



Patient Guide to
SEVERE, MALIGNANT
OSTEOPETROSIS (SMO)

Learn about the condition
and how you can take control



ACTiMUNE[®]
(Interferon gamma-1b)

Please see Important Safety Information on page 2.

Important Safety Information

Approved Uses for ACTIMMUNE® (Interferon gamma-1b)

Chronic Granulomatous Disease (CGD)

ACTIMMUNE® is approved by the US Food and Drug Administration to reduce the frequency and severity of serious infections associated with Chronic Granulomatous Disease. CGD is a genetic disorder that affects the functioning of some cells of the immune system.

Severe, Malignant Osteopetrosis (SMO)

ACTIMMUNE® is approved by the US Food and Drug Administration to slow the worsening of severe, malignant osteopetrosis. SMO is a genetic disorder that affects normal bone formation.

Important Safety Information (ISI)

The most common side effects with ACTIMMUNE® are “flu-like” symptoms such as fever, headache, chills, myalgia (muscle pain), or fatigue, which may decrease in severity as treatment continues. Bedtime administration of ACTIMMUNE® may minimize some of these symptoms. Acetaminophen may be helpful in preventing fever and headache.

ACTIMMUNE® can cause severe allergic reactions and/or rash. Do not use ACTIMMUNE® if you are allergic to interferon-gamma, *E. coli*-derived products, or any component of the product. (See Full Prescribing Information for a list of components). If you develop a serious reaction to ACTIMMUNE®, discontinue it immediately and contact your doctor or seek medical help.

At high doses, ACTIMMUNE® can cause (flu-like) symptoms, which may worsen some pre-existing heart conditions. Tell your doctor if you have a cardiac condition, such as irregular heartbeat, heart failure, or decreased blood flow to your heart.

ACTIMMUNE® may cause reversible changes to your nervous system, including decreased mental status, walking disturbances, and dizziness. Tell your doctor if you have a history of seizures or other neurologic disorders.

Bone marrow function may be suppressed with ACTIMMUNE® and decreased production of cells important to the body may occur. This effect, which can be severe, is usually reversible when the drug is discontinued or the dose is reduced. Tell your doctor if you have, or have had, reduced bone marrow function. Your doctor will monitor these cells with blood tests at the beginning of therapy and at 3 month intervals thereafter.

Taking ACTIMMUNE® may cause reversible changes to your liver function, particularly in patients less than one year old. Your doctor will monitor your liver function with blood tests at the beginning of therapy and at 3 month intervals. If the patient is 1 year or less, monitoring will be done on a monthly basis.

If you are pregnant or plan to become pregnant or plan to nurse you should consult your physician.

If you are receiving ACTIMMUNE® at home, your doctor will provide to you or your caregiver appropriate instructions on the administration of the drug and disposal of the container, needles, and syringes.

You are encouraged to report negative side effects of prescription drugs to the FDA.

Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

This information is not intended to replace discussions with your doctor. For additional information about ACTIMMUNE®, please consult the Full Prescribing Information and the Information for the Patient/Caregiver and talk to your doctor. ACTIMMUNE® is available by prescription only.

Visit www.ACTIMMUNE.com to download a copy of the ACTIMMUNE® Full Prescribing Information.

Severe, Malignant Osteopetrosis (SMO) & ACTIMMUNE® (Interferon gamma-1b)

This introductory guide was created to help you learn about SMO and how ACTIMMUNE® may help you and your healthcare provider manage the disease.

For additional information, please talk with your healthcare provider.

This brochure will help you learn about

- What SMO is and what causes it
- The signs and symptoms of SMO and how it is diagnosed
- How SMO may be managed
- ACTIMMUNE®, its effectiveness, and safety profile
- How to dose and administer ACTIMMUNE®

Find out about the COMPASSSM (Comprehensive Personalized Patient Prescription Advocacy & Support Services) Program and resources available to SMO patients on ACTIMMUNE®.

TIP: As you read this brochure, you can find definitions of the medical terms (shown in bold type) you may not be familiar with in the glossary in the back of this brochure.

What is Severe, Malignant Osteopetrosis (SMO)?

