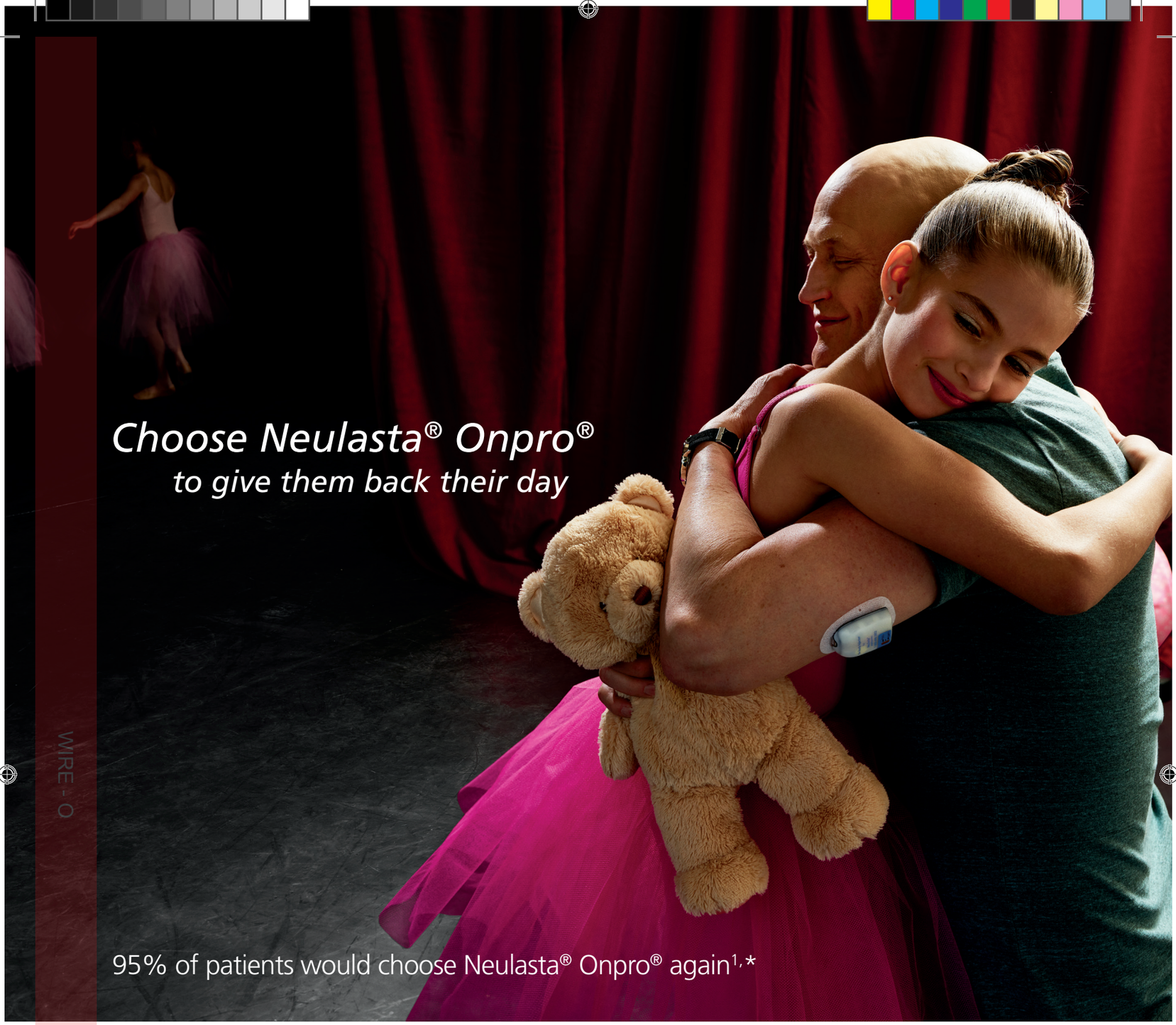


Indication

Neulasta® and NEUPOGEN® are 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 clinically significant incidence of febrile neutropenia.

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

*2016 data from interviews with oncology patients who have had experience with Neulasta® (N=227, PFS n=150, Neulasta® Onpro® n=77). Patients who had received Neulasta® via Neulasta® Onpro® were asked to answer the question: Based on your personal experience getting your Neulasta® with Neulasta® Onpro®, if your doctor said you needed to use Neulasta® again in the future, would you request getting it with Neulasta® Onpro® again? (Study Design 1)[1]
PFS, prefilled syringe.

Please see full Important Safety Information on pages 18-19.

See pages 22-23 for full study designs.

AMGEN®

Neulasta® (pegfilgrastim) injection Onpro® kit

Patient-chosen

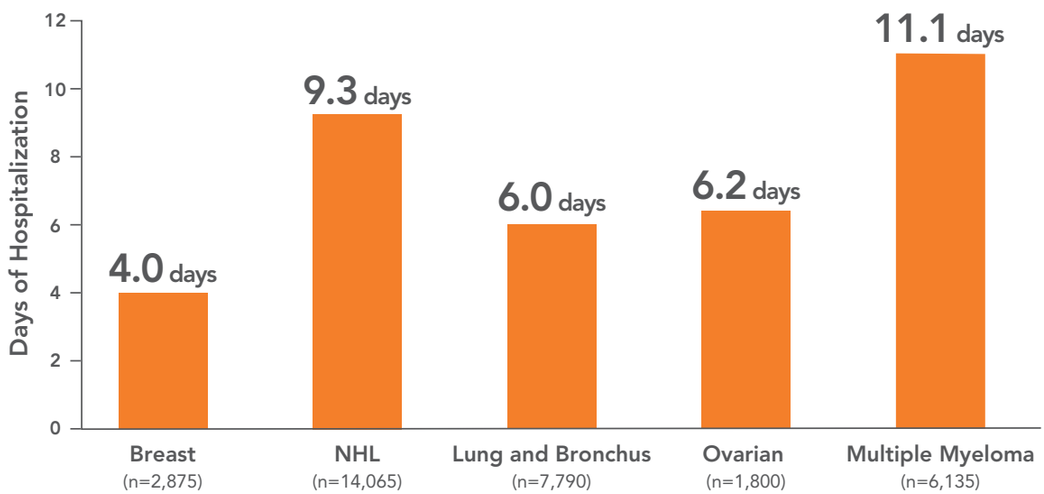
Can more be done to reduce the impact of febrile neutropenia?

91,000+ hospitalizations among adult patients with cancer-related neutropenia in the United States in 2012[2,*]

Leading to an average hospital stay of **nearly 10 days, with an average cost of almost $25,000***

Average length of stay and cost for FN hospitalizations among adult patients with select tumor types*

Medicare, commercial insurance, and other types of coverage based on hospital discharge data



Cost of hospital stay	$8,033	$25,676	$12,532	$12,579	$30,042

A retrospective cohort study (N=91,560 patients) conducted with 2012 hospital discharge data from the Agency for Healthcare Research and Quality Nationwide Inpatient Sample all-payer database. Hospitalizations may or may not have been caused by chemotherapy (Study Design 2).[2]

***Subjects in these studies may or may not have received G-CSF support prior to FN hospitalization.**
FN, febrile neutropenia; G-CSF, granulocyte colony-stimulating factor; NHL, non-Hodgkin's lymphoma.

See pages 22-23 for full study designs.

