING FOR ADULTS

6 mg

Once per chemotherapy cycle

Do not administer NYVEPRIA between **14 days before** and **24 hours after administration of cytotoxic chemotherapy**

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

Please see the full NYVEPRIA Prescribing Information for additional details.

Please see Important Safety Information and Indication on pages 25-27 and full Prescribing Information, Patient Information, and Instructions for Use, also available at NyvepriaHCP.com.

SELECTED SAFETY INFORMATION

Warnings and Precautions (continued)

Potential for Tumor Growth Stimulatory Effects on Malignant Cells

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

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Introduction

Dosing and Administration

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NYVEPRIA® (pegfilgrastim-apgf) has an identical dosing and administration schedule to Neulasta® (pegfilgrastim)[1]

DOSING FOR PEDIATRIC PATIENTS WEIGHING LESS THAN 45 KG*		
Body weight	**NYVEPRIA dose**	**Volume to administer**
Less than 10 kg†	See below†	See below†
10-20 kg	1.5 mg	0.15 mL
21-30 kg	2.5 mg	0.25 mL
31-44 kg	4 mg	0.40 mL

INJECTION: 6 mg/0.6 mL of a sterile, clear, colorless, preservative-free solution in a single-dose prefilled syringe with BD UltraSafe Plus™ Passive Needle Guard for manual use only

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

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

Please see the full NYVEPRIA Prescribing Information for additional details.

Please see Important Safety Information and Indication on pages 25-27 and full Prescribing Information, Patient Information, and Instructions for Use, also available at NyvepriaHCP.com.

SELECTED SAFETY INFORMATION

Warnings and Precautions (continued)

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

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Introduction

Dosing and Administration

Ordering and Product Information

NYVEPRIA® (pegfilgrastim-apgf) is available in a single-dose prefilled syringe[1,3,6]

Ordering NYVEPRIA—What you need to know

Unit of Sale	6 mg/0.6 mL prefilled syringe
Unit of Sale NDC	0069-0324-01
Unit of Sale Quantity	1 prefilled syringe
Unit of Sale List Price*	$3,925
HCPCS Code	Q5122
OPPS Status	340B pass-through payment

OPPS=Outpatient Prospective Payment System.
*As of October 2022.

Please see Important Safety Information and Indication on pages 25-27 and full Prescribing Information, Patient Information, and Instructions for Use, also available at NyvepriaHCP.com.

SELECTED SAFETY INFORMATION

Warnings and Precautions (continued)

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 (eg, c-reactive protein and white blood cell count)
- Consider aortitis in patients who develop these signs and symptoms without known etiology. Discontinue NYVEPRIA if aortitis is suspected

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Introduction

Dosing and Administration

Ordering and Product Information

NYVEPRIA® (pegfilgrastim-apgf) is available in a single-dose prefilled syringe[1,3,6]

Storage and handling

Store refrigerated between 36 °F to 46 °F (2 °C to 8 °C) in the carton to protect from light

Do not shake the prefilled syringe

Discard syringes stored at room temperature for more than 15 days

Avoid freezing; if frozen, thaw in the refrigerator before administration. Discard syringe if frozen more than once

- The NYVEPRIA syringe plunger stopper and needle cover are not made with natural rubber latex

Please see the full NYVEPRIA Prescribing Information for detailed storage and handling information.

Please see Important Safety Information and Indication on pages 25-27 and full Prescribing Information, Patient Information, and Instructions for Use, also available at NyvepriaHCP.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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An FDA-approved biosimilar to Neulasta® (pegfilgrastim)[1]

A totality of evidence supports biosimilarity to Neulasta[1,7]

Biosimilarity established based on a totality of evidence[1,7]

Similar structure and function[3]

Studies in support of biosimilarity in healthy volunteers

NYVEPRIA PD/PK data supports no clinically meaningful differences in efficacy vs Neulasta-EU and Neulasta-US[3]

Studies in support of biosimilarity in healthy volunteers

NYVEPRIA had a comparable safety profile vs Neulasta across adverse event categories[3]

PD=pharmacodynamic; PK=pharmacokinetic.

Please see Important Safety Information and Indication on pages 25-27 and full Prescribing Information, Patient Information, and Instructions for Use, also available at NyvepriaHCP.com.

