



Understanding **Thalidomide** **Therapy**



"Until There is a Cure...There is the IMF"

Notes

My Health Care Team

Doctor _____ Phone _____

Nurse _____ Phone _____

Hospital _____ Main Phone _____

Other _____ Phone _____

Emergency Contacts

_____ Phone _____

_____ Phone _____

Other Medications I Am Taking

Thalidomide Dosing Schedule

Dose (eg, 100 mg) _____

Number of Capsules (eg, 2 x 50 mg) _____

Schedule: Morning___ Every Other Day___ Other___

Important Reminders When Taking Thalidomide

The use of thalidomide for the treatment of myeloma is currently under investigation in clinical trials. This booklet is meant to provide the patient with general information on thalidomide treatment. It is not part of, nor is it meant to substitute for any part of, the System for Thalidomide Education and Prescribing Safety (S.T.E.P.S.[®]) program. All patients must be advised of, agree to, and comply with the requirements of the S.T.E.P.S.[®] program in order to receive thalidomide.

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North Hollywood, California

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Introduction

Using thalidomide to treat *myeloma** is a new idea, but thalidomide itself has been studied for many decades. Much has been learned about how thalidomide works in the treatment of different diseases and how its *side effects* can be treated. Additionally, we now understand how important it is to prevent women who may be pregnant from being exposed to thalidomide.

Thalidomide is currently approved for the treatment of *erythema nodosum leprosum*, an *inflammatory* condition seen in some patients with leprosy. However, thalidomide is actively being investigated for the treatment of myeloma. Many patients with myeloma have benefited from this therapy.

This booklet is intended to provide a basic understanding of thalidomide therapy:

- What thalidomide is and how it works to treat myeloma
- How to handle thalidomide safely
- What side effects might be expected while taking thalidomide
- How doctors can minimize side effects
- How thalidomide may be used with other therapies

The information in this booklet may be useful not only to patients, but also to friends, family, loved ones, and other caregivers. Please remember that myeloma, like all cancers, is a complicated disease. Specific questions about treatment should be addressed by a doctor or nurse.

*All words that appear in italics are defined in the glossary at the back of this booklet.

What Is Thalidomide?

Thalidomide is a drug that was first used in the late 1950s in Europe for the treatment of morning sickness. It was later withdrawn from use when it was reported that the drug produced severe, life-threatening birth defects.

Today, the medical community has a better understanding of this drug and how it works. Thalidomide is classified as an *immunomodulatory agent*, which means it affects the levels of certain chemicals in the body that control the activity of *cells*. We know that thalidomide can produce many other effects that are helpful, such as slowing or stopping the growth of new blood vessels, called angiogenesis. Today, a program called the *System for Thalidomide Education and Prescribing Safety (S.T.E.P.S.®)* helps to ensure that every effort is made to use the drug safely.

Is Thalidomide the Same as Chemotherapy?

Chemotherapy works by killing cells that are dividing. These cells include cancer cells as well as some normal cells in the body. Hair loss, nausea and vomiting, and gastric upset are common side effects that occur, because some healthy cells are affected by chemotherapy. Thalidomide is not considered a form of chemotherapy. It is instead considered a new kind of treatment, because it can affect the levels of certain proteins that the body normally uses to control the activity of cells.

Who Can Benefit From Thalidomide Therapy?