The impact of febrile neutropenia extends beyond initial hospitalization

A SEPARATE STUDY SHOWED

Following discharge from the hospital, FN-related care can add **another 32%** to the initial cost of hospitalization[3]

Retrospective observational study using 2001–2003 claims data from the Ingenix database representing medical and pharmacy claims from a national health plan (n=373) (Study Design 3).[3]

IN A SEPARATE STUDY

Approximately **24% of patients** were readmitted to the hospital within 30 days[4,*,†]

Retrospective cohort study conducted with 2007–2010 hospital discharge data from the Premier database. Included 16,273 patients hospitalized with FN. Tumor types included breast, lung, colorectal, ovarian, NHL, and Hodgkin's lymphoma. Primary endpoints included length of stay for each patient's first FN-related hospitalization.[4]

***Subjects in these studies may or may not have received G-CSF support prior to FN hospitalization.**
†All-cause readmission.

See pages 22-23 for full study designs.

National guidelines recommend assessing risk of febrile neutropenia before every cycle[5,6]

According to the American Society of Clinical Oncology (ASCO) and the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Evaluate the risk of FN and administer primary CSF prophylaxis in first and subsequent cycles for patients at approximately > 20% risk[5,6]

When assessing risk, evaluate both chemotherapy regimen and patient risk factors[6]

Select chemotherapy regimens associated with a HIGH RISK OF FN

Breast cancer

- TC (docetaxel + cyclophosphamide)[6,7]
- TCH (docetaxel + carboplatin + trastuzumab)[6]
- TAC (docetaxel + doxorubicin + cyclophosphamide) Q3W[6,8]

Non-Hodgkin's lymphoma

- BR (bendamustine + rituximab)[9,*]
- CHOP ± R (cyclophosphamide + doxorubicin + vincristine + predniso[lo]ne with or without rituximab) Q3W[10,11,†]
- Dose-adjusted EPOCH (etoposide + prednisone + vincristine + cyclophosphamide + doxorubicin)[6]

Non-small cell lung cancer

- Carboplatin + paclitaxel Q3W[12,†]

Small cell lung cancer

- Topotecan[6]

Select chemotherapy regimens associated with an INTERMEDIATE RISK OF FN

Breast cancer

- AC (doxorubicin + cyclophosphamide) + sequential docetaxel[13]

Prostate cancer

- Cabazitaxel[6]
- Docetaxel + prednisone[14,*]

Small cell lung cancer

- Carboplatin + etoposide[6]

Testicular cancer

- Etoposide + cisplatin[6]

Neulasta® 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 clinically significant incidence of febrile neutropenia. Neulasta® is not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation.

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

*Select regimens not listed by the NCCN.
†Select regimens listed by the NCCN as intermediate risk.
CSF, colony-stimulating factor; FN, febrile neutropenia; NCCN, National Comprehensive Cancer Network; Q3W, once every 3 weeks.

Important Safety Information

Contraindication

- Neulasta® or NEUPOGEN® are contraindicated in patients with a history of serious allergic reactions to human granulocyte colony-stimulating factors (G-CSFs), such as pegfilgrastim or filgrastim

Splenic Rupture

- Splenic rupture, including fatal cases, can occur following the administration of Neulasta® and NEUPOGEN®
- Evaluate for an enlarged or ruptured spleen in patients who report left upper abdominal or shoulder pain

Please see full Important Safety Information on pages 18-19.

Even one of these select risk factors can increase risk:[6,*]

- Baseline cytopenias[5,6,15,16]
- Poor performance status (ECOG ≥ 2)[5,6,17,18]
- Age ≥ 65 years[5,6]
- COPD[19,†]
- Chronic immunosuppression in the post-transplant setting, including organ transplant[6]
- Liver disease[5,6,19]
- Renal disease[5,6,15]
- Cardiovascular disease[5,19,†]
- Diabetes[19,20,†]
- Prior chemotherapy[5,6,20]
- Prior radiotherapy[5,6]
- Poor nutritional status[5,†]
- Decreased serum albumin[18,21,†]
- Open wounds/recent surgery[5,6]
- Active infections[5,21,†]
- HIV[5,6]
- Metastatic[5,†]
- Elevated lactate dehydrogenase[15,18,21,†]

NCCN Guidelines: If your patient is on an **intermediate-risk regimen** and has **1 or more risk factors**, consider pegfilgrastim (Neulasta® or Neulasta® Onpro®)[6]

*The patient risk factors included here have been identified through published literature and clinical guidelines. This list is not exhaustive. There may be other risk factors that apply based on available research and the clinical judgment of the treating physicians.
†Risk factors not listed by the NCCN.
COPD, chronic obstructive pulmonary disease; ECOG, Eastern Cooperative Oncology Group; HIV, human immunodeficiency virus.

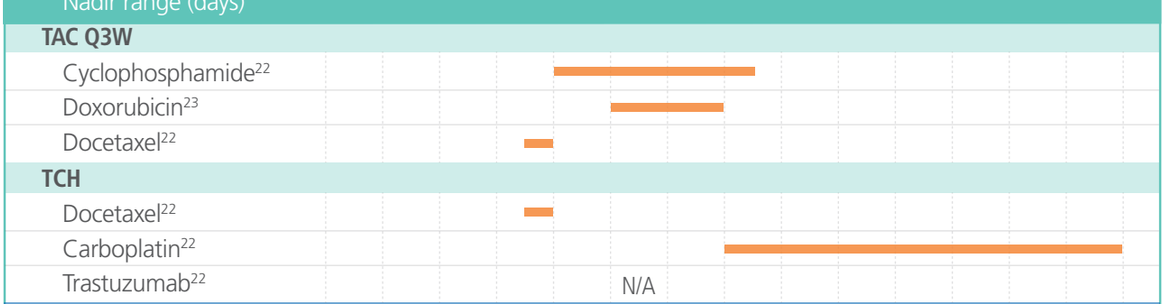
Neulasta® (pegfilgrastim) injection Onpro® kit

WIRE - O

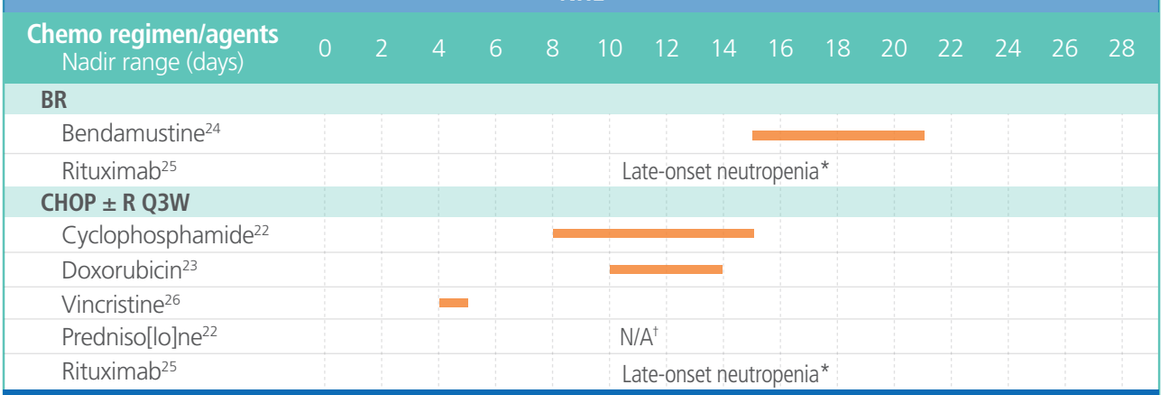
Neutrophil nadirs can be unpredictable and vary by chemotherapy agent

Select chemotherapy regimens associated with a HIGH RISK OF FN

BREAST CANCER

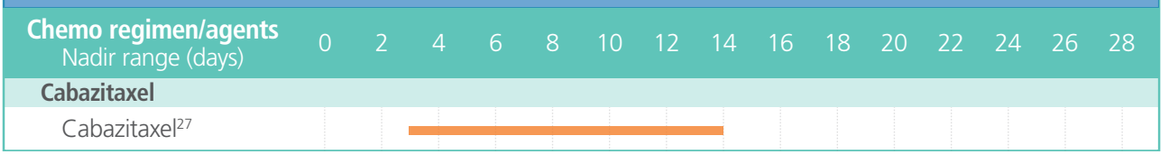


NHL



Select chemotherapy regimens associated with an INTERMEDIATE RISK OF FN

PROSTATE CANCER



*Rituximab has been associated with late-onset neutropenia (defined as occurring at least 60 days after the last treatment). In a retrospective evaluation of patients with diffuse large B-cell lymphoma receiving CHOP-R, the median time to neutrophil nadir (ANC=0.66 x 10^9/L) was 129 days.[25]
†Not an antineoplastic agent.