SELECTED SAFETY INFORMATION
Most Common Adverse Reactions
- Bone pain
- Pain in extremity

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An FDA-approved biosimilar to Neulasta® (pegfilgrastim)[1]

NYVEPRIA® (pegfilgrastim-apgf) was approved by the FDA based on the totality of evidence demonstrating it is highly similar to Neulasta[1,3]

ADDITIONAL CLINICAL STUDIES	**NYVEPRIA showed no clinically meaningful differences to Neulasta-US**[3] • In healthy subjects, no clinically meaningful differences in immunogenicity risk were observed between NYVEPRIA and Neulasta-US • No evidence of NAbs was observed in any subject
CLINICAL PHARMACOLOGY (PD/PK)	**NYVEPRIA demonstrated PD and PK equivalence to Neulasta-EU* and Neulasta-US in a phase I study**[3] • In this study, all PD and PK parameters were within the bioequivalence window of 80 % to 125 %
NONCLINICAL	**NYVEPRIA is similar to Neulasta-EU and Neulasta-US based on TK and toxicity**[3] • A comparative 4-week, repeat-dose toxicity study in rats demonstrated comparable toxicity, TK, PD, and antipegfilgrastim antibody profiles
ANALYTICAL	**NYVEPRIA is highly similar to Neulasta-EU and Neulasta-US in terms of structure and function**[3] • NYVEPRIA, Neulasta-EU, and Neulasta-US have a highly similar higher-order structure (protein folding) and have equivalent in vitro potency

- No comparative safety and efficacy study was conducted for this biosimilar program. A comparative human PD and PK study was conducted in healthy subjects using a relevant PD measure followed by a comparative immunogenicity study in healthy subjects, per FDA guidance[3]

Click to enlarge

NAb=neutralizing antibody; TK=toxicokinetic.
*Product sourced from the EU is often used as a comparator in trials to demonstrate biosimilarity.

Please see Important Safety Information and Indication on pages 25-27 and full Prescribing Information, Patient Information, and Instructions for Use, also available at NyvepriaHCP.com.

SELECTED SAFETY INFORMATION

Contraindications

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

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ADDITIONAL CLINICAL STUDIES

NYVEPRIA showed no clinically meaningful differences to Neulasta-US[3]

- In healthy subjects, no clinically meaningful differences in immunogenicity risk were observed between NYVEPRIA and Neulasta-US
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CLINICAL PHARMACOLOGY (PD/PK)

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NAb=neutralizing antibody; TK=toxicokinetic.

*Product sourced from the EU is often used as a comparator in trials to demonstrate biosimilarity.

CLOSE

- Reactions have included anaphylaxis

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Biosimilars: Highly similar versions of existing biologic medicines[7]

- 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[7,8]

Development pathways

- The goal of biosimilar development is to demonstrate that there are no clinically meaningful differences based on the totality of evidence[7,8]
- Analytical studies are the foundation of biosimilar development and provide the greatest sensitivity for detecting differences between a biosimilar and its reference product[7,8]

Click to enlarge

Please see Important Safety Information and Indication on pages 25-27 and full Prescribing Information, Patient Information, and Instructions for Use, also available at NyvepriaHCP.com.

SELECTED SAFETY INFORMATION

Warnings and Precautions

Splenic Rupture

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

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CLOSE

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- Evaluate for an enlarged spleen or splenic rupture in patients who report left upper abdominal or shoulder pain after receiving NYVEPRIA

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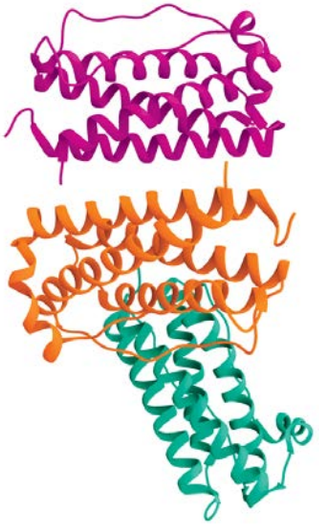
NYVEPRIA® (pegfilgrastim-apgf) and Neulasta® (pegfilgrastim) have a highly similar higher-order structure (protein folding)[3]

X-ray crystallography



- NYVEPRIA, Neulasta-EU, and Neulasta-US have equivalent in vitro potency
- NYVEPRIA showed no clinically meaningful differences in immunogenicity risk vs Neulasta in healthy subjects
- NYVEPRIA showed comparable incidence of adverse events of special interest vs Neulasta-EU and Neulasta-US in healthy subjects

Please see Important Safety Information and Indication on pages 25-27 and full Prescribing Information, Patient Information, and Instructions for Use, also available at NyvepriaHCP.com.