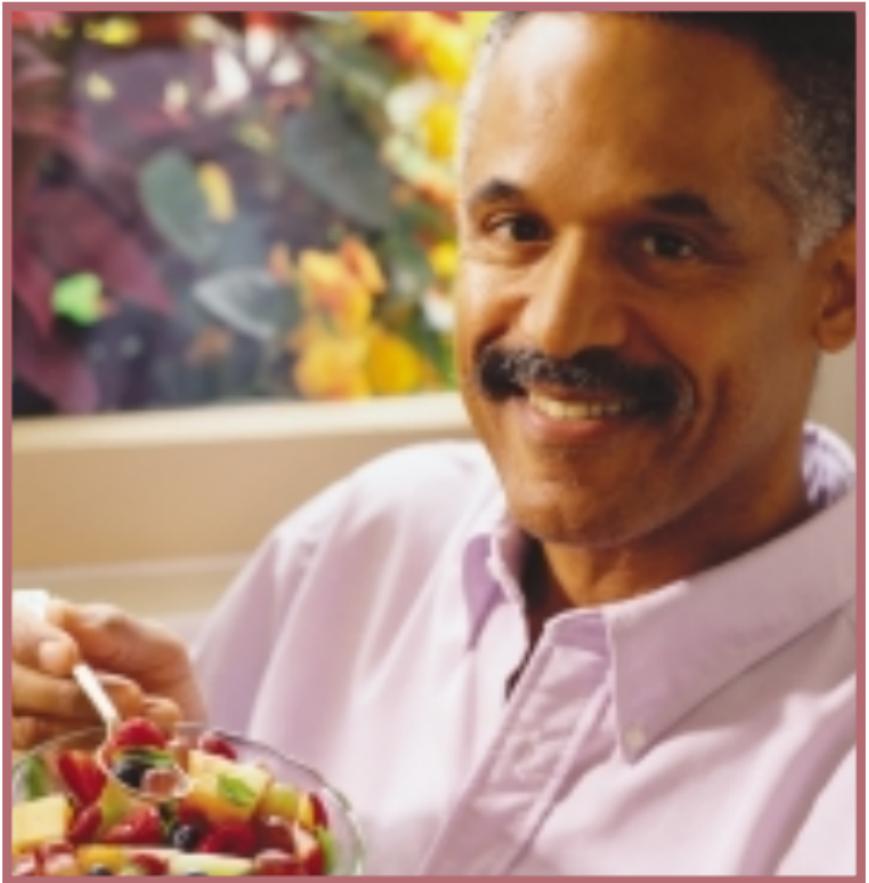
Today, thalidomide is approved for the treatment of erythema nodosum leprosum. However, thalidomide has also been studied in a number of other diseases, including cancer.

Clinical trials have shown that thalidomide is active against myeloma and can produce lasting *complete or partial responses*, as well as *disease stabilization*. In these trials, thalidomide has been found to be effective in patients with different stages of myeloma, including:

- Patients with newly diagnosed myeloma
- Patients who have not responded to other treatments
- Patients in whom myeloma has returned after initial successful treatment

Additionally, thalidomide has been successful in treating myeloma either when given alone or when given in combination with the drug dexamethasone, a type of steroid. Selection of an





appropriate treatment is made on a case-by-case basis. The ideal daily dose of thalidomide is under investigation. In some cases, low doses have been found to be effective alone and in combination.

Response to thalidomide therapy takes time. Generally, improvement in the disease is seen after about 3 months of treatment; however, improvements have been noted as early as 2 weeks and as late as 8 months. Once a response is achieved, the physician will determine if ongoing, or maintenance, therapy is needed. It is important to note, however, that not everyone who takes thalidomide will have a response and other therapies may be considered.

How Does Thalidomide Work?

Although scientists are still trying to understand exactly how thalidomide fights cancer,

thalidomide is known to work on 2 important levels. First, thalidomide is believed to boost the body's immune response to cancer. Second, it helps block the blood supply of cancerous tumors. Cancer cells, like normal cells, need to get nutrients and oxygen from the blood to survive and multiply. Some tumors send chemicals into the body that can trigger the formation of new blood vessels. As more blood vessels grow into the tumor, it can become larger. It is thought that one way thalidomide may help to limit tumor growth is by hindering new blood vessel growth within tumors.

Thalidomide is also believed to act in several other ways against myeloma, including targeting the myeloma cells and the molecules that allow them to grow. However, these exact effects are not clear and scientists are actively studying them.

What Are the Possible Side Effects of Thalidomide?

The most common side effects associated with thalidomide are:

- Drowsiness – feelings of sleepiness or fatigue
- *Peripheral neuropathy* – tingling or numbness in the arms, hands, legs, and/or feet
- Dizziness – sensation of unsteadiness
- Constipation – delayed or infrequent passage of hardened feces
- Rash – an eruption on the skin
- *Leukopenia* – a low level of *white blood cells*

Other side effects have been reported, although infrequently. Any side effects a patient experiences while receiving treatment should be discussed with a doctor or nurse as soon as possible. In addition, any changes in overall health or well-being should be reported to a health care professional. Prescription medications and over-the-counter products that are being taken should also be reported.

Drowsiness

Thalidomide often causes feelings of drowsiness. These methods may help relieve this side effect:

- Taking thalidomide at bedtime
- Avoiding use of other drugs that may cause drowsiness while taking thalidomide
- At the discretion of a doctor or nurse, taking other drugs to help alleviate drowsiness
- Avoiding alcohol



Situations in which drowsiness may be a problem should be avoided. Mental and physical abilities needed to perform dangerous tasks, such as driving a car, may be impaired.