ANC, absolute neutrophil count; FN, febrile neutropenia; NHL, non-Hodgkin's lymphoma; Q3W, once every 3 weeks.

Important Safety Information

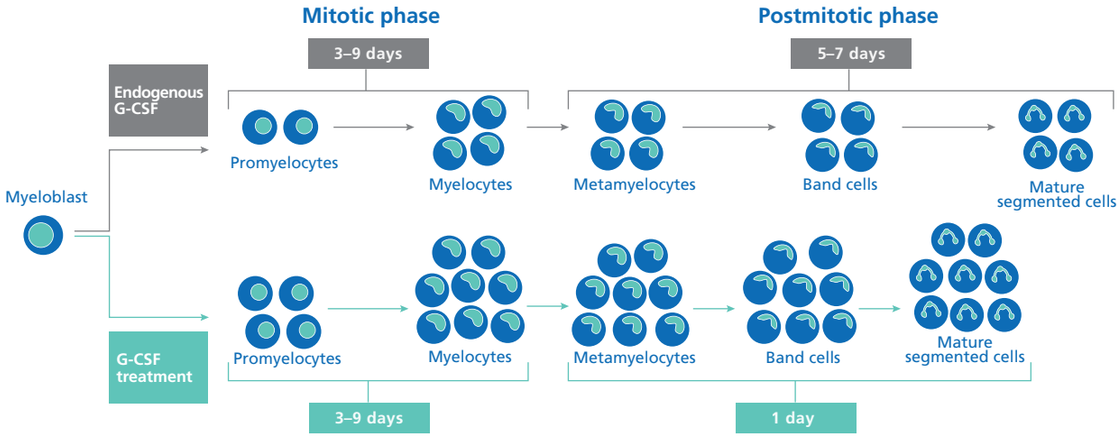
Acute Respiratory Distress Syndrome (ARDS)

- ARDS has occurred in patients receiving Neulasta® and NEUPOGEN®
- Evaluate patients who develop a fever and lung infiltrates or respiratory distress after receiving Neulasta® or NEUPOGEN®
- Discontinue Neulasta® or NEUPOGEN® in patients with ARDS

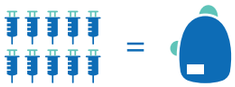
Please see full Important Safety Information on pages 18-19.

A missed dose of a short-acting G-CSF can cause a rapid decline of neutrophil counts during the neutrophil nadir[28-31]

Neutrophil development is sensitive to stimulation with a G-CSF[28-31]



After discontinuation of a short-acting G-CSF, circulating neutrophils may decrease by 50% within 1 to 2 days and return to pretreatment levels within 1 week[32,33]



Rate of FN increases when a patient receives fewer than 10–11 doses of NEUPOGEN®, based on clinical trials[34,35,*]

On average, patients only receive 3 injections of NEUPOGEN® or Zarxio® in each cycle of chemotherapy[36,†]

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Myeloid Growth Factors recommend the use of prophylactic G-CSFs for select patients

There are studies that show that shorter duration of short-acting G-CSFs may be less efficacious[6,37]

Administer NEUPOGEN® 24 hours after cytotoxic chemotherapy, and daily for up to 2 weeks until ANC has reached 10,000/mm^3 following expected chemotherapy-induced neutrophil nadir.[32]

*Based on a retrospective analysis of claims data from approximately 18,000 patients receiving more than 58,000 cycles of chemotherapy from January 1, 2004, to April 30, 2010 HIRD, and January 1, 2001, to August 31, 2009 (OptumInsight) (Study Design 4).[35]
†Based on an analysis of the OSCER database. The total sample used is based on cycles of myelosuppressive chemotherapy treated with NEUPOGEN® and Zarxio® (652 cycles and 186 cycles respectively). This study is unprojected and limited to community-based oncology clinics; it is only reflective of treatment practices contained within OSCER (Study Design 5).[36]

G-CSF, granulocyte colony-stimulating factor; HIRD, HealthCore Integrated Research Database; NCCN, National Comprehensive Cancer Network; OSCER, Oncology Services Comprehensive Electronic Records.

See pages 22-23 for full study designs.

Indication

Patients with Cancer Receiving Myelosuppressive Chemotherapy

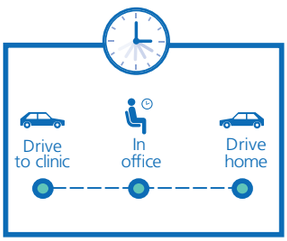
NEUPOGEN® is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever.

Please see full Important Safety Information on pages 18-19.

Neulasta® (pegfilgrastim) injection Onpro® kit

Give them back the day after chemotherapy with Neulasta® Onpro®[1,38]

9 OUT OF 10 patients reported feeling tired, fatigued, drained, and exhausted after receiving chemotherapy[39,*]



Traveling for injections the day after chemotherapy is time-consuming for patients and caregivers[40,†]

- Patients and caregivers may need to make several arrangements for a next-day G-CSF treatment

Nearly 2/3 of patients had a companion drive them to the clinic[40]

How would your day change if you had fewer next-day injection appointments?

*Data from interviews with Neulasta® treatment-experienced oncology patients (N=227, PFS n=150, Neulasta® Onpro® n=77) conducted in November 2016 (Study Design 6).[39]
†Total time spent in the office, including wait time and time spent traveling for a return visit for G-CSF injection, was reported by respondents in a prospective cohort study of 598 adult patients with ESBC. 33.5% (~1/3rd) of patients drove themselves to the clinic; 64.5% (~2/3rd) of patients had a companion drive to the clinic. Patients included those treated with daily-dose filgrastim and those receiving once-per-cycle pegfilgrastim injections. On average, patients spend 1.73 hours per clinic visit for a G-CSF injection.[40]
ESBC, early-stage breast cancer; G-CSF, granulocyte colony-stimulating factor; PFS, prefilled syringe.

See pages 22-23 for full study designs.

Important Safety Information

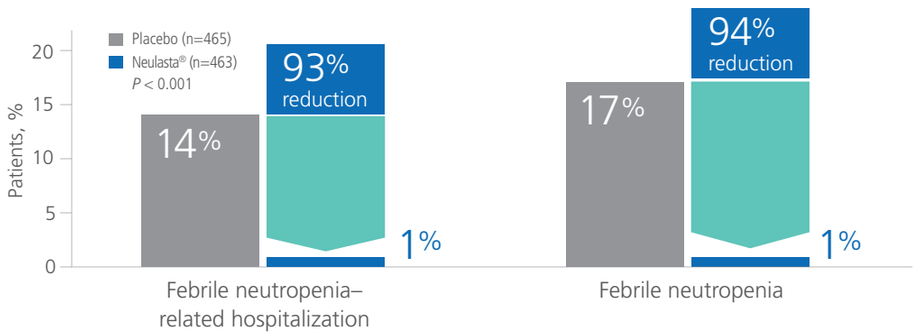
Serious Allergic Reactions

- Serious allergic reactions, including anaphylaxis can occur in patients receiving Neulasta® and NEUPOGEN®
- Provide symptomatic treatment for allergic reactions
- Majority of events occurred upon initial exposure and can recur within days after discontinuation of initial anti-allergic treatment
- Permanently discontinue Neulasta® or NEUPOGEN® in patients with serious allergic reactions

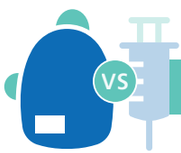
Please see full Important Safety Information on pages 18-19.