SELECTED SAFETY INFORMATION

Warnings and Precautions (continued)

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 NYVEPRIA
- Discontinue NYVEPRIA in patients with ARDS

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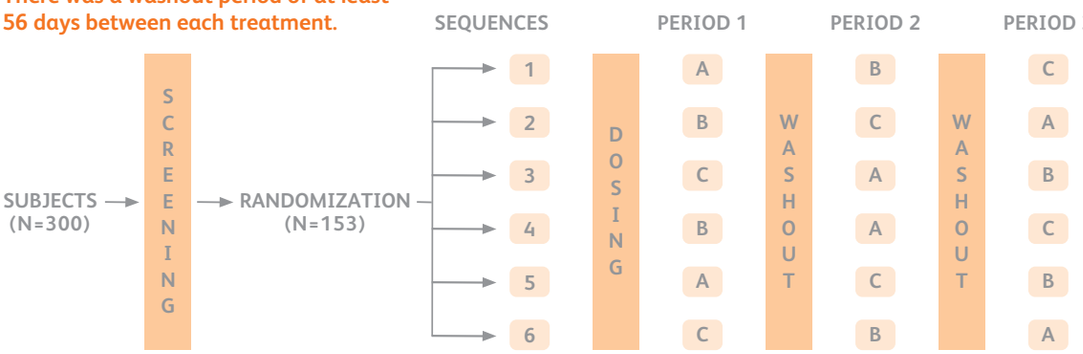
Study to assess PD/PK similarity in healthy subjects[3]

Study design

There was a washout period of at least 56 days between each treatment.



- Treatment A: NYVEPRIA, 6 mg, single SC injection in the deltoid region
- Treatment B: Neulasta-US, 6 mg, single SC injection in the deltoid region
- Treatment C: Neulasta-EU, 6 mg, single SC injection in the deltoid region*

Study description

- A single-center, randomized, open-label, single-dose, comparator-controlled, 3-treatment, 3-period, 6-sequence crossover study that assessed the PD and PK profiles of NYVEPRIA compared with Neulasta-US and Neulasta-EU following SC administration in healthy subjects

SC=subcutaneous.

*Product sourced from the EU is often used as a comparator in trials to demonstrate biosimilarity.

Study Design
PD Equivalence
PK Equivalence

Please see Important Safety Information and Indication on pages 25-27 and full Prescribing Information, Patient Information, and Instructions for Use, also available at NyvepriaHCP.com.

SELECTED SAFETY INFORMATION

Warnings and Precautions (continued)

Serious Allergic Reactions

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

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Study to assess PD/PK similarity in healthy subjects[3]

Primary PD/PK endpoints

- The primary PD endpoints were $AUEC_{ANC}$ from the time of dose administration to 288 hours after dose administration and the maximum observed value for ANC (ANC_C_{max})
  - PD equivalence was assessed by constructing the 90% CIs for the GMR (test/reference) for $AUEC_{ANC}$ and ANC_C_{max}
- The primary PK endpoints were $AUC_{0-\infty}$ and C_{max}
  - PK equivalence was assessed by constructing the 90% CIs for the GMR (test/reference) for $AUC_{0-\infty}$ and C_{max}. PK equivalence was concluded if the 90% CIs for both $AUC_{0-\infty}$ and C_{max} were completely contained within the acceptance limits of 80% to 125%

ANC=absolute neutrophil count; AUEC=area under the effect curve; CI=confidence interval; C_{max}=maximum observed serum pegfilgrastim concentration; GMR=geometric mean ratio.

