Patient Information About

LEUKINE®

Leukine®
sargramostim

Please see Important Safety Information for LEUKINE on page 9 and accompanying full Prescribing Information available at www.leukine.com.

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Introduction

This brochure has been created for you and patients like you whose doctors have prescribed LEUKINE® (sargramostim) as part of their treatment regimen. The brochure includes answers to the questions most commonly asked by patients using LEUKINE. We hope it will help you understand why your doctor has prescribed LEUKINE and what you can expect from using it.

Your nurse is an excellent resource while you are taking LEUKINE. He or she can answer questions (or refer them to your doctor), provide additional patient education materials, and perhaps most importantly, become one of your greatest supporters as you undergo treatment.

Why did my doctor prescribe LEUKINE?

Cancer treatments can compromise your immune system. This is because some cancer treatments—including chemotherapy, which targets and destroys fast-growing cancerous cells—can also kill healthy white blood cells (WBCs), including neutrophils. WBCs, which are made in your bone marrow, are responsible for fighting infections by initiating an immune response. Because they are also fast growing, WBCs may also be affected by chemotherapy.

The high rate of infection is the primary reason your healthcare team will closely monitor your immune system, using blood tests that measure the levels of various cell types. Because neutrophils are the most abundant WBC, the risk for infection is often assessed with a blood test called the absolute neutrophil count (ANC).

If your ANC drops too low, your immune system is less able to protect you against organisms and your chance of getting a severe or life-threatening infection increases. Your doctor has prescribed LEUKINE to help your body make more neutrophils, which in turn, can help protect against infections.

Indication

LEUKINE is used to help increase the number and function of white blood cells after bone marrow transplantation, in cases of bone marrow transplantation failure or engraftment delay, before and after peripheral blood stem cell transplantation, and following induction chemotherapy in older patients with acute myelogenous leukemia. Your doctor may also choose to treat other conditions with LEUKINE.

Important Safety Information for LEUKINE

You should not use LEUKINE if you have high levels of abnormal white blood cells, called leukemic blasts, in the bone marrow or blood. You should not use LEUKINE if you have had an allergic reaction to GM-CSF, other products made from yeast, or any ingredient used to make LEUKINE. If you are also receiving chemotherapy or radiation therapy, do not take your LEUKINE in the period 24 hours before through 24 hours after the administration of your chemotherapy or radiation therapy.

What is LEUKINE® (sargramostim)?

LEUKINE is a man-made form of colony-stimulating factor (CSF). A CSF is a type of protein known as a growth factor that your body produces to help increase the number and function of your WBCs. LEUKINE is known as a granulocyte-macrophage colony-stimulating factor, or GM-CSF.

How does LEUKINE work?

LEUKINE affects important aspects of your immune system that may enhance your recovery.

LEUKINE increases the number and activity of 3 types of WBCs: neutrophils, macrophages, and dendritic cells. Each of these 3 cells has a distinct purpose and function within the immune system.

White Blood Cells Stimulated by LEUKINE

Neutrophil *Macrophage* *Dendritic Cell*

Function of white blood cells

- Neutrophils are the most abundant WBCs and are the first to respond to the site of an infection. Their purpose is to capture and digest foreign invaders such as bacteria
- Monocytes/macrophages also capture and digest foreign invaders but are longer acting and recognize more invaders than neutrophils. Macrophages enhance the first-line response of neutrophils
- Dendritic cells (DCs) make up less than 1% of WBCs but are extremely important. DCs continuously scan their environment and alert other cells when they find something foreign, such as an invading organism

How is LEUKINE administered?

LEUKINE is given as a part of a daily treatment regimen. Your doctor will determine how LEUKINE will be administered to you. Depending on the treatment plan, LEUKINE may be administered either:

- Subcutaneously (SC), which means by injections directly beneath the skin, or
- Intravenously (IV), which means by infusion through a needle or catheter placed into a vein

Important Safety Information for LEUKINE

A generalized allergy is an uncommon but potentially serious reaction to LEUKINE. This may include a skin rash over your entire body, hives, trouble breathing, a fast pulse, sweating, and feeling faint. In severe cases a generalized allergy may be life-threatening. If you think you are having a generalized allergy to LEUKINE, stop taking LEUKINE and notify your doctor immediately.