SMO is a disease of the bones. It is considered a genetic disorder—meaning a person is born with it. There are several different forms of osteopetrosis (not to be confused with the more common osteoporosis, a very different condition). All forms of osteopetrosis involve an abnormal increase in bone density.¹

This condition is rare. It is estimated that 1 out of 250,000 children are born with severe, malignant osteopetrosis.¹

During normal bone development, existing bone material is constantly being replaced by new bone. Cells called **osteoblasts** cause new bone formation. Other cells called **osteoclasts** remove old bone through a process called **resorption**.^{1,2}

In people with osteopetrosis, this balance is not maintained because their osteoclasts do not function properly. As a result, abnormal bone development occurs, which may cause many problems in the body such as¹

- Blood disorders
- Decreased ability to fight infection
- Bone fractures
- Problems with vision and hearing
- Abnormal appearance of the face and head

Common Characteristics

In SMO, the abnormal buildup of bone materials tends to narrow the space inside the bone. This means there is less space to make bone marrow, which is where new blood cells are formed. This can lead to³

- Anemia because of low red blood cells. Symptoms of anemia include pale skin and lack of energy
- Bleeding problems because of low platelets. Platelets are blood cells needed for clotting to help stop bleeding
- Many infections due to low white blood cells. White blood cells are needed to fight infections

Also, there can be narrowing of the “tunnels” within bones of the skull (called **foramina**) through which the nerves for vision and hearing pass. When these nerves are compressed by the overdevelopment of bones due to SMO, vision and hearing problems can result.^{1,2,4}

Patients with SMO often suffer serious effects from the disease. These may include^{1,4}

- Failure to thrive, slow growth in childhood
- Impaired vision or blindness
- Hearing loss
- Abnormal head shape
- Bone marrow failure, anemia
- Frequent and recurrent infections
- Frequent and recurrent bone fractures

SMO is associated with diminished life expectancy, with most untreated children dying within the first decade of their life.¹



Diagnosing Severe, Malignant Osteopetrosis

Severe, malignant osteopetrosis is generally diagnosed in infants, often within the first year of life and frequently within the first 3 months. The first signs of the disease commonly noticed by parents are⁴

- Vision problems
- Failure to thrive
- Slow growth

Other early signs include recurrent infections, bone fractures, nasal congestion, and unusual facial features.⁴

To diagnose that a person has severe, malignant osteopetrosis, the doctor may order an X-ray. By examining the X-ray images, doctors can look for the abnormal bone development that is characteristic of the disease. That information, combined with the patient's physical signs and symptoms, usually leads to a firm diagnosis. This diagnosis can be definitively confirmed through genetic testing.¹

**ACTIMMUNE® IS THE ONLY
MEDICINE APPROVED BY
THE US FOOD AND DRUG
ADMINISTRATION TO DELAY
THE TIME TO DISEASE
PROGRESSION IN CHILDREN
WITH SMO.⁵**

What Is ACTIMMUNE® (Interferon gamma-1b)?

ACTIMMUNE® is a biologically manufactured protein called interferon gamma that is similar to a protein your body makes naturally. In the body, interferon gamma is produced by cells of the immune system. ACTIMMUNE® (Interferon gamma-1b) is indicated for delaying time to disease progression in patients with severe, malignant osteopetrosis.⁵

The precise way that ACTIMMUNE® works to slow the worsening of SMO is not fully understood, but ACTIMMUNE® is believed to work by modifying the cellular function of various cells, including those that help form your bones.^{2,5}

Managing SMO

Therapies available for SMO can help to manage the complications that occur, delay progression of the disease, and prolong survival. Doctors may prescribe **corticosteroid medications** or high doses of calcitriol (a special form of vitamin D) in order to slow the progression of the disease. Problems caused by bone marrow failure may be treated with blood transfusions. Special treatments for vision, hearing, and dental problems may be required.^{1,4}

ACTIMMUNE® is the only medicine approved by the US Food and Drug Administration to slow the worsening of severe, malignant osteopetrosis (SMO). SMO is a genetic disorder that affects normal bone formation.⁵

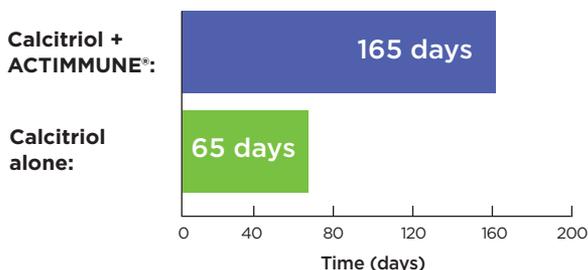
ACTIMMUNE® (Interferon gamma-1b) plus calcitriol may provide benefits for patients with SMO by^{1,2}

- Increasing bone resorption
- Stabilizing hemoglobin and platelet levels
- Lowering the risk of serious bacterial infections associated with (or caused by) SMO

For some patients, **HSCT** (often referred to as BMT) may be considered. BMT provides a possible cure for SMO, but there are associated risks, including rejection of the transplanted cells.^{1,2,4} Ask your healthcare provider for more information.

