HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use ROLVEDON™ safely and effectively. See full prescribing information for ROLVEDON.

ROLVEDON™ (eflapegrastim-xnst) injection, for subcutaneous use
Initial U.S. Approval: 2022

----------INDICATIONS AND USAGE----------

Rolvedon is a leukocyte growth factor indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in adult patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with clinically significant incidence of febrile neutropenia. (1)

Limitations of Use

Rolvedon is not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation. (1)

----------DOSAGE AND ADMINISTRATION----------

- Recommended Dose: 13.2 mg administered subcutaneously once per chemotherapy cycle. (2.1)
- Administer approximately 24 hours after cytotoxic chemotherapy. Do not administer within the period from 14 days before to 24 hours after administration of cytotoxic chemotherapy. (2.1)

----------DOSAGE FORMS AND STRENGTHS----------

Injection: 13.2 mg/0.6 mL solution in a single-dose prefilled syringe. (3)

----------CONTRAINDICATIONS----------

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

----------WARNINGS AND PRECAUTIONS----------

- Fatal splenic rupture: Evaluate patients who report left upper abdominal or shoulder pain for an enlarged spleen or splenic rupture. (5.1)
- Acute respiratory distress syndrome (ARDS): Evaluate patients who develop fever, lung infiltrates, or respiratory distress. Discontinue Rolvedon in patients with ARDS. (5.2)
- Serious allergic reactions, including anaphylaxis: Permanently discontinue Rolvedon in patients with serious allergic reactions. (5.3)
- Sickle Cell Crisis in Patients with Sickle Cell Disorders: Discontinue Rolvedon if sickle cell crisis occurs. (5.4)
- Glomerulonephritis: Evaluate and consider dose-reduction or interruption of Rolvedon if causality is likely. (5.5)
- Leukocytosis: Monitor complete blood count (CBC) during Rolvedon therapy. (5.6)
- Thrombocytopenia: Monitor platelet counts. (5.7)
- Myelodysplastic Syndrome (MDS) and Acute Myeloid Leukemia (AML): Monitor patients with breast and lung cancer using Rolvedon in conjunction with chemotherapy and/or radiotherapy for signs and symptoms of MDS/AML. (5.10)

----------ADVERSE REACTIONS----------

The most common adverse reactions (≥20%) are fatigue, nausea, diarrhea, bone pain, headache, pyrexia, anemia, rash, myalgia, arthralgia, and back pain. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Spectrum Pharmaceuticals, Inc. at 1-888-713-0688 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

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

Revised: 09/2022

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Rolvedon is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in adult patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with clinically significant incidence of febrile neutropenia.

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

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

The recommended dosage of Rolvedon is a single subcutaneous injection of 13.2 mg administered once per chemotherapy cycle. Administer approximately 24 hours after cytotoxic chemotherapy. Do not administer within the period from 14 days before to 24 hours after administration of cytotoxic chemotherapy.

2.2 Administration

Rolvedon is administered subcutaneously via a single-dose prefilled syringe by a healthcare professional.

Prior to use, remove the carton from the refrigerator (keeping the prefilled syringe inside the carton) for a minimum of 30 minutes to allow the product to reach room temperature. Discard any prefilled syringe left at room temperature for greater than 12 hours. Do not shake. If Rolvedon is accidentally frozen, do not use. Remove the tray from box and carefully remove the prefilled syringe from the tray. If you drop the prefilled syringe onto a hard surface, do not use it. Use a new syringe for the injection.

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

Administer the entire contents of the prefilled syringe.

If the patient or caregiver misses a dose of Rolvedon, instruct them to contact their healthcare provider.

The Rolvedon prefilled syringe does not bear graduation marks and is intended only to deliver the entire contents of the syringe (13.2 mg/0.6 mL) for direct administration.

Not made with natural rubber latex.

3 DOSAGE FORMS AND STRENGTHS

Injection: 13.2 mg/0.6 mL as a clear, colorless, preservative-free solution in a single-dose prefilled syringe.