Choose Neulasta® Onpro® every cycle to help ensure next-day Neulasta® delivery[38]

Next-day Neulasta® reduced the incidence of FN* and FN-related hospitalization when used every cycle[41]



Phase 3, multicenter, multinational, double-blind, placebo-controlled trial of patients with breast cancer (Neulasta® or placebo) receiving 100 mg/m^2 docetaxel Q3W for up to 4 cycles. The key endpoint was the percentage of patients who developed FN.* A key secondary endpoint was the incidence of hospitalization (Study Design 7).[41]



Adherence to G-CSF therapy was

higher with Neulasta® Onpro®

than with the PFS[42]

- Adherence is defined as proportion of patients receiving treatment according to Clinical Practice Guidelines[43]
- Adherence in this analysis was based on a comparative analysis of Neulasta® doses administered by PFS versus Neulasta® Onpro® and was conducted using data from OSCER on 389,000 oncology patients who were seen in 2016. Percentage of dose administered was calculated by taking the sum of patients' chemotherapy cycles with Neulasta® and dividing by the sum of their total chemotherapy cycles. Both arms were assumed to have received the treatment as prescribed (Study Design 8)[42]

How might a missed PFS appointment affect infection risk?

*FN = temperature ≥ 38.2°C and ANC < 0.5 x 10^9/L.[41]
ANC, absolute neutrophil count; FN, febrile neutropenia; IV, intravenous; OSCER, Oncology Services Comprehensive Electronic Records; Q3W, once every 3 weeks.

See pages 22-23 for full study designs.

Important Safety Information

Allergies to Acrylics

- On-body Injector for Neulasta® uses acrylic adhesives
- Patients who are allergic to acrylic adhesives may have a significant reaction

Use in Patients with Sickle Cell Disorders

- In patients with sickle cell trait or disease, sickle cell crisis, in some cases fatal, can occur in patients receiving Neulasta® and NEUPOGEN®. Discontinue if sickle cell crisis occurs.

Please see full Important Safety Information on pages 18-19.

Neulasta® (pegfilgrastim) injection Onpro® kit

Febrile neutropenia risk increases when Neulasta® is not administered the day after chemotherapy[41,44]

NCCN Guidelines® state that based on clinical trial data, pegfilgrastim (Neulasta®) should be administered the day after chemotherapy (category 1 recommendation)[6]

23% of Neulasta® cycles were administered on days other than the day after chemotherapy[44]

The study included **over 200,000 Neulasta® cycles** from 2 patient databases. Over 90% of patients were ≤ 65 years of age.

18% increased risk of FN when Neulasta® was administered on days other than the day after chemotherapy[44,*]

FN rate for the day after chemotherapy vs all other days of Neulasta® administration was 2.53% and 3.04%, respectively[44]

Retrospective cohort analysis based on health care claims from IMS PharMetrics Plus™ and Truven Health Analytics MarketScan® Commercial and Medicare Supplemental Databases. The collective data include health care claims from private US health plans, covering over 30 million persons and over 200,000 cycles of chemotherapy annually between July 1, 2010, and September 30, 2015 (Study Design 9).[44]

Do not administer Neulasta® between 14 days before and 24 hours after administration of chemotherapy.[38]

Neulasta® Onpro® is designed to deliver **27 hours after application** in accordance with labeling[38]

*18% is the increase in the odds of FN comparing administration on day 1 (the day after the last day of chemotherapy; absolute risk 2.53%) to other days (including same day [the last day of chemo administration] and days 2–5 [after the last day of chemo administration]; absolute risk 3.04%). The 18% result was estimated using an adjusted analysis (using generalized estimating equations) to account for differences in patient, cancer, and treatment characteristics.[44]

†Do not administer Neulasta® the same day as chemotherapy.[38]

ANC, absolute neutrophil count; CHOP-R, cyclophosphamide + doxorubicin + vincristine + prednisone + rituximab; CI, confidence interval; FN, febrile neutropenia; NCCN, National Comprehensive Cancer Network; NHL, non-Hodgkin's lymphoma.

See pages 22-23 for full study designs.

Important Safety Information

Glomerulonephritis

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

Please see full Important Safety Information on pages 18-19.

Febrile neutropenia risk increases when Neulasta® is not administered every cycle[45,46]

Neulasta® treatment first two cycles only:[45]

3.6x increased risk of febrile neutropenia in an open-label, phase 3 noninferiority study of patients with breast cancer receiving select myelosuppressive chemotherapy regimens[45]

10% of patients developed FN when given Neulasta® every cycle (n=84)[45]

36% of patients developed FN when given Neulasta® in the first 2 cycles only (n=83)[45]

Patients with breast cancer at risk of FN were randomly assigned to Neulasta® throughout all chemotherapy cycles (n=84) or Neulasta® in cycles 1 and 2 only (n=83). A 6-mg fixed dose of Neulasta® was administered 24–30 hours after chemotherapy administration. Primary endpoint was the percentage of patients who developed FN.[45]
Fever = body temperature ≥ 38.5°C once or ≥ 38.0°C for > 12 hours.[45]
Neutropenia = ANC ≤ 0.5 x 10^9/L or ANC ≤ 1.0 x 10^9/L and expected to fall below 0.5 within the next 24 hours.[45]

Neulasta® treatment at physician's discretion:[46]

2.5x increased risk of febrile neutropenia in an open-label, phase 4, prospective study of patients with NHL treated with CHOP-R[46]

15% of patients developed FN when given Neulasta® every cycle (n=73; 95% CI, 8%–25%)[46]

37% of patients developed FN when given Neulasta® at physician's discretion (n=73; 95% CI, 26%–49%)[46]

Open-label, randomized, phase 4, prospective, multicenter, community-based study of patients with solid tumors or NHL (N=852). Patients were randomized to every-cycle Neulasta®, or Neulasta® in any cycle after cycle 1 at the physician's discretion. Data shown are for a post hoc subset analysis of patients with NHL (n=73 patients in each study arm). Most NHL patients (82%, n=120) received CHOP-R. The primary endpoint was the incidence of patients experiencing FN.[46]
FN = ANC < 1.0 x 10^9/L and temperature ≥ 38°C occurring on the same day.[46]

ANC, absolute neutrophil count; CHOP-R, cyclophosphamide + doxorubicin + vincristine + prednisone + rituximab; CI, confidence interval; FN, febrile neutropenia; NCCN, National Comprehensive Cancer Network; NHL, non-Hodgkin's lymphoma.

See pages 22-23 for full study designs.

Important Safety Information

Capillary Leak Syndrome (CLS)

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

Please see full Important Safety Information on pages 18-19.