Peripheral neuropathy

Impairment of the nerves in the extremities (hands, arms, legs, feet) is known as peripheral neuropathy. This side effect can be mild, causing tingling in the hands and feet; more rarely, it can be severe and painful. It typically occurs after a long period of taking thalidomide, but it can sometimes occur sooner. These strategies may help alleviate symptoms of peripheral neuropathy:

- Walking and other forms of exercising
- Avoiding tight shoes and socks with elastic
- At the discretion of a doctor, reducing the dose of thalidomide
- At the discretion of a doctor or nurse, taking additional medications

A physician should be notified if any symptoms of peripheral neuropathy occur. If side effects are severe, thalidomide therapy may need to be stopped altogether.

Dizziness

Dizziness may occur while taking thalidomide. Sitting up and waiting a few minutes before getting out of bed may help reduce dizziness.

Constipation

Constipation may occur during treatment with thalidomide; however, constipation is rarely severe. Prevention is the key to management.

These strategies may help alleviate constipation:

- Drinking at least 8 glasses of fluid daily
- Adding plenty of dietary fiber every morning, such as prune juice, apple juice, and bran
- Exercising
- At the recommendation of a doctor or nurse, taking stool softeners and laxatives

If constipation becomes severe, the dose of thalidomide may be lowered or temporarily discontinued.

Rash

In some cases, a rash may develop while taking thalidomide. A mild rash (red or discolored skin, with or without raised bumps) usually begins on the trunk and spreads to the arms and legs. Mild rashes may be relieved in the following ways:

- At the recommendation of a doctor or nurse, taking antihistamines and topical corticosteroids
- To alleviate dry skin, using Calendra lotion, cocoa butter cream, oatmeal soap, Eucerin[®] cream, and Acid Mantle[®]

Rashes often resolve spontaneously after about 10 to 14 days of treatment. Some rashes are a potentially serious reaction to thalidomide treatment. Rare reactions include Stevens-Johnson syndrome and toxic epidermal necrolysis (TEN). Symptoms of Stevens-Johnson syndrome include persistent fever, rash, blisters, or red splotches on the skin and blisters in the mouth, eyes, ears, nose, and genital area. TEN is characterized by blistering and peeling of large sections of skin.

A doctor should be contacted immediately if a fever and/or drop in blood pressure occur.