4 CONTRAINDICATIONS

Rolvedon is contraindicated in patients with a history of serious allergic reactions to eflapegrastim, pegfilgrastim, or filgrastim products. Reactions may include anaphylaxis *[see Warnings and Precautions (5.3)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Splenic Rupture

Splenic rupture, including fatal cases, can occur following the administration of recombinant human granulocyte colony-stimulating factor (rhG-CSF) products, such as Rolvedon. Evaluate for an enlarged spleen or splenic rupture in patients who report left upper abdominal or shoulder pain after receiving Rolvedon.

5.2 Acute Respiratory Distress Syndrome

Acute respiratory distress syndrome (ARDS) can occur in patients receiving rhG-CSF products, such as Rolvedon. Evaluate patients who develop fever and lung infiltrates or respiratory distress after receiving Rolvedon for ARDS. Discontinue Rolvedon in patients with ARDS.

5.3 Serious Allergic Reactions

Serious allergic reactions, including anaphylaxis, can occur in patients receiving rhG-CSF products, such as Rolvedon. Permanently discontinue Rolvedon in patients with serious allergic reactions. Rolvedon is contraindicated in patients with a history of serious allergic reactions to eflapegrastim, pegfilgrastim, or filgrastim products *[see Contraindications (4)]*.

5.4 Sickle Cell Crisis in Patients with Sickle Cell Disorders

Severe and sometimes fatal sickle cell crises can occur in patients with sickle cell disorders receiving rhG-CSF products, such as Rolvedon. Discontinue Rolvedon if sickle cell crisis occurs.

5.5 Glomerulonephritis

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

5.6 Leukocytosis

White blood cell (WBC) counts of 100 x 10^9/L or greater have been observed in patients receiving rhG-CSF products. Monitor complete blood count (CBC) during Rolvedon therapy. Discontinue Rolvedon treatment if WBC count of 100 x 10^9/L or greater occurs.

5.7 Thrombocytopenia

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

5.8 Capillary Leak Syndrome

Capillary leak syndrome has been reported after administration of rhG-CSF 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 capillary leak syndrome should be closely monitored and receive standard symptomatic treatment, which may include a need for intensive care.

5.9 Potential for Tumor Growth Stimulatory Effects on Malignant Cells

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

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

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

5.11 Aortitis

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

5.12 Nuclear Imaging

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

6 ADVERSE REACTIONS

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

- Splenic rupture *[see Warnings and Precautions (5.1)]*
- Acute respiratory distress syndrome *[see Warnings and Precautions (5.2)]*
- Serious allergic reactions *[see Warnings and Precautions (5.3)]*
- Sickle cell crisis in patients with sickle cell disorders *[see Warnings and Precautions (5.4)]*
- Glomerulonephritis *[see Warnings and Precautions (5.5)]*
- Leukocytosis *[see Warnings and Precautions (5.6)]*
- Thrombocytopenia *[see Warnings and Precautions (5.7)]*
- Capillary leak syndrome *[see Warnings and Precautions (5.8)]*
- Potential for tumor growth stimulatory effects on malignant cells *[see Warnings and Precautions (5.9)]*
- Myelodysplastic Syndrome (MDS) and Acute Myeloid Leukemia (AML) in Patients with Breast and Lung Cancer *[see Warnings and Precautions (5.10)]*
- Aortitis *[see Warnings and Precautions (5.11)]*
- Nuclear Imaging *[see Warnings and Precautions (5.12)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

The safety of Rolvedon was evaluated in Study 1 and Study 2 *[see Clinical Studies (14)]*. Patients with early-stage breast cancer received Rolvedon 13.2 mg by subcutaneous injection (n=314) or pegfilgrastim 6 mg by subcutaneous injection (n=326) on Day 2 of each cycle after docetaxel 75 mg/m^2 and cyclophosphamide 600 mg/m^2 (TC) chemotherapy.

Among patients receiving Rolvedon, a total of 272 patients received four 21-day treatment cycles.
The most common adverse reactions (≥20%) were fatigue, nausea, diarrhea, bone pain, headache, pyrexia, anemia, rash, myalgia, arthralgia, and back pain. Table 1 summarizes the adverse reactions that occurred in Studies 1 and 2.