Neulasta® (pegfilgrastim) injection Onpro® kit

WIRE - O

Neulasta® Onpro®: Patient-chosen protection[1,*]

95% of patients and nurses would choose Neulasta® Onpro® again[1,47,†,‡]

Not having to return to the doctor’s office the day after chemotherapy just for an injection was the most important factor for patients when choosing a G-CSF[1,§]

- Patients also valued **how much experience** their doctor has with the G-CSF they will receive and **being informed** by the doctor or nurse of all available ways to receive the G-CSF[1]

The National Comprehensive Cancer Network® (NCCN®) recognizes the On-body Injector as an appropriate option for delivering the full dose of pegfilgrastim (Neulasta®) the day after chemotherapy[6]

*In a key study of 928 patients with breast cancer, when given once every chemotherapy cycle, 17% of patients got infections when not treated with Neulasta®—while only 1% of patients got infections when treated with Neulasta®.[41]
†2016 data from interviews with oncology patients who have had experience with Neulasta® (N=227, PFS n=150, Neulasta® Onpro® n=77). Patients who had received Neulasta® via Neulasta® Onpro® were asked to answer a survey (Study Design 10).[1]
‡Data from interviews with oncology nurses (N=250) conducted in October 2016. Respondents were asked if they agree with this statement: Based on my Neulasta® Onpro® experience, when my patients are appropriate for Neulasta® (PFS or Neulasta® Onpro®), I would choose Neulasta® Onpro® (Study Design 10).[47]
§November 2016 data from interviews with oncology patients who have had experience with Neulasta® (N=227, PFS n=150, Neulasta® Onpro® n=77). Patients were asked a multiple-choice selection prompt (Study Design 11).[1]
G-CSF, granulocyte colony-stimulating factor; PFS, prefilled syringe.

See pages 22-23 for full study designs.

Important Safety Information

Thrombocytopenia

- Thrombocytopenia has been reported in patients who received NEUPOGEN®
- Monitor platelet counts

Please see full Important Safety Information on pages 18-19.

Amgen: Unwavering dedication to every patient, every time

Joan

Shelley

Safiya

Patients like these have benefited from 35 years of our G-CSF innovation, culminating in Neulasta® Onpro®

NEUPOGEN® (FILGRASTIM) INJECTION
FDA APPROVED
February 1991
The first biologic approved to reduce the incidence of chemotherapy-induced FN

Neulasta® (pegfilgrastim) injection
FDA APPROVED
January 2002
Enabled patients to receive just 1 G-CSF injection instead of 10 to 11[34,35,*]

Neulasta® (pegfilgrastim) injection Onpro® kit
FDA APPROVED
December 2014
Redefined the patient experience by giving them an opportunity to not return to the office just for their Neulasta® shot the day after chemotherapy

Neulasta® (pegfilgrastim) injection Onpro® kit
Enhancements to Neulasta® Onpro®
November 2016
Designed to improve ease of use for healthcare providers

Comprehensive Support

- Helping patients access Amgen medicines whenever possible
- Best-in-class resources for patients[48]

*Please see information on page 7.
FN, febrile neutropenia; G-CSF, granulocyte colony-stimulating factor.

Important Safety Information

Leukocytosis

- White blood cell counts of ≥ 100,000/mm^3 have been observed in patients who received NEUPOGEN® and Neulasta®
- Monitor CBCs during Neulasta® therapy and at least twice weekly for NEUPOGEN®
- Adjust NEUPOGEN® dosing as clinically indicated to help mitigate risk of leukocytosis
- Dosages of NEUPOGEN® that increase the absolute neutrophil count (ANC) beyond 10,000/mm^3 may not result in any additional clinical benefit
- Discontinuation of NEUPOGEN® 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 full Important Safety Information on pages 18-19.

Amgen is committed to being the partner of choice for you and your patients

Commitment

- Amgen has an ongoing commitment to deliver guaranteed supply to our customers

zero supply shortages in the last decade[49]

- Amgen maintains a surplus of inventory and operates an integrated network of manufacturing facilities to ensure product availability

Amgen makes significant investments in risk mitigation to ensure safety and supply

- Despite a major hurricane damaging Puerto Rico in 2017, Amgen did not experience shortages of products, in part, because of continuity plans[50]

Amgen employees displaying the first batch of product produced after Hurricane Maria in 2017

- Amgen supported the local community with resources in the hurricane aftermath, and the Amgen Foundation pledged $5 million to support both urgent and long-term Hurricane Maria relief efforts[50]

Important Safety Information

Cutaneous Vasculitis

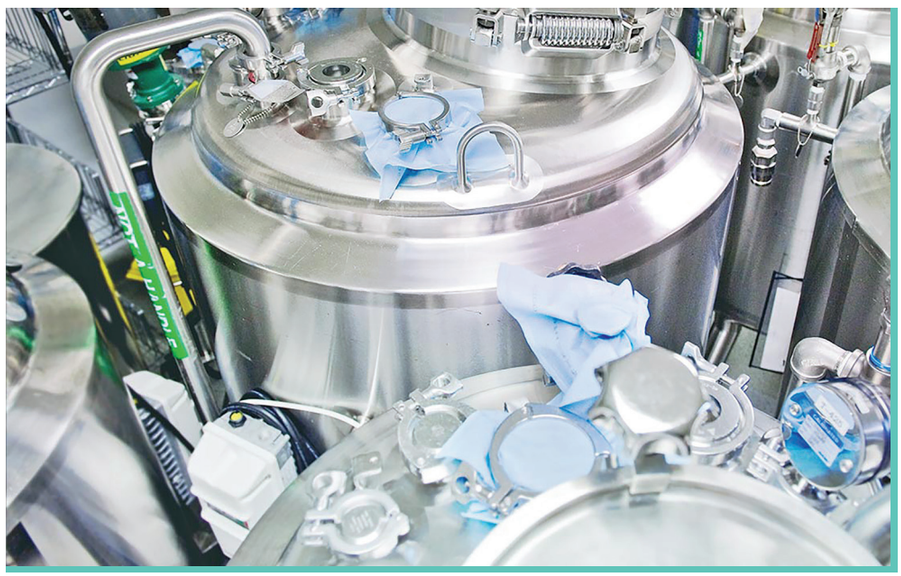
- Moderate or severe cases of cutaneous vasculitis have been reported in patients treated with NEUPOGEN®
- Most reports involved patients with severe chronic neutropenia on long-term NEUPOGEN® therapy
- Hold NEUPOGEN® therapy in patients with cutaneous vasculitis
- NEUPOGEN® dose may be reduced when the symptoms resolve and ANC has decreased

Please see full Important Safety Information on pages 18-19.

Amgen demonstrates dedication to excellence through sophisticated, global manufacturing

Expertise

- At the forefront of modern biotechnology, helping set the standard for the future of the industry[51,52]
  - Amgen manufactures therapeutic and fusion proteins, monoclonal antibodies, peptibodies, and immunotherapies
- More than 250 quality checks to ensure consistency of product[51,53]
  - Proteins are very sensitive to their conditions of synthesis and handling, and a series of critical culturing and purification steps is required to produce a consistent, high-quality active ingredient[53-55]



Drug substance manufacturing bioreactors at Amgen

- State-of-the-art, next-generation manufacturing
  - Biologic medicines are complex; they are manufactured using living cells that have been engineered to produce therapeutic proteins in large quantities[52,53]

Important Safety Information

Potential Effect on Malignant Cells

- G-CSF receptor has been found on tumor cell lines
- The possibility that NEUPOGEN® or Neulasta® acts as a growth factor for any tumor type, including myeloid malignancies and myelodysplasia, cannot be excluded

Please see full Important Safety Information on pages 18-19.