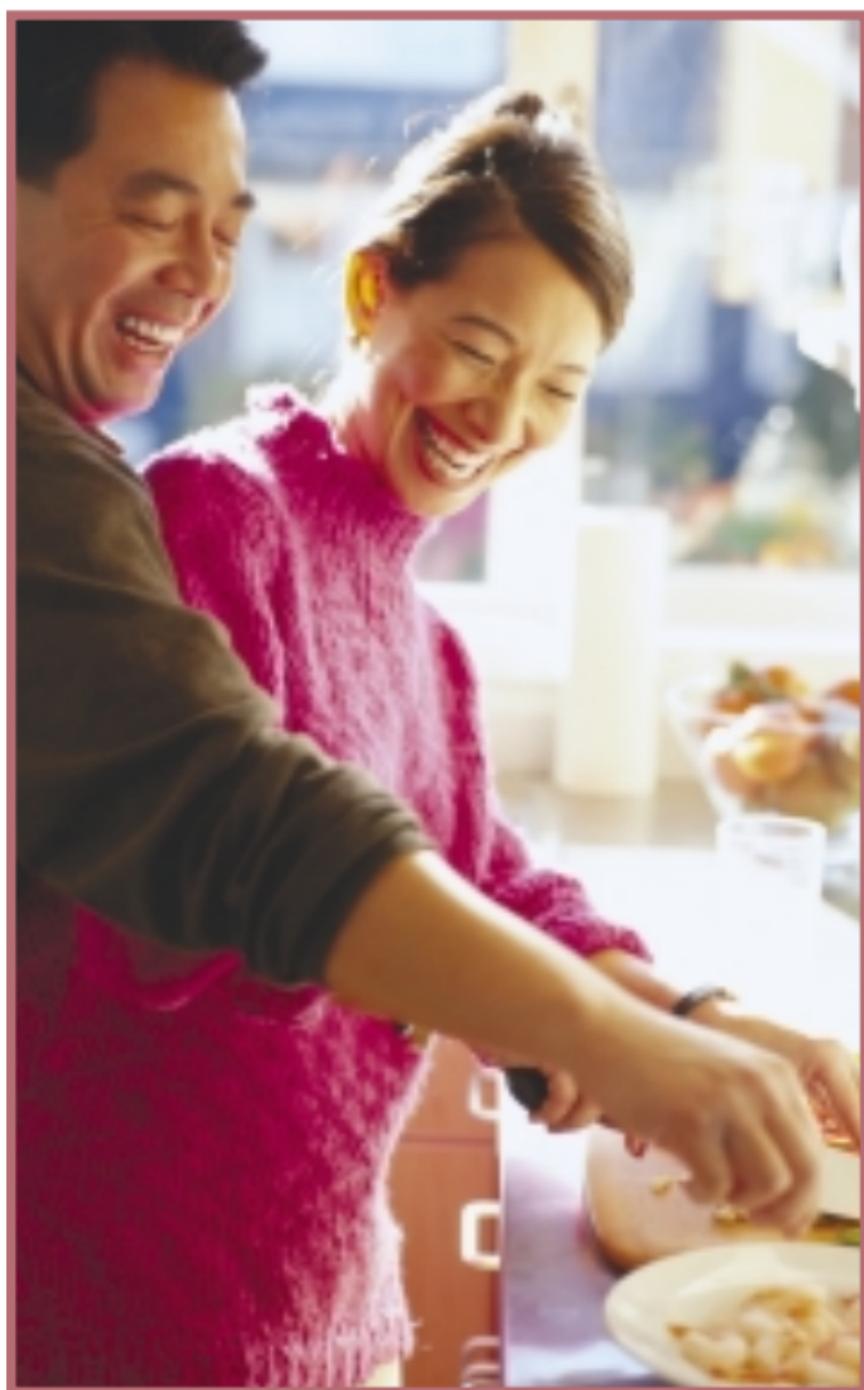
Leukopenia

Thalidomide can sometimes cause a decrease in white blood cells. This condition is called leukopenia. Because of this possibility, blood tests need to be done regularly. If the white blood cell count becomes too low, the dose of thalidomide may have to be changed or the treatment may need to be interrupted.



Who Should Not Take Thalidomide?

If thalidomide is taken during pregnancy, it can cause severe birth defects or death to an unborn baby. Thalidomide should never be used by women who are pregnant or who could become pregnant while taking the drug. Thalidomide may be detected in male sperm. Therefore, both men and women are required to follow strict rules for birth control while taking thalidomide.



Only physicians and pharmacists who are registered with the special program called S.T.E.P.S.[®] can prescribe or dispense thalidomide. Physicians and pharmacists may register with the S.T.E.P.S.[®] program by calling Celgene Corporation, the manufacturer of thalidomide, at 888-4-CELGENE (888-423-5436). Both men and women must agree to follow this program before receiving thalidomide. To minimize the risk of exposing an unborn child to thalidomide, the S.T.E.P.S.[®] program includes the following elements:

- Patients must provide informed consent, complete confidential enrollment, and complete follow-up surveys throughout treatment
- Women of childbearing age must have pregnancy tests every week during the first month of thalidomide therapy and monthly afterwards (every 2 weeks for women with irregular menstrual cycles)
- Women of childbearing age must receive contraceptive counseling and use 2 methods of birth control 4 weeks before, during, and at least 4 weeks after completing therapy
- Men who are sexually involved with women of childbearing age must use a latex condom during and at least 4 weeks after completing thalidomide therapy

How Is Thalidomide Given?

Thalidomide is available as a capsule. The dose, or number of capsules to be taken every day, will be determined by whether thalidomide is being given alone or in combination with other drugs. How the drug is tolerated by the body will also determine the dose.

The dose may be gradually increased over time. A gradual increase ensures the most effective dose is given as safely as possible.

If side effects occur, a doctor or nurse should be notified immediately. The dose may need to be lowered, or even discontinued, if the side effects are severe. The dose should only be changed under the direction of a doctor.

Can Thalidomide Be Taken With Other Cancer Treatments?

Yes, thalidomide can be taken alone or in combination with chemotherapy, radiation therapy, or biologic treatments. A doctor will advise on the appropriate treatment for each individual.

Will Insurance Cover the Cost of Thalidomide?

Insurance coverage varies. Individual insurance companies can provide information regarding thalidomide coverage. Celgene Corporation also offers a therapy assistance program. For more information about this program, call 888-4-CELGENE (888-423-5436).

A Final Note

Thalidomide is an important treatment for a number of diseases. However, like any drug, it can cause harm if misused. It is important that all advice from health care professionals be followed while taking this drug. Any questions should be promptly addressed by a doctor or nurse.

Questions and concerns regarding thalidomide treatment may arise once treatment begins. Some of these concerns may be about thalidomide itself. Others may be about the outcome of treatment and its side effects. Still other concerns may be more emotional or financial in nature.

Many resources are available. Concerns should