Table 1. Common Adverse Reactions with a Frequency of ≥10% Through Week 14 in Patients with Early-Stage Breast Cancer in Study 1 and Study 2

Adverse Reaction	Rolvedon (N = 314) %	Pegfilgrastim** (N=326) %
Fatigue *	181 (58%)	192 (59%)
Nausea	162 (52%)	166 (51%)
Diarrhea	125 (40%)	126 (39%)
Bone pain	119 (38%)	121 (37%)
Headache*	92 (29%)	90 (28%)
Pyrexia *	87 (28%)	84 (26%)
Anemia*	77 (25%)	52 (16%)
Rash*	77 (25%)	99 (30%)
Myalgia	69 (22%)	49 (15%)
Arthralgia	66 (21%)	48 (15%)
Back pain*	63 (20%)	55 (17%)
Decreased appetite	61 (19%)	50 (15%)
Peripheral edema*	57 (18%)	53 (16%)
Abdominal pain*	53 (17%)	67 (21%)
Dizziness *	50 (16%)	38 (12%)
Dyspnea*	49 (16%)	44 (13%)
Cough*	48 (15%)	51 (16%)
Thrombocytopenia*	44 (14%)	17 (5%)
Pain	37 (12%)	42 (13%)
Pain in extremity	36 (11%)	42 (13%)
Local administration reactions*	34 (11%)	27 (8%)
Flushing	32 (10%)	27 (8%)

*Grouped Terms
**Study 1 and Study 2 were not designed to evaluate meaningful comparisons of the incidence of adverse reactions in the Rolvedon and the pegfilgrastim treatment groups.

Permanent discontinuation due to an adverse reaction occurred in 4% of patients who received Rolvedon. The adverse reaction requiring permanent discontinuation in 3 patients who received Rolvedon was rash.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available data on Rolvedon use in pregnant women; however, data from published studies with use of other recombinant human granulocyte colony-stimulating factor (rhG-CSF) products in pregnant women have not identified any drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes.

Animal reproduction studies were conducted in rats and rabbits. In rats, eflapegrastim-xnst did not adversely affect embryofetal and/or postnatal development when administered from organogenesis throughout lactation at doses that produced maternal exposures up to 7 times the exposure at the recommended clinical dose. In rabbits, eflapegrastim-xnst caused embryofetal lethality and reduced fetal weight when administered during the organogenesis period at approximately 6 times the exposure at the clinical dose *(see Data)*.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risks of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Data

Animal Data

In an embryofetal developmental study in rabbits, eflapegrastim-xnst was administered subcutaneously every other day during the period of organogenesis at doses up to 10 times the clinical exposure at the maximum recommended dose of 13.2 mg. Increased post-implantation loss, reduced number of live fetuses, and reduced fetal body weights were observed at 6 times the clinical exposure, based on AUC. No malformations were observed up to 10 times the clinical exposure, based on AUC.

In an embryofetal developmental study in rats, eflapegrastim-xnst administered subcutaneously every other day during the period of organogenesis did not adversely affect embryofetal development at doses up to 7 times clinical exposure, based on AUC.

In a pre- and post-natal development study in rats, eflapegrastim-xnst administered subcutaneously once weekly from organogenesis through lactation did not adversely affect behavioral, developmental, or reproductive parameters at doses up to 7 times the clinical exposure, based on AUC.

8.2 Lactation

Risk Summary

There are no data on the presence of eflapegrastim-xnst in human milk, the effects on the breastfed child, or the effects on milk production. Endogenous granulocyte colony-stimulating factor (G-CSF) is present in human milk. Other recombinant human granulocyte colony-stimulating factor (rhG-CSF) products are present in human milk at low levels and are not orally absorbed by infants. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Rolvedon and any potential adverse effects on the breastfed child from Rolvedon or from the underlying maternal condition.

8.4 Pediatric Use
Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use
Of the 314 patients in clinical studies of Rolvedon, 39% were 65 and over, while 6% were 75 and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects.

10 OVERDOSAGE

Overdose of Rolvedon may result in leukocytosis and bone pain. In the event of overdose, general supportive measures should be instituted as necessary. Monitor the patient for adverse reactions *[see Adverse Reactions (6)]*.