Neulasta® (pegfilgrastim) injection Onpro® kit

Loratadine may help alleviate bone pain[56]

Bone pain was the most common AE for Neulasta®[38]

- Neulasta® stimulates neutrophil development in the bone marrow, which may lead to bone pain for some patients[38,57-59]

ADVERSE REACTIONS WITH ≥ 5% HIGHER INCIDENCE IN NEULASTA® PATIENTS COMPARED WITH PLACEBO[38]

Event	Placebo (n=461)	Neulasta® 6 mg SC on day 2 (n=467)
Bone pain	26%	**31%**
Pain in extremity	4%	**9%**

- Taxane therapy may be associated with bone pain[56]

Treatment with loratadine should be considered to help prevent bone pain in patients receiving chemotherapy and pegfilgrastim[56]

Randomized, phase 2 study to estimate the effect of prophylactic naproxen or loratadine versus no prophylactic treatment on bone pain in patients with early-stage breast cancer receiving chemotherapy and pegfilgrastim. The primary endpoint of the study was bone pain (all grades combined) in cycle 1, captured as part of AE reporting.[56]

AE, adverse event; SC, subcutaneous.

See pages 22-23 for full study designs.

Important Safety Information

Simultaneous Use with Chemotherapy and Radiation Therapy Not Recommended

- Safety and efficacy of NEUPOGEN® given simultaneously with cytotoxic chemotherapy and radiation have not been established
- Do not use NEUPOGEN® 24 hours before or after cytotoxic chemotherapy
- Avoid simultaneous use of NEUPOGEN® with chemotherapy and radiation

Please see full Important Safety Information on pages 18-19.

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Important Safety Information

Contraindication

- Neulasta® or NEUPOGEN® are contraindicated in patients with a history of serious allergic reactions to human granulocyte colony-stimulating factors (G-CSFs), such as pegfilgrastim or filgrastim

Splenic Rupture

- Splenic rupture, including fatal cases, can occur following the administration of Neulasta® and NEUPOGEN®
- Evaluate for an enlarged or ruptured spleen in patients who report upper abdominal or shoulder pain

Acute Respiratory Distress Syndrome (ARDS)

- ARDS has occurred in patients receiving Neulasta® and NEUPOGEN®
- Evaluate patients who develop fever and lung infiltrates or respiratory distress after receiving Neulasta® or NEUPOGEN®
- Discontinue Neulasta® or NEUPOGEN® in patients with ARDS

Serious Allergic Reactions

- Serious allergic reactions, including anaphylaxis can occur in patients receiving Neulasta® and NEUPOGEN®
- Provide symptomatic treatment for allergic reactions
- Majority of events occurred upon initial exposure and can recur within days after the discontinuation of initial anti-allergic treatment
- Permanently discontinue Neulasta® or NEUPOGEN® in patients with serious allergic reactions

Allergies to Acrylics

- On-body Injector for Neulasta® uses acrylic adhesives
- Patients who are allergic to acrylic adhesives may have a significant reaction

Use in Patients with Sickle Cell Disorders

- In patients with sickle cell trait or disease, sickle cell crisis, in some cases fatal, can occur in patients receiving Neulasta® and NEUPOGEN®
- Discontinue if sickle cell crisis occurs

Glomerulonephritis

- Has occurred in patients receiving NEUPOGEN® and Neulasta®
- Diagnoses were based upon azotemia, hematuria, proteinuria, and renal biopsy
- Generally, events resolved after dose reduction or discontinuation of NEUPOGEN® and Neulasta®
- If suspected, evaluate for cause and if cause is likely, consider dose-reduction or interruption of NEUPOGEN® or Neulasta®

Capillary Leak Syndrome (CLS)

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

Thrombocytopenia

- Thrombocytopenia has been reported in patients who received NEUPOGEN®
- Monitor platelet counts

Leukocytosis

- White blood cell counts of $\geq 100{,}000/mm^3$ have been observed in patients who received NEUPOGEN® and Neulasta®
- Monitor CBCs during Neulasta® therapy and at least twice weekly for NEUPOGEN®
- Adjust NEUPOGEN® dosing as clinically indicated to help mitigate risk of leukocytosis
- Dosages of NEUPOGEN® that increase the absolute neutrophil count (ANC) beyond $10{,}000/mm^3$ may not result in any additional clinical benefit
- Discontinuation of NEUPOGEN® 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

Cutaneous Vasculitis

- Moderate or severe cases of cutaneous vasculitis have been reported in patients treated with NEUPOGEN®
- Most reports involved patients with severe chronic neutropenia on long-term NEUPOGEN® therapy
- Hold NEUPOGEN® therapy in patients with cutaneous vasculitis
- NEUPOGEN® may be reduced when the symptoms resolve and ANC has decreased

Potential Effect on Malignant Cells

- G-CSF receptor has been found on tumor cell lines
- The possibility that NEUPOGEN® or Neulasta® acts as a growth factor for any tumor type, including myeloid malignancies and myelodysplasia, cannot be excluded

Important Safety Information (cont'd)

Simultaneous Use with Chemotherapy and Radiation Therapy Not Recommended

- Safety and efficacy of NEUPOGEN® given simultaneously with cytotoxic chemotherapy and radiation have not been established
- Do not use NEUPOGEN® 24 hours before or after cytotoxic chemotherapy
- Avoid simultaneous use of NEUPOGEN® with chemotherapy and radiation

Nuclear Imaging

- Increased hematopoietic activity of the bone marrow in response to growth factor therapy has been associated with transient positive bone-imaging changes which have been seen in patients taking Neulasta® or NEUPOGEN®
- Consider when interpreting bone-imaging results

Potential Device Failures

- Missed or partial doses have been reported in patients receiving pegfilgrastim via the on-body injector (OBI) due to the device not performing as intended
- In the event of a missed or partial dose, patients may be at increased risk of events such as neutropenia, febrile neutropenia and/or infection than if the dose had been correctly delivered
- Instruct patients to notify their healthcare professional immediately in order to determine the need for a replacement dose if they suspect that the device may not have performed as intended

Aortitis

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

Most common adverse reactions in patients taking NEUPOGEN®

- Anemia, constipation, diarrhea, oral pain, vomiting, asthenia, malaise, peripheral edema, decreased hemoglobin, decreased appetite, oropharyngeal pain, and alopecia

Most common adverse reactions in patients taking Neulasta®

- Bone pain
- Pain in extremity

Please see accompanying full Prescribing Information for Neulasta® and NEUPOGEN®.

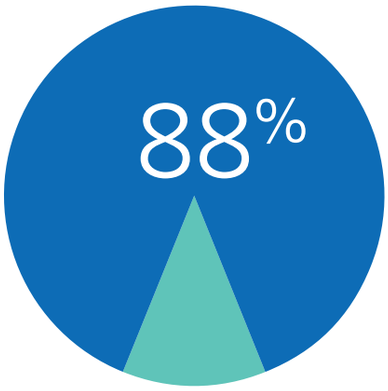
Special Instructions for the On-body Injector (OBI) for Neulasta®

- A healthcare provider must fill the on-body injector (OBI) with Neulasta® using the co-packaged prefilled syringe and then apply the OBI to the patient's skin (abdomen or back of arm). The back of the arm may only be used if there is a caregiver available to monitor the status of the OBI. Approximately 27 hours after the OBI is applied to the patient's skin, Neulasta® will be delivered over approximately 45 minutes. A healthcare provider may initiate administration with the OBI on the same day as the administration of cytotoxic chemotherapy, as long as the OBI delivers Neulasta® no less than 24 hours after the administration of cytotoxic chemotherapy.
- The prefilled syringe co-packaged in the Neulasta® Onpro® kit contains additional solution to compensate for liquid loss during delivery through the OBI. If this syringe is used for manual subcutaneous injection, the patient will receive an overdose. If the prefilled syringe for manual use is used with the OBI, the patient may receive less than the recommended dose.
- Do not use the OBI to deliver any other drug product except the Neulasta® prefilled syringe co-packaged with the OBI. Use of the OBI has not been studied in pediatric patients. The OBI should be applied to intact, non-irritated skin on the arm or abdomen.
- A missed dose could occur due to an OBI failure or leakage. Instruct patients using the OBI to notify their healthcare professional immediately in order to determine the need for a replacement dose of pegfilgrastim if they suspect that the device may not have performed as intended. If the patient misses a dose, a new dose should be administered by single prefilled syringe for manual use as soon as possible after detection.
- Review the Patient Information and Patient Instructions for Use with the patient and provide the instructions to the patient.
- Refer to the Healthcare Provider Instructions for Use for the OBI for full administration information.
- For any OBI problems, call Amgen at 1-800-772-6436 or 1-844-MYNEULASTA (1-844-696-3852).