ACTIMMUNE® has been shown to delay disease progression in patients with SMO⁵:

Median time to disease progression



- A clinical trial showed that the median time to disease progression was significantly delayed in the ACTIMMUNE® plus calcitriol group versus patients taking calcitriol alone⁵
- In an analysis that combined data from a second study, 19 of 24 patients treated with ACTIMMUNE® (± calcitriol) for at least 6 months had reduced **trabecular bone** volume compared to baseline⁵

Safety of ACTIMMUNE®

The safety profile of ACTIMMUNE® in patients with SMO was found to be similar to patients with CGD treated with ACTIMMUNE®.⁵

The most common side effects seen with ACTIMMUNE® are “flu-like” symptoms such as fever, headache, chills, myalgia (muscle pain), or fatigue, which may reduce in severity as treatment continues. Administering

ACTIMMUNE® at bedtime may also help minimize some of these symptoms. Acetaminophen may be helpful in preventing fever and headache.⁵

ACTIMMUNE® can cause severe allergic reactions and/or rash; flu-like symptoms, which may worsen pre-existing heart conditions; reversible changes to the nervous system (such as decreased mental status, walking disturbances, and dizziness); reversible severe bone marrow toxicity; decreased production of important cells in the body; and reversible changes to liver function (particularly in patients less than one year old).⁵

If you develop a serious reaction, discontinue immediately; call your doctor or seek medical help. Tell your doctor if you have any allergies to interferon-gamma or E. coli-derived products; a cardiac condition (such as irregular heartbeat, heart failure, or decreased blood flow to your heart); history of seizures or other neurologic disorders; or reduced bone marrow function. If you are pregnant or plan to become pregnant or plan to nurse, you should consult your doctor.

For a full list of side effects with ACTIMMUNE®, please see Full Prescribing Information.

Most common side effects in patients with CGD^{5,6}

SIDE EFFECT	PERCENTAGE OF PATIENTS	
	ACTIMMUNE® (n=63)	Placebo (n=65)
Fever	52	28
Headache	33	9
Rash	17	6
Chills	14	0
Injection site erythema or tenderness	14	2
Fatigue	14	11
Diarrhea	14	12
Vomiting	13	5
Nausea	10	2
Muscle Pain	6	0
Joint Pain	2	0
Injection site pain	0	2

Administering ACTIMMUNE® (Interferon gamma-1b)

ACTIMMUNE® is administered as a **subcutaneous** injection. For best results, injections should be given 3 times weekly (for example, Monday, Wednesday, and Friday).⁵

IMPORTANT: Don't administer ACTIMMUNE® until a healthcare provider has shown you how. He or she will give you detailed instructions on how to^{5,7}

- Measure the dose
- Select the injection site
- Administer the injection
- Store ACTIMMUNE®
- Properly dispose of the unused portion of each vial
- Properly dispose of the used syringe and needle after each injection

TIP: A Sharps Container will be provided to you for easy disposal of your used syringes at no cost when you enroll in COMPASSSM.

See page 15 for more details.



ACTIMMUNE® at bedtime may also help minimize some of these symptoms. Acetaminophen may be helpful in preventing fever and headache.⁵

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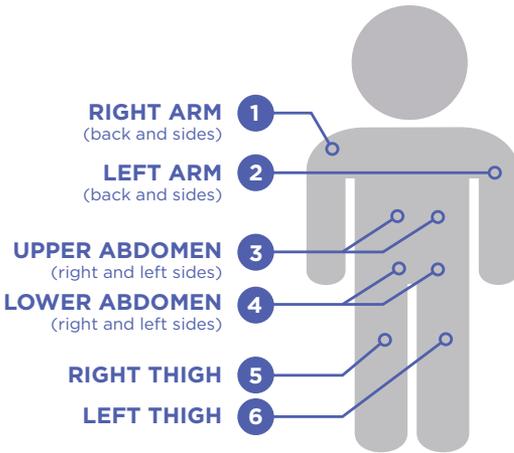
If you develop a serious reaction, discontinue immediately; call your doctor or seek medical help. Tell your doctor if you have any allergies to interferon-gamma or E. coli-derived products; a cardiac condition (such as irregular heartbeat, heart failure, or decreased blood flow to your heart); history of seizures or other neurologic disorders; or reduced bone marrow function. If you are pregnant or plan to become pregnant or plan to nurse, you should consult your doctor.