11 DESCRIPTION

Eflapegrastim-xnst is a granulocyte colony-stimulating factor (G-CSF) produced by covalent coupling of a human G-CSF analog (18.6 kDa) and an Fc fragment of human immunoglobulin G4 (IgG4) (49.8 kDa), both derived from recombinant *E. coli*, via a single 3.4 kDa polyethylene glycol linker. The recombinant G-CSF domain in eflapegrastim-xnst is a variant of human G-CSF with two serine substitutions at positions 17 and 65, and no additional N-terminal methionine. Eflapegrastim-xnst has a molecular weight of approximately 72 kDa.

Rolvedon (eflapegrastim-xnst) injection is a sterile, preservative-free, clear, colorless solution supplied in a single-dose prefilled syringe for subcutaneous use. Each 0.6 mL single-dose prefilled syringe contains 13.2 mg of eflapegrastim-xnst, citric acid monohydrate (2.52 mg), mannitol (30 mg), polysorbate 80 (0.72 mg) and sodium chloride (5.26 mg) in Water for Injection. Sodium hydroxide may be used to adjust pH to 5.5 during manufacturing.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Eflapegrastim-xnst is a recombinant human granulocyte growth factor that binds to G-CSF receptors on myeloid progenitor cells and neutrophils, triggering signaling pathways that control cell differentiation, proliferation, migration and survival.

12.2 Pharmacodynamics

Eflapegrastim-xnst has been shown to elevate neutrophil counts in healthy subjects and in cancer patients. Absolute neutrophil count (ANC), C_{max} and area under the effect curve ($AUEC_{last}$) increased with increasing doses of eflapegrastim-xnst in a linear, but less than dose-proportional, manner over a dose range of 45 to 350 mcg/kg.

12.3 Pharmacokinetics

The pharmacokinetics of eflapegrastim-xnst was studied in healthy subjects and patients with breast cancer. After subcutaneous (SC) dosing, the pharmacokinetics of eflapegrastim-xnst was nonlinear and exposure increases were not dose-proportional over the dose range of 45 to 350 mcg/kg.

Absorption
The median T_{max} of eflapegrastim-xnst is 25 hours (6 to 144 hours) in patients with breast cancer following administration of the recommended dosage.

Distribution
The volume of distribution of eflapegrastim-xnst is 1.44 L.

Elimination
The geometric mean half-life of eflapegrastim-xnst in patients with breast cancer is 36.4 hours (Range: 16.1 to 115 hours) during Cycle 1. Eflapegrastim-xnst clearance decreased with increasing doses following single dose administration, suggesting target-mediated clearance of eflapegrastim-xnst by neutrophils. Following repeat administration, clearance increased in Cycle 3 as compared to Cycle 1, potentially due to the subsequent increase in neutrophils. In *in vitro* studies, the IgG4 Fc fragment in eflapegrastim-xnst binds to the neonatal Fc receptor (FcRn), facilitating the FcRn-mediated transcytosis of eflapegrastim-xnst.

Metabolism
Eflapegrastim-xnst is expected to be metabolized by endogenous degradation following receptor-mediated internalization by cells bearing the G-CSF receptor.

Excretion
Eflapegrastim-xnst was not detected in urine.

Drug Interaction Studies

No studies evaluating the drug interaction potential of eflapegrastim-xnst have been conducted.

12.6 Immunogenicity
The observed incidence of anti-drug antibodies is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of anti-drug antibodies in the studies described below with the incidence of anti-drug antibodies in other studies, including those of eflapegrastim-xnst or of other eflapegrastim products.

Antibodies to eflapegrastim-xnst were detected using bridging enzyme-linked immunosorbent assay (ELISA) with a sensitivity of 65 ng/mL. During the 12-week treatment period in the two randomized studies, twenty-one of 297 (7.1%) patients treated with eflapegrastim-xnst developed antibodies. At the 12-month follow-up visit after the last dose of treatment in the two randomized studies, 28 of 297 (9.4%) patients treated with eflapegrastim-xnst developed antibodies.