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SELECTED SAFETY INFORMATION
Warnings and Precautions (continued)
Use in Patients with Sickle Cell Disorders

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

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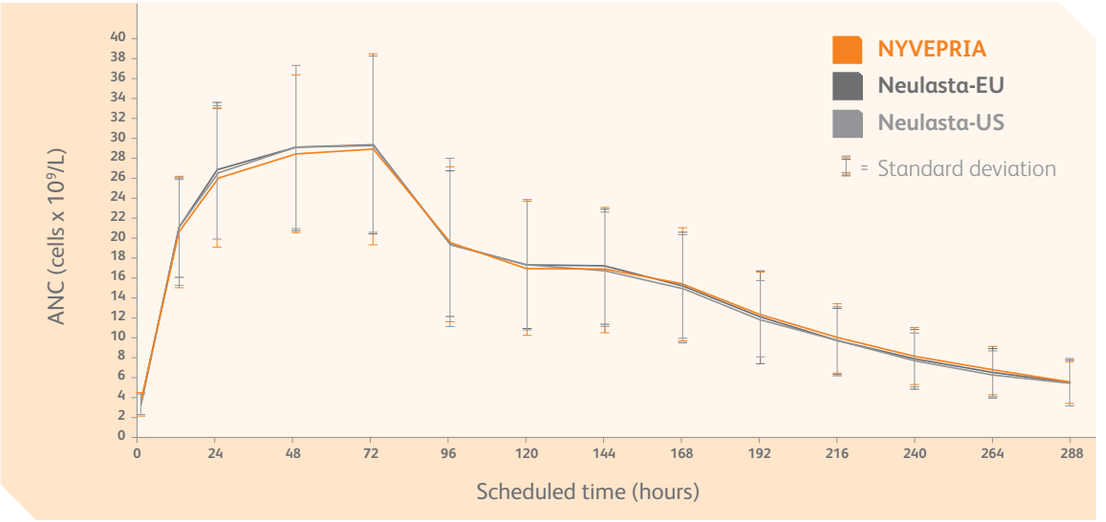
Introduction
Data Summary
FDA Evaluation
Similar Structure and Function
PD/PK Profiles
Immunogenicity
Safety Evaluation

NYVEPRIA® (pegfilgrastim-apgf) PD analysis established equivalence to Neulasta® (pegfilgrastim) in support of biosimilarity[3]

Mean ANC over time in healthy subjects*



The 90% CIs for $AUEC_{ANC}$ and ANC_C_{max} were completely contained within the predefined equivalence limit of 80% to 125% for all study drug comparisons.

*A total of 143 subjects, assigned to 1 of the 6 sequence groups, were included in the PD and PK populations; 10 subjects confirmed positive for antipegfilgrastim antibodies were excluded from PD and PK analyses.

Study Design
PD Equivalence
PK Equivalence

Please see Important Safety Information and Indication on pages 25-27 and full Prescribing Information, Patient Information, and Instructions for Use, also available at NyvepriaHCP.com.

SELECTED SAFETY INFORMATION

Warnings and Precautions (continued)

Glomerulonephritis

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

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Introduction
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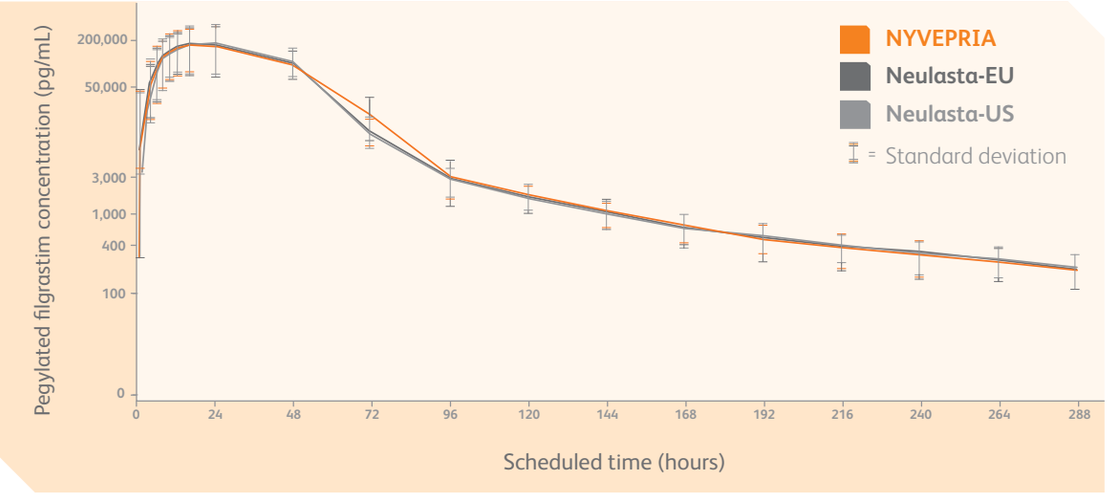
Safety Evaluation