Please see Important Safety Information for LEUKINE on page 9 and accompanying full Prescribing Information available at www.leukine.com.

Your doctor may recommend that you self administer LEUKINE® (sargramostim) at home. When you give yourself a SC injection, it is important to use a different injection site each time to help avoid soreness or redness in one area. Select injection sites on your stomach or thigh; the stomach is the optimal injection site. Do not use any site that is red, tender, or swollen. If a skin reaction occurs, contact your doctor. If the potential sites on the stomach are tender, switch to a site on the thigh.

When is therapy started?

Depending on your diagnosis and overall treatment plan, your doctor will determine when your LEUKINE therapy will begin.

When is therapy stopped?

Your doctor will monitor the number of neutrophils in your blood with regular blood tests to determine when the WBCs reach a level that is high enough to help fight infections. Generally, that is the point at which LEUKINE therapy is stopped.

What happens if I miss a dose?

LEUKINE works best if you stay on the schedule prescribed by your doctor. Notify your doctor immediately if you are unable to make your appointment and/or if you miss a dose of LEUKINE.

Questions about safety

Are there patients who should not use LEUKINE?

You should not use LEUKINE if you have high levels of abnormal white blood cells, called leukemic blasts, in the bone marrow or blood. You should not use LEUKINE if you have had an allergic reaction to GM-CSF, other products made from yeast, or any ingredient used to make LEUKINE. LEUKINE should be used with caution, and your doctor should monitor you if you have preexisting fluid buildup, heart or lung conditions, or kidney or liver disease. Your doctor will monitor your white blood cell and platelet counts with blood tests during LEUKINE treatment. If your white blood cell or platelet counts rise above certain levels, your doctor may stop your LEUKINE treatment, or may reduce the dose. If your doctor detects progression of your disease, he/she may stop your LEUKINE therapy. Liquid solutions containing benzyl alcohol, including LEUKINE liquid or lyophilized LEUKINE reconstituted with Bacteriostatic Water For Injection, USP should not be administered to newborns.

Are there possible drug interactions with LEUKINE?

Drugs that can increase WBCs, such as lithium and corticosteroids, should be used with caution while receiving LEUKINE. Interactions between LEUKINE and other drugs have not been fully evaluated.

If you are also receiving chemotherapy or radiation therapy, do not take your LEUKINE® (sargramostim) in the period 24 hours before through 24 hours after the administration of your chemotherapy or radiation therapy.

What are some of the side effects of LEUKINE?

Some patients taking LEUKINE may experience unwanted side effects, most of which are mild to moderate and not serious. Some of the more common side effects include bone pain, feeling like you have the flu, feeling tired or weak, muscle aches, diarrhea, stomach upset, weight loss, or loss of appetite. You may also get a low-grade fever (less than 100.5°F or 38°C) about 1 to 4 hours after an injection, or you may have swelling, redness, and/or discomfort where LEUKINE was injected.

Some side effects or symptoms may be serious. These include developing a high fever (over 100.5°F or 38°C), signs of infection including chills, sore throat, or congestion (such as stuffy nose), having trouble breathing, wheezing, or fainting, or developing extensive skin rash, hives, or other signs of an allergic reaction, experiencing sudden weight gain or other signs of fluid buildup, such as swollen legs or feet, having chest pain, chest discomfort, or a rapid or irregular pulse. These may be due to LEUKINE, your illness, or other treatments that you may have received. Many of these side effects can be managed. These or other side effects you may be concerned about should be reported promptly to your doctor, nurse, or pharmacist.

How can LEUKINE side effects be managed?

The following techniques may be used by the person administering your injection to manage some of the common side effects of LEUKINE treatment.