Neutralizing antibodies were detected by a cell-based assay with a sensitivity of 1.95 mcg/mL. One patient out of 297 (0.3%) in the eflapegrastim-xnst arm tested positive for neutralizing antibodies post-treatment. Treatment-emergent anti-PEG antibodies were detected by a direct binding ELISA in 126 out of 268 patients (47%) treated with eflapegrastim-xnst. There was no identified clinically significant effect of anti-drug antibodies on pharmacokinetics, pharmacodynamics, safety or effectiveness of Rolvedon over the treatment duration of 12 weeks. There was no identified clinically significant effect of anti-drug antibodies on the safety profile of Rolvedon during the 12-month follow-up period after the last dose.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No long-term carcinogenicity studies have been performed with eflapegrastim-xnst.

Eflapegrastim-xnst was not mutagenic or clastogenic in a standard battery of genotoxicity tests (bacterial mutagenicity (Ames), Chinese hamster ovary cells chromosomal aberration, rat bone marrow micronucleus).

Eflapegrastim-xnst did not affect reproductive performance or fertility in male or female rats at weekly doses up to 7 times the clinical exposure at the maximum recommended dose of 13.2 mg.

14 CLINICAL STUDIES

Patients with Cancer Receiving Myelosuppressive Chemotherapy

The efficacy of Rolvedon to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs was evaluated in two 1:1 randomized, open-label, active-controlled non-inferiority studies of similar design (Study 1 [NCT02643420] and Study 2 [NCT02953340]) that enrolled a total of 643 patients with early-stage breast cancer. Docetaxel 75 mg/m^2 and cyclophosphamide 600 mg/m^2 (TC) were administered intravenously every 21 days (on Day 1 of each cycle) for up to 4 cycles. A fixed dose of Rolvedon 13.2 mg/0.6 mL or pegfilgrastim (6 mg/0.6 mL) was administered subcutaneously on Day 2 of each cycle after TC chemotherapy.

The median age of patients enrolled in the two randomized studies was 60 years (Range: 24 to 88), the majority of patients were female (>99%), 77% were White and 12% were Black or African American.

Study 1 enrolled 406 patients; 196 patients to the Rolvedon arm and 210 patients to the pegfilgrastim arm. Study 2 enrolled 237 patients; 118 patients to the Rolvedon arm and 119 patients to the pegfilgrastim arm. Efficacy for both trials was based on the duration of severe neutropenia (DSN) in Cycle 1.

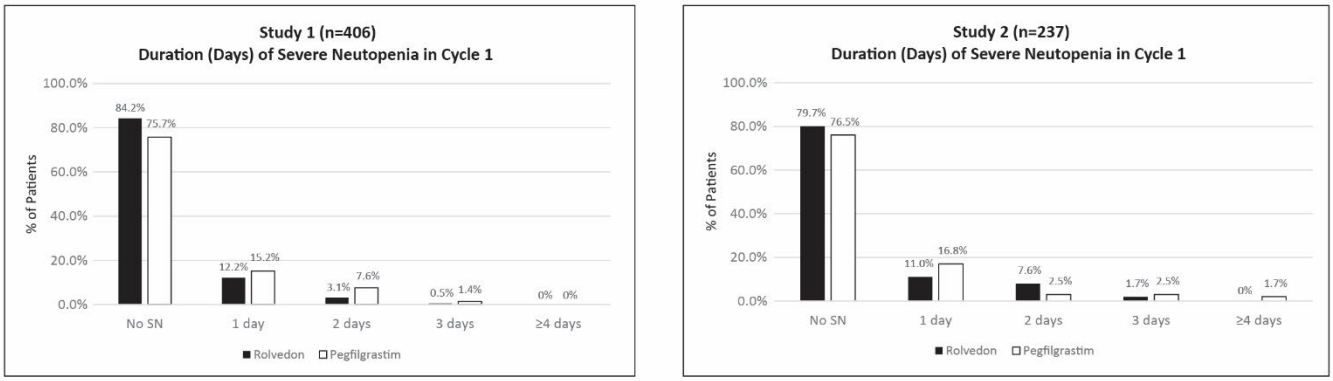
Efficacy results are shown in Table 2. In both studies, Rolvedon was non-inferior to pegfilgrastim. The distributions of the severe neutropenia events in percentage from Cycle 1 for Study 1 and Study 2 are presented in Figure 1.