Neulasta® (pegfilgrastim) injection Onpro® kit

WIRE - O

Most patients pay $0 out of pocket (OOP) per dose for Neulasta® Onpro®[60]



of commercially insured patients pay $0 OOP costs per dose of Neulasta® Onpro®[60,*]

Broad nationwide coverage:

100% of Medicare Part B lives[61]

and

99% of commercial benefit lives covered[62]

Neulasta® Onpro® is available at no extra cost beyond that of the Neulasta® PFS.

*Data based on Decision Resources Group Remittance Database of 124,287 commercial, medical, and pharmacy claims identified between January 1, 2016, and December 31, 2016. Claims included in this analysis were categorized according to patient OOP costs for Neulasta® or Neulasta® Onpro®. Based on typical practices, one claim was assumed to represent a single dose of Neulasta® PFS or Neulasta® Onpro®.[60]
PFS, prefilled syringe.

Financial access resources for patients

With Neulasta FIRST STEP®, eligible patients could pay $5 or less per dose of Neulasta®

Help your eligible* commercially insured patients reduce their out-of-pocket costs for Neulasta®

The Neulasta FIRST STEP® Program

- For eligible commercially insured patients only*
- No out-of-pocket cost for the first dose or cycle, and $5 out-of-pocket cost for subsequent dose or cycle
- Maximum benefit of $10,000 per calendar year
- No income eligibility requirement

Here's what you need to qualify for Neulasta FIRST STEP®†

- Must be prescribed Neulasta®
- Must have private commercial health insurance that covers medication costs for Neulasta®
- Must not be a participant in any federal-, state-, or government-funded healthcare program such as Medicare, Medicare Advantage, Medicare Part D, Medicaid, Medigap, VA, the DoD, or Tricare
- May not seek reimbursement for value received from the Neulasta FIRST STEP® Program from any third-party payers, including flexible spending accounts or healthcare savings accounts. If at any time patients begin receiving coverage under any federal-, state-, or government-funded healthcare program, patients will no longer be eligible to participate in the Neulasta FIRST STEP® Program and must call 1-888-65-STEP1 (1-888-657-8371) Monday through Friday, 9 AM to 8 PM ET to stop participation. Restrictions may apply. This is not health insurance. Program invalid where otherwise prohibited by law

Coverage Limits:

- Program covers out-of-pocket medication costs for the Amgen product only
- Program does not cover any other costs related to office visit or administration of the Amgen product
- No out-of-pocket cost for first dose or cycle; $5 out-of-pocket cost for subsequent dose or cycle; maximum benefit of $10,000 per patient per calendar year. Patient is responsible for costs above these amounts
- Ongoing activation of the Neulasta FIRST STEP® card is contingent on the submission of the required EOB form by your healthcare provider's office within 45 days of use of the Neulasta FIRST STEP® card. Patients will be responsible for reimbursing the program for all amounts paid out if the EOB for the date of service is not received by the program within 45 days

AMGEN ASSIST 360™

Amgen Assist 360™: Tools, information, and support for Amgen products

Benefit verification
- Submit, store, and retrieve benefit verifications for all your patients currently on an Amgen product

Amgen reimbursement specialists
- Connect with an Amgen Reimbursement Counselor or schedule a visit with a Field Reimbursement Specialist

Patient resource guide
- Find co-pay and reimbursement resources‡ for patients with different kinds of insurance or no insurance at all

AMGEN® Safety Net Foundation
Serving Patients in Need™

Amgen Safety Net Foundation

- Provides Neulasta® at no cost to qualifying patients with no or limited drug coverage who meet income eligibility requirements

Eligibility for returns of damaged On-body Injector for Neulasta®

The Neulasta® Onpro® kit, purchased directly from Amgen or an authorized distributor, is eligible for return and credit or a replacement shipment due to malfunction or failure of an On-body Injector for Neulasta®, including situations where it did not perform as described in the Instructions for Use. New return policy effective October 1, 2017, allows Customer to obtain replacement if product is mishandled or improperly stored, patient no-show or refusal, and similar situations.

visit **AmgenAssist360.com**

or

Call 1-888-4ASSIST (1-888-427-7478)
Monday to Friday
9:00 AM to 8:00 PM ET

*For Neulasta® only: Neulasta FIRST STEP® program.
†Other restrictions apply. Not valid where prohibited by law. Amgen reserves the right to revise or terminate this program, in whole or in part, without notice at any time.
‡Provided through independent nonprofit patient assistance programs; program eligibility is based on the nonprofit's criteria. Amgen has no control over these programs and provides referrals as a courtesy only.
EOB, explanation of benefits; DoD, Department of Defense; VA, Veterans Affairs.

Neulasta® (pegfilgrastim) injection Onpro® kit

WIRE - O

Access Solutions

Study Designs

PAGE 1: Study Design 1
2016 data from interviews with oncology patients who have had experience with Neulasta® (N=227, PFS n=150, Neulasta® Onpro® n=77). Patients who had received Neulasta® via Neulasta® Onpro® were asked to answer the question: Based on your personal experience getting your Neulasta® with Neulasta® Onpro®, if your doctor said you needed to use Neulasta® again in the future, would you request getting it with Neulasta® Onpro® again?[1]

PAGE 2: Study Design 2
Based on a retrospective cohort study conducted with 2012 hospital discharge data from the Agency for Healthcare Research and Quality Nationwide Inpatient Sample all-payer database. The total study population included 91,560 hospital discharge records for adult patients (≥ 18 years) with a primary or secondary diagnosis of cancer (including select tumor types) and a diagnosis of neutropenia or a fever of unknown origin. Hospitalizations may or may not have been caused by chemotherapy. Primary payer types included Medicare, commercial insurance, Medicaid, self-pay, and other. Study endpoints focused on characteristics of cancer-related neutropenia hospitalizations, including the mean length of stay.[2]

PAGE 3: Study Design 3
Based on a separate retrospective observational study using 2001–2003 claims data from the Ingenix database representing medical and pharmacy claims from a national health plan. The study population included cancer patients receiving a course of chemotherapy (including first and subsequent cycles). A subset of 373 patients were identified on the basis of the first hospitalization for FN during their chemotherapy course (first or subsequent cycle). FN hospitalization was defined as those with a primary or secondary diagnosis code for neutropenia, fever, or infection. The primary outcome measures in the study were the total cost of FN, including costs reimbursed by the payer for initial hospitalization, postdischarge care through end of cycle, and FN-related care in all subsequent cycles. Results showed that postdischarge neutropenia-related care following an FN-related hospitalization within the same cycle represented an additional 32% of the cost of the initial hospitalization.[3]

PAGE 7: Study Design 4
Based on a retrospective analysis of claims data from approximately 18,000 patients receiving more than 58,000 cycles of chemotherapy from January 1, 2004 to April 30, 2010 (HIRD) and January 1, 2001 to August 31, 2009 (OptumInsight). Patients were ≥ 18 years old with NHL, Hodgkin's lymphoma (OptumInsight data only) and solid tumors receiving myelosuppressive chemotherapy. Odds ratios reported in the study were calculated using general estimating equation. FN was defined as a primary or secondary diagnosis of neutropenia or fever of unknown origin or infection.[35]