NYVEPRIA® (pegfilgrastim-apgf) PK analysis established equivalence to Neulasta® (pegfilgrastim) in support of biosimilarity[3]

Primary PK endpoint of mean serum concentration over time was similar across treatments among healthy subjects



The 90% CIs for $AUC_{0-\infty}$ and C_{max} were completely contained within the predefined equivalence limit of 80% to 125% for all study drug comparisons.

Study Design
PD Equivalence
PK Equivalence

Please see Important Safety Information and Indication on pages 25-27 and full Prescribing Information, Patient Information, and Instructions for Use, also available at NyvepriaHCP.com.

SELECTED SAFETY INFORMATION

Warnings and Precautions (continued)

Leukocytosis

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

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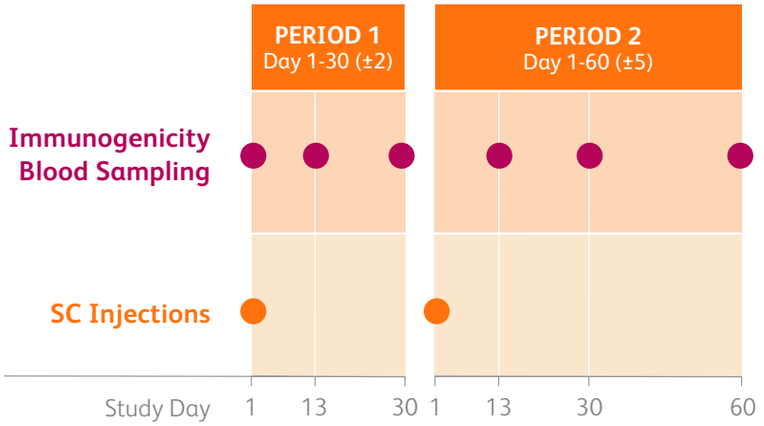
*A comparative clinical study assessed the immunogenicity of NYVEPRIA® (pegfilgrastim-apgf) vs Neulasta® (pegfilgrastim) in healthy subjects[3]**



Primary endpoint

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

Secondary endpoint

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

*Based on an open-label, randomized, multiple-dose, parallel design, noninferiority, 2-treatment, 2-period study of 422 healthy subjects.

Study Design
Study Results

Please see Important Safety Information and Indication on pages 25-27 and full Prescribing Information, Patient Information, and Instructions for Use, also available at NyvepriaHCP.com.

SELECTED SAFETY INFORMATION

Warnings and Precautions (continued)

Thrombocytopenia

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

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Introduction
Data Summary
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Similar Structure and Function
PD/PK Profiles
Immunogenicity
Safety Evaluation

No clinically meaningful differences in immunogenicity risk observed between NYVEPRIA® (pegfilgrastim-apgf) and Neulasta® (pegfilgrastim)[3]

	NYVEPRIA n (%) (n=208)	Neulasta n (%) (n=209)	Risk difference (%)	90% CI
Antipegfilgrastim antibody	12 (5.9) (n=204)	15 (7.5) (n=201)	-1.580	-5.915-2.675
Positive NAb	0 (n=204)	0 (n=201)	0	

- The upper bound of the 90 % CI of risk difference was below the prespecified margin of 10 %, establishing the noninferiority of NYVEPRIA to Neulasta-US
- No evidence of NAbs was observed in any subject

Study Design
Study Results

Please see Important Safety Information and Indication on pages 25-27 and full Prescribing Information, Patient Information, and Instructions for Use, also available at NyvepriaHCP.com.