- For temperature elevation (less than 100.5°F or 38°C) and/or bone pain, your healthcare provider may recommend pain relievers such as acetaminophen. Please consult with your healthcare team before taking any medications for fever or pain while you are receiving LEUKINE therapy
- To minimize injection site discomfort, the person administering the injections should:
  - Allow LEUKINE to come to room temperature before injection
  - Rotate injection sites from one injection to the next
  - Avoid rubbing or pinching the skin before or after injection
  - Apply ice to the site for one minute immediately prior to and after the injection
  - Inject LEUKINE slowly (30–60 seconds)

When should I contact my healthcare provider?

During your treatment, some serious but rare side effects or symptoms may occur that may be due to LEUKINE® (sargramostim), your illness, or other treatments you may be receiving. Call your doctor immediately if you:

- Notice any signs of infection, which can include chills, sore throat, congestion, inflammation (warmth or redness) of an area of the body or development of a fever as defined by your healthcare provider
- Have trouble breathing or experience wheezing, fainting, skin rash, hives, or feel you are having an allergic reaction of any kind
- Experience sudden weight gain or other signs of fluid buildup such as swollen legs or feet
- Develop chest pain, chest discomfort, or a rapid or irregular pulse
- Develop any other unexpected symptoms

Important Safety Information for LEUKINE

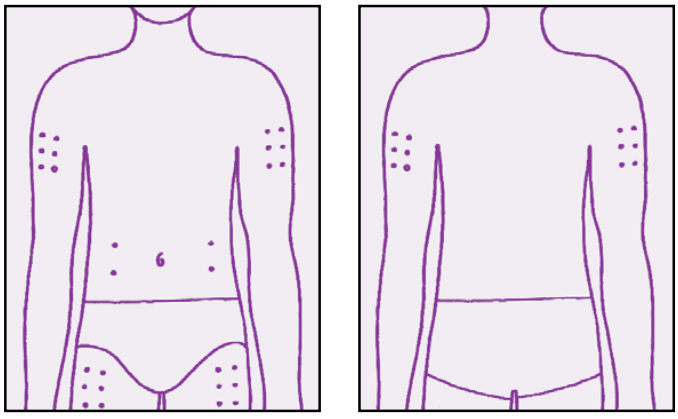
Liquid solutions containing benzyl alcohol, including LEUKINE liquid or lyophilized LEUKINE reconstituted with Bacteriostatic Water For Injection, USP should not be administered to newborns.

LEUKINE should be used with caution, and your doctor should monitor you if you have preexisting fluid buildup, heart or lung conditions, or kidney or liver disease.

Medical diary

LEUKINE injection record

The tables on page13 will help you track your LEUKINE injections. Using the illustrations as a guide, note the injection site on the table, together with the date, dose, and the time of the injection. The best areas for self-injecting LEUKINE are the thighs or stomach. The navel or waistline should be avoided. If a caregiver is helping with the injections you may use the back portion of the upper arms. It is important to use a new injection site for each injection to avoid soreness in any one area. **Please see the LEUKINE Information for Patients available at www.leukine.com.**



LEUKINE® (sargramostim) injection record

Before using LEUKINE for the first time, talk to your doctor, nurse, or pharmacist about how to use it, what to expect when using it, possible side effects, and what to do if side effects occur. You must be instructed and trained properly in how to prepare and inject LEUKINE by your doctor, nurse, or pharmacist prior to using it. Do not attempt to self-administer LEUKINE until you are sure that you understand the instructions for giving an injection to yourself. Your dose has been selected to meet your individual needs. Do not change your dose without consulting your doctor. If you are unsure about the amount (mL or cc) or dose to be used, how to inject yourself, or how often to inject yourself, talk to your doctor, nurse, or pharmacist.

It is extremely important that you do not reuse syringes or needles. Do not attempt to put the needle cover back on the needle. Throw away used syringes and needles in a puncture-resistant container as instructed by your doctor, nurse, or pharmacist.
For more information, please see the LEUKINE Information for Patients available at www.leukine.com.