For a full list of side effects with ACTIMMUNE®, please see Full Prescribing Information.

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Nausea	10	2
Muscle Pain	6	0
Joint Pain	2	0
Injection site pain	0	2

How to choose the injection site



It's important to select the correct place on the body to inject ACTIMMUNE® (Interferon gamma-1b). We understand that an injection can be uncomfortable, so make sure you inject ACTIMMUNE® into an area of the body that is fatty. Fatty areas have the fewest nerve endings; using them as injection sites will minimize any discomfort.

The above diagram shows recommended injection sites.⁵ The sites are numbered to help you identify their locations when recording them on the calendar. Use a different injection site each time you administer ACTIMMUNE®. Rotating the injection site helps each area recover fully before the same site is used again, and helps minimize localized side effects.

Using the Injection Site Rotation Calendar

ACTIMMUNE® injections should be administered 3 times weekly. To help you keep track of when and where on the body you have administered ACTIMMUNE®, we've provided you with a laminated Injection Site Rotation Calendar. Use a dry-erase marker so you can erase marks and reuse the calendar.

- After each injection, write on the calendar the site number and side where you injected ACTIMMUNE®

Example: If you gave an injection in the left side of the upper abdomen, label it 3L (3L = *upper abdomen, left side*; 3R = *upper abdomen, right side*).

Keep in mind



Do contact your physician or healthcare provider if you have any questions about the information in this brochure



Do administer ACTIMMUNE® at same days of the week and same time of day

- For example, if you choose Monday, Wednesday, and Friday at 1 PM as your injection days and time, make sure this schedule remains the same for the upcoming months. Consistent timing helps make injections a regular part of your routine



Do consider administering ACTIMMUNE® just before going to bed in order to minimize some of the “flu-like” side effects



Do rotate the injection site consistently and use a different area on the body for each injection. It helps each area fully recover before the same site is used again, and helps minimize localized side effects



Do properly dispose of the unused portion of the ACTIMMUNE® vial after each injection as instructed by your healthcare provider. Each vial can be safely used for one injection only



Do properly dispose of the used syringe and needle after each injection as instructed by your healthcare provider. You may wish to use a Sharps (syringe) Container, which is provided to you at no cost when you enroll in COMPASSSM (see page 15)



Do not discontinue any of your prescribed medications without consulting your healthcare provider

Occasionally, a problem may develop at the injection site. Inform your healthcare provider immediately if you see⁷

- A lump or swelling that does not go away
- Bruising that does not go away
- Any signs of infection or inflammation (pus, persistent redness, surrounding skin that's hot to the touch, persistent pain after the injection)

Storing ACTIMMUNE® (Interferon gamma-1b)^{5,6}

- ACTIMMUNE® must be refrigerated immediately upon receipt of the vials
- Unused ACTIMMUNE® vials should not be left at room temperature for more than 12 hours
- Refrigerate at typical refrigerator temperatures: 36°F to 46°F (2°C to 8°C)
- **Do not freeze** ACTIMMUNE® vials
- **Do not shake** ACTIMMUNE® vials
- **Do not store** ACTIMMUNE® in the syringe

ACTIMMUNE® is supplied in single-use vials. The unused portion of each vial should be disposed of as instructed by your healthcare provider. If you have any questions, contact your healthcare provider.⁵

Helping you get ACTIMMUNE® so ACTIMMUNE® can help you

Horizon Pharma is committed to getting patients and families the help they need to obtain ACTIMMUNE®.

The COMPASSSM (Comprehensive Personalized Patient Prescription Advocacy & Support Services) Program offers eligible ACTIMMUNE® patients, their families, and healthcare providers one-stop convenient access to support services, ongoing health education, and financial resources.