Table 2. Duration of Severe Neutropenia (DSN) in Cycle 1 (Study 1 and Study 2)

	Study 1		**Study 2**	
	Rolvedon (n=196)	Pegfilgrastim (n=210)	Rolvedon (n=118)	Pegfilgrastim (n=119)
Mean DSN (SD) (Days)	0.20 (0.503)	0.35 (0.683)	0.31 (0.688)	0.39 (0.949)
Median DSN (Range) (Days)	0 (0, 3)	0 (0, 3)	0 (0, 3)	0 (0, 7)
Difference in DSN (Days)	-0.148		-0.073	
*95% Confidence Interval[a]	-0.265, -0.033		-0.292, 0.129	

[a]Confidence intervals were obtained using 2.5 percentile and 97.5 percentile of the 100,000 bootstrap samples with treatment as stratification factor.
*The non-inferiority of Rolvedon to pegfilgrastim was to be declared if the upper bound of 95% CI of the difference in mean DSN between the treatment arms was <0.62 days.

Figure 1. Duration of Severe Neutropenia (DSN) by Day in Cycle 1 (Study 1 and Study 2)



16 HOW SUPPLIED/STORAGE AND HANDLING

Rolvedon (eflapegrastim-xnst) injection is a clear, colorless solution supplied in a single-dose prefilled syringe containing 13.2 mg of eflapegrastim-xnst in 0.6 mL solution, with 29-gauge 1/2 inch pre-attached (staked) needle with a needle guard.

Rolvedon is provided in a dispensing pack containing one sterile 13.2 mg/0.6 mL prefilled syringe (NDC 76961-101-01).

Store refrigerated at 36°F to 46°F (2°C to 8°C) in the carton to protect from light. Do not shake. Discard syringes stored at room temperature for more than 12 hours. Do not freeze; discard syringe if frozen.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information). Rolvedon should only be given by a healthcare professional. Inform patients to contact their healthcare provider with any questions.

Advise patients of the following risks and potential risks with Rolvedon:

- Splenic rupture and splenomegaly *[see Warnings and Precautions (5.1)]*
- Acute respiratory distress syndrome *[see Warnings and Precautions (5.2)]*
- Serious allergic reactions *[see Warnings and Precautions (5.3)]*
- Sickle cell crisis *[see Warnings and Precautions (5.4)]*
- Glomerulonephritis *[see Warnings and Precautions (5.5)]*
- Leukocytosis *[see Warnings and Precautions (5.6)]*
- Thrombocytopenia *[see Warnings and Precautions (5.7)]*
- Capillary leak syndrome *[see Warnings and Precautions (5.8)]*
- Potential for tumor growth stimulatory effects on malignant cells *[see Warnings and Precautions (5.9)]*
- Increased risk of myelodysplastic syndrome and/or acute myeloid leukemia in patients with breast and lung cancer who receive Rolvedon in conjunction with chemotherapy and/or radiation therapy *[see Warnings and Precautions (5.10)]*
- Aortitis *[see Warnings and Precautions (5.11)]*

Manufactured by:
Spectrum Pharmaceuticals, Inc.

18200 Von Karman Avenue, Suite 700
Irvine, CA 92612 USA

U.S. License No. 2312

PATIENT INFORMATION
Rolvedon™ (roll veh don)
(eflapegrastim-xnst)
injection

What is Rolvedon?
Rolvedon is a man-made form of granulocyte colony-stimulating factor (G-CSF). G-CSF is a substance produced by the body. It stimulates the growth of neutrophils, a type of white blood cell important in the body's fight against infection.

It is not known if Rolvedon is safe and effective in children.

Do not take Rolvedon if you have had a serious allergic reaction to eflapegrastim, pegfilgrastim or filgrastim products.