Date	Dose	Time	Injection Site

Blood count record

Your doctor will take blood tests regularly to monitor certain components in your blood while you are taking LEUKINE® (sargramostim) therapy. You may find it helpful to discuss the normal ranges with your doctor and track the results of these tests.

WBC = white blood cell count (the number of infection-fighting cells in your blood)

ANC = absolute neutrophil count (the number of neutrophils, which are infection-fighting WBCs)

PLT = platelets (the cells that are responsible for blood clotting)

HGB = hemoglobin (a protein in red blood cells that carries oxygen throughout the body)

Important Safety Information for LEUKINE

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Date	WBC	ANC	PLT	HGB

Indication

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Important Safety Information for Leukine® (sargramostim)

- Leukine is contraindicated in patients with excessive leukemic myeloid blasts in bone marrow or peripheral blood (≥10%); in patients with known hypersensitivity to GM-CSF, yeast-derived products, orany component of Leukine; and for concomitant use with chemotherapy and radiotherapy.
- Serious allergic or anaphylactic reactions have been reported with Leukine. If any serious allergic or anaphylactic reactions occur, Leukine therapy should be immediately discontinued and appropriate therapy initiated.
- Liquid solutions containing benzyl alcohol (including liquid Leukine) or lyophilized Leukine reconstituted with Bacteriostatic Water for Injection, USP (0.9% benzyl alcohol) should not be administered to neonates.
- Leukine should be used with caution and monitored in patients with preexisting fluid retention, pulmonary infiltrates, or congestive heart failure, respiratory symptoms or disease; cardiac symptoms or disease; and renal or hepatic dysfunction.
- Edema, capillary leak syndrome, pleural and/or pericardial effusion, sequestration of granulocytes in the pulmonary circulation, and dyspnea have been reported in patients after Leukine administration. Occasional transient supraventricular arrhythmia has been reported during Leukine administration. Leukine has induced the elevation of serum creatinine or bilirubin and hepatic enzymes in some patients. Monitoring of renal and hepatic function in patients with preexisting renal or hepatic dysfunction is recommended at least every other week during Leukine administration.
- Adverse events occurring in >10% of patients receiving Leukine in controlled clinical trials and reported in a higher frequency than placebo were: in AML patients – (fever, skin reactions, metabolic disturbances, nausea, vomiting, weight-loss, edema, anorexia); in Autologous BMT patients – (asthenia, malaise, diarrhea, rash, peripheral edema, urinary tract disorder); and in Allogeneic BMT patients – (abdominal pain, chills, chest pain, diarrhea, nausea, vomiting, hematemesis, dysphagia, GI hemorrhage, pruritus, bone pain, arthralgia, eye hemorrhage, hypertension, tachycardia, bilirubinemia, hyperglycemia, increased creatinine, hypomagnesemia, edema, pharyngitis, epistaxis, dyspnea, insomnia, anxiety, high BUN, and high cholesterol).
- If ANC > 20,000 cells/mm^3 or if platelet counts > 500,000/mm^3, Leukine administration should be interrupted or the dose reduced by half. Twice weekly monitoring of CBC with differential should be performed.
- Leukine therapy should be discontinued if disease progression is detected during treatment.
- Drugs that can increase WBCs, such as lithium and corticosteroids, should be used with caution while receiving Leukine. Interactions between Leukine and other drugs have not been fully evaluated.

Please see accompanying full Prescribing Information available at www.leukine.com.

Leukine® sargramostim

For Support

Call *LEUKLine* — A toll-free line to answer LEUKINE questions

- Healthcare professionals available Monday through Friday from 8:00 AM to 6:00 PM ET

1-877-3LEUKINE (1-877-353-8546) Or visit us at www.leukine.com

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For Reimbursement Questions

Call *LEUKINE* Direct — A one-stop information resource for reimbursement questions

- Available Monday through Friday from 9:00 AM to 7:00 PM ET

1-888-4RxLEUKINE (1-888-479-5385), option 3

Please see Important Safety Information for LEUKINE on page 9 and accompanying full Prescribing Information available at www.leukine.com.

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