COMPASSSM

Comprehensive Personalized Patient Prescription Advocacy & Support Services

Help is only a phone call away

You or your doctor can enroll you in the COMPASSSM Program. Once enrolled, eligible patients will have access to the following services at no cost.*

Clinical Nurse Program

Once enrolled in COMPASSSM, you can opt-in to get connected with a Registered Nurse who can provide personalized support, answer questions, and share helpful resources on how to manage your condition.

Reimbursement Hotline

Eligible patients will be assigned to a dedicated Program Coordinator and automatically referred for Co-Pay Assistance. Your COMPASSSM Program Coordinator can provide help with prior authorizations and appeals, and benefit investigation within 48 hours.

Co-Pay Assistance Program

COMPASSSM will help you minimize your out-of-pocket costs by covering the co-pay amount and co-insurance (you will pay \$0 per month). The co-pay amount and co-insurance are automatically applied by your pharmacy. There are no financial eligibility requirements under this program.

The Co-Pay Assistance Program is not available to Medicare, Medicaid, TRICARE, or any other government-insured patients.

Patient Assistance Program (PAP)

For eligible patients without insurance or rendered uninsured due to payer denial, COMPASSSM may provide medication at no cost. At your request, this program can also assist you in finding insurance coverage. Proof of income is required (with Form 1040 or W-2).

Prescription Refill Reminders

To help you keep track of your ACTIMMUNE[®] refills while managing your busy schedule, you can opt-in to receive refill reminders via text and/or email, once you enroll in COMPASSSM.

Sharps Container Program

Because proper disposal of used syringes is important, this program is available to ACTIMMUNE[®] patients. Once enrolled in COMPASSSM, you can opt-in to have a Sharps Container and return shipping materials shipped directly to you at no cost.

Take advantage of these programs.

Call a COMPASSSM Program Coordinator at (877) 305-7704 Monday-Friday 8 AM to 6 PM Eastern Time or visit www.compassforpatients.com.

*In order for you to receive support through COMPASSSM, the prescribing physician must fax the Service Request Form to (877) 305-7706.



Helpful information and support

You can find more information and support groups for families affected by SMO through these organizations.

[Osteopetrosis.org](https://www.osteopetrosis.org)

An organization that gives patients and families facing osteopetrosis a source for helpful information.

[Ryan Wersten MIOP Foundation](https://www.ryanwerstenmiopfoundation.org)

Created in memory of Ryan Wersten, who lived for only 6 months after being diagnosed with SMO—which is also known as **Malignant** Infantile Osteopetrosis (MIOP)—the group is dedicated to supporting current research as well as families who have a child with MIOP.

[Mason Shaffer Foundation](https://www.masonshafferfoundation.org)

A nonprofit organization devoted to creating a support network for families of children with osteopetrosis.

[Global Genes/RARE Project](https://www.globalgenes.org)

A leading patient advocacy organization working to connect and empower rare disease patients and caregivers by providing tools, resources, and information. The group's mission is to build and unify a global rare and genetic disease community while positively impacting patients in their lifetime.



If you have any questions, want to enroll in COMPASSSM, or make use of COMPASSSM, please call (877) 305-7704.

CARD PLACEMENT

Helpful definitions

Bone marrow—the soft, fatty tissue that fills most bone cavities and is the source of red blood cells and white blood cells

Corticosteroid medications—medications that closely resemble cortisol, a hormone that is produced by the adrenal glands in the human body

Foramina (plural of foramen)—tunnel-like passages or openings through which blood vessels pass

HSCT—the transplantation of potent hematopoietic stem cells, usually derived from bone marrow, peripheral blood, or umbilical cord blood

Malignant—in this instance refers to severity of the disease and a condition that can become progressively worse. Malignant here is not a term related to cancer

Osteoblasts—a type of cell within bones that helps form new bone material

Osteoclasts—a type of cell within bones that breaks down old bone material through a process called resorption

Resorption—the process by which osteoclasts break down old bone material

Subcutaneous—pertaining to the fatty layer of tissue just under the skin

Trabecular bone—a type of structural tissue that helps form bones

Thank you!

We hope that this information has helped you learn about SMO and how ACTIMMUNE® (Interferon gamma-1b) can help prevent infections.

If you would like more information about SMO or ACTIMMUNE®, please visit www.ACTIMMUNE.com or call (877) 305-7704.

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