SELECTED SAFETY INFORMATION

Warnings and Precautions (continued)

Capillary Leak Syndrome (CLS)

- CLS has been reported after granulocyte-colony stimulating factor (G-CSF) administration, including pegfilgrastim 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 a need for intensive care

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TEAEs were comparable in a pooled analysis of 2 comparative studies[3]

TEAEs (TREATMENT RELATED) IN ≥5% OF HEALTHY SUBJECTS

Preferred Term	NYVEPRIA (n=358) n (%)	Neulasta® (pegfilgrastim) (n=356) n (%)
Abdominal pain	15 (4.2)	19 (5.3)
Nausea	34 (9.5)	31 (8.7)
Injection site pain	30 (8.4)	25 (7.0)
Back pain	133 (37.2)	132 (37.1)
Musculoskeletal pain	163 (45.5)	153 (43.0)
Myalgia	26 (7.3)	35 (9.8)
Pain in extremity	37 (10.3)	35 (9.8)
Dizziness	20 (5.6)	6 (1.7)
Headache	206 (57.5)	200 (56.2)

- Adverse events for NYVEPRIA were consistent with the known safety profile of Neulasta
- The incidence of TEAEs of special interest was comparable between NYVEPRIA and Neulasta
- No new significant safety information as compared to the established safety profile of Neulasta was identified

TEAEs=treatment-emergent adverse events.

Please see Important Safety Information and Indication on pages 25-27 and full Prescribing Information, Patient Information, and Instructions for Use, also available at NyvepriaHCP.com.

SELECTED SAFETY INFORMATION

Warnings and Precautions (continued)

Potential for Tumor Growth Stimulatory Effects on Malignant Cells

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

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Important Safety Information and Indication

Contraindications

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

Warnings and Precautions

Splenic Rupture

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

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 NYVEPRIA
- Discontinue NYVEPRIA 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
- Allergic reactions, including anaphylaxis, can recur within days after the discontinuation of initial anti-allergic treatment
- Permanently discontinue NYVEPRIA in patients with serious allergic reactions
- Do not administer NYVEPRIA to patients with a history of serious allergic reactions to pegfilgrastim products or filgrastim products

Use in Patients with Sickle Cell Disorders

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

Please see Important Safety Information and Indication on pages 25-27 and full Prescribing Information, Patient Information, and Instructions for Use, also available at NyvepriaHCP.com.

SELECTED SAFETY INFORMATION

Warnings and Precautions (continued)

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

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Important Safety Information and Indication

Glomerulonephritis

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

Leukocytosis

- White blood cell counts of 100 x 10^9/L or greater have been observed in patients receiving pegfilgrastim products
- Monitoring of complete blood count (CBC) during NYVEPRIA 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 granulocyte-colony stimulating factor (G-CSF) administration, including pegfilgrastim 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 a need for intensive care

Potential for Tumor Growth Stimulatory Effects on Malignant Cells

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

Please see Important Safety Information and Indication on pages 25-27 and full Prescribing Information, Patient Information, and Instructions for Use, also available at NyvepriaHCP.com.

SELECTED SAFETY INFORMATION
Warnings and Precautions (continued)

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 (eg, c-reactive protein and white blood cell count)
- Consider aortitis in patients who develop these signs and symptoms without known etiology. Discontinue NYVEPRIA if aortitis is suspected

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Important Safety Information and Indication

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

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- 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 NYVEPRIA 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

INDICATION

NYVEPRIA 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

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

Please see Important Safety Information and Indication on pages 25-27 and full Prescribing Information, Patient Information, and Instructions for Use, also available at NyvepriaHCP.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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NYVEPRIA® (pegfilgrastim-apgf): Pfizer Oncology's commitment to building onto the clinical experience of pegfilgrastim

Pfizer

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

Favorable coverage[3]

Potential savings[3]

Support for you and your patients

Approved for the eligible indication of Neulasta® (pegfilgrastim), with an identical dosing and administration schedule[1]

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

Please see Important Safety Information and Indication on pages 25-27 and full Prescribing Information, Patient Information, and Instructions for Use, also available at NyvepriaHCP.com.

SELECTED SAFETY INFORMATION

Most Common Adverse Reactions

- Bone pain
- Pain in extremity

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Summary

References

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SELECTED SAFETY INFORMATION

Contraindications

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

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