PAGE 7: Study Design 5
Based on an analysis of the OSCER database, which contains the EHRs for patients treated in 54 networks of community-based oncology clinics, representing records for about 700,000 cancer patients. The total sample used for this study is unprojected and limited to community-based oncology clinics; it is only reflective of treatment practices contained within OSCER. A logarithmic transformation of administrations per cycle was used to calculate the standard deviation due to the positively skewed nature of the underlying distribution. The sample is based on 652 cycles of myelosuppressive chemotherapy treated with NEUPOGEN® and 186 cycles of myelosuppressive chemotherapy treated with Zarxio®.[36]

PAGE 8: Study Design 6
Data from interviews with Neulasta® treatment-experienced oncology patients (N=227, PFS n=150, Neulasta® Onpro® n=77) conducted in November 2016. All patients in the study were asked to list one-word adjectives or short phrases that best described how they felt after receiving chemotherapy. 86% of patients surveyed recalled feeling tired, fatigued, drained, and exhausted after receiving chemotherapy.[39]

PAGE 9: Study Design 7
Phase 3, multicenter, multinational, double-blind, placebo-controlled trial of patients with breast cancer (Neulasta® [n=463] or placebo [n=465]) receiving 100 mg/m^2 docetaxel Q3W for up to 4 cycles. The key endpoint was the percentage of patients who developed FN (Neulasta® 1% versus placebo 17%, $P < 0.001$). Also, secondary endpoints were lower for Neulasta®-treated patients as compared to placebo-treated patients (the incidence of hospitalization [1% versus 14%] and IV anti-infective use [2% versus 10%] respectively).[41]

FN = temperature ≥ 38.2°C and ANC < 0.5 x 10^9/L.[41]

PAGE 9: Study Design 8
A comparative analysis of Neulasta® doses administered by PFS versus Neulasta® Onpro® was conducted using data from OSCER ending in December 2016, unprojected. OSCER contains data from EHRs processed by QuintilesIMS, provides monthly statistics regarding oncology drug treatment, and contains data on 389,000 oncology patients, who were seen in 2016. Patients who completed a course of therapy from May 2016 through October 2016 were included. Percentage of dose administered was calculated by taking the sum of patients' chemotherapy cycles with Neulasta® and dividing by the sum of their total chemotherapy cycles. Standard deviation calculation was used to assess margin of error.[42]

ANC, absolute neutrophil count; EHR, electronic health record; FN, febrile neutropenia; HIRD, HealthCore Integrated Research Database; IV, intravenous; NHL, non-Hodgkin's lymphoma; OSCER, Oncology Services Comprehensive Electronic Records; PFS, prefilled syringe; Q3W, once every 3 weeks.

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PAGE 10: Study Design 9

Retrospective cohort analysis based on healthcare claims IMS PharMetrics Plus™ and Truven Health Analytics MarketScan® Commercial and Medicare Supplemental Database. The collective data include healthcare claims from private US health plans, covering over 30 million persons annually. The data included all patients ≥ 18 years who, between July 1, 2010, and September 30, 2015, initiated ≥ 1 course of myelosuppressive chemotherapy for a primary solid tumor or NHL. All patients who received a selected chemotherapy regimen with a risk of FN and pegfilgrastim prophylaxis in ≥ 1 cycles of chemotherapy were selected for inclusion in the study population. FN requiring inpatient care was identified based on an inpatient admission with a diagnosis (principal or secondary) of neutropenia, fever, or infection using ICD-9 and ICD-10 codes. FN requiring outpatient care only was ascertained based on an encounter in the outpatient setting with a diagnosis of neutropenia, fever, or infection and—on the same date—code for IV administration of antimicrobial therapy. 18% is the increase in relative risk comparing administration on day 1 (the day after the last day of chemotherapy) to other days including day 0 (the last day of chemo administration) and days 2-5 (after the last day of chemo administration) estimated using GEE, to account for correlation among repeated measures for the same subject, and adjusted using backward selection of patient, cancer, and treatment characteristics.[42]

PAGE 11: Study Design 10

2016 data from interviews with oncology patients who have had experience with Neulasta® (N=227, PFS n=150, Neulasta® Onpro® n=77). Patients who had received Neulasta® via Neulasta® Onpro® were asked to answer the question: Based on your personal experience getting your Neulasta® with Neulasta® Onpro®, if your doctor said you needed to use Neulasta® again in the future, would you request getting it with Neulasta® Onpro® again?[1]

Data from interviews with oncology nurses (N=250) conducted in October 2016. Respondents were asked if they agree with this statement: Based on my Neulasta® Onpro® experience, when my patients are appropriate for Neulasta® PFS or Neulasta® Onpro®, I would choose Neulasta® Onpro®.[47]

PAGE 11: Study Design 11

Data from interviews with oncology patients who have had experience with Neulasta® (N=227, PFS n=150, Neulasta® Onpro® n=77) conducted in November 2016. Patients were asked a multiple-choice selection prompt: If your doctor felt you should receive a G-CSF medication, please select the 3 most important factors to you (other than safety and how well it works) when considering G-CSF care to boost your white blood cell count after chemotherapy. Patients then completed a follow-up prompt: Of the 3 most important factors you selected, we would like to know which is the most important. Please rank these from most important (1) to least important (3).[1]

G-CSF, granulocyte colony-stimulating factor; GEE, generalized estimating equations; ICD-9, International Classification of Diseases, Ninth Revision; ICD-10, International Classification of Diseases, Tenth Revision; NHL, non-Hodgkin's lymphoma.

Consider what Neulasta® Onpro® can offer patients and practices

	Neulasta® Onpro®	Prefilled Syringe
9 of 10 patients report feeling fatigued the day after chemo. Provides option to automatically deliver G-CSF at home[38,39,*]	✓	
May eliminate the time patients and caregivers spend traveling for G-CSF appointments[40]	✓	
Fewer next-day injection appointments[40]	✓	
Designed for automatic next-day delivery of pegfilgrastim (Neulasta®) in accordance with guidelines and labeling[38,*]	✓	
Would be chosen again by 95% of Neulasta® Onpro® patients if they needed Neulasta® again[1,†]	✓	
Is the product of 3 decades of innovation and commitment to enhancing patient experience[51,52,‡]	✓	
Appropriate for patients who don't want to wear a device[63]		✓
Suitable for patients who prefer to receive G-CSF in their doctor's office[63]		✓
May provide G-CSF support through the nadir[34]	✓	✓

*Incomplete doses have been reported with Neulasta® Onpro® due to the device not performing as intended. This may increase risk of neutropenia, febrile neutropenia, and/or infection.[38]
†2016 data from interviews with oncology patients who have had experience with Neulasta® (N=227, PFS n=150, Neulasta® Onpro® n=77). Patients who had received Neulasta® via Neulasta® Onpro® were asked to answer a survey.[1]
‡NEUPOGEN® was approved in 1991; Neulasta® Onpro® was approved in 2014.[32,64]
G-CSF, granulocyte colony-stimulating factor; PFS, prefilled syringe.

Important Safety Information

Potential Device Failures

- Missed or partial doses have been reported in patients receiving pegfilgrastim via the on-body injector (OBI) due to the device not performing as intended
- In the event of a missed or partial dose, patients may be at increased risk of events such as neutropenia, febrile neutropenia and/or infection than if the dose had been correctly delivered
- Instruct patients to notify their healthcare professional immediately in order to determine the need for a replacement dose if they suspect that the device may not have performed as intended

Please see full Important Safety Information on pages 18-19.

AMGEN®

Neulasta® (pegfilgrastim) injection Onpro® kit