Before receiving Rolvedon, tell your healthcare provider about all of your medical conditions, including if you:
- have a sickle cell disorder
- have kidney problems
- are pregnant or plan to become pregnant. It is not known if Rolvedon can harm your unborn baby. Tell your healthcare provider right away if you become pregnant during treatment with Rolvedon.
- are breastfeeding or plan to breastfeed. It is not known if Rolvedon passes into your breast milk.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How will I receive Rolvedon?
- Rolvedon is given as an injection under your skin (subcutaneous injection) by a healthcare provider.
- You will receive 1 injection of Rolvedon for each cycle of chemotherapy.
- You will receive your injection of Rolvedon about **24 hours after you finish receiving your chemotherapy**.
- You should not receive Rolvedon for 14 days before or within 24 hours after your dose of chemotherapy.
- If you miss a dose of Rolvedon, talk to your healthcare provider about when you should receive your next dose.

What are the possible side effects of Rolvedon?

Rolvedon may cause serious side effects, including:

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

- swelling or puffiness and are urinating less than usual
- trouble breathing
- swelling of your stomach area (abdomen) and feeling of fullness
- dizziness or feeling faint
- a general feeling of tiredness

- **Myelodysplastic syndrome and acute myeloid leukemia.** If you have breast cancer or lung cancer, when Rolvedon is used with chemotherapy and radiation therapy, or with radiation therapy alone, you may have an increased risk of developing a precancerous blood condition called myelodysplastic syndrome (MDS) or a blood cancer called acute myeloid leukemia (AML). Symptoms of MDS and AML may include tiredness, fever, and easy bruising or bleeding. Call your healthcare provider if you develop these symptoms during treatment with Rolvedon.

- **Inflammation of the aorta (aortitis).** Inflammation of the aorta (the large blood vessel which transports blood from the heart to the body) has been reported in patients who received pegfilgrastim products. Symptoms may include fever, abdominal pain, feeling tired, and back pain. Call your healthcare provider if you experience these symptoms.

The most common side effects of Rolvedon include:

- tiredness
- nausea
- diarrhea
- bone pain
- headache
- fever
- decreased red blood cell count
- rash
- muscle and joint pain
- back pain

These are not all the possible side effects of Rolvedon.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of Rolvedon.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. You can ask your pharmacist or healthcare provider for information about Rolvedon that is written for health professionals.

What are the ingredients in Rolvedon?

Active ingredient: eflapegrastim-xnst

Inactive ingredients: citric acid monohydrate, mannitol, polysorbate 80, sodium chloride in Water for Injection. Sodium hydroxide may be used to adjust pH to 5.5 during manufacturing.

Manufactured by: Spectrum Pharmaceuticals, Inc. 18200 Von Karman Avenue, Suite 700, Irvine, CA 92612 USA

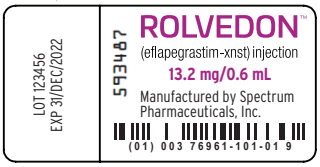
U.S. License No. 2312

For more information, go to www.rolvedon.com or call 1-888-713-0688.

This Patient Information has been approved by the U.S. Food and Drug Administration. Issued: 09/2022

Reference ID: 5044179

Unvarnished area.
Leave blank.



ROLVEDON™

(eflapegrastim-xnst) injection

13.2 mg/0.6 mL

For subcutaneous injection
by a healthcare provider only
Sterile Solution – No Preservative

One 0.6 mL Single-dose
Pre-filled Syringe

NDC 76961-101-01 Rx only

Each 0.6 mL single-dose pre-filled syringe contains 13.2 mg of eflapegrastim-xnst in a sterile, clear, colorless, preservative-free solution consisting of citric acid monohydrate (2.52 mg), mannitol (30 mg), polysorbate 80 (0.72 mg), and sodium chloride (5.26 mg) in Water for Injection. Sodium hydroxide may be used to adjust pH to 5.5 during manufacturing.

Dosage See prescribing information

Store refrigerated at 36°F to 46°F (2°C to 8°C)
in original carton to protect from light.
Do Not Freeze. Do Not Shake.

2DM

Product of Republic of Korea
Manufactured by Spectrum Pharmaceuticals, Inc.
Irvine, CA 92612 USA U.S. License No. 2312

688170

(01) 003 76961-101-01 9

Lot:
Exp:

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

LISA B YANOFF
09/12/2022 02:50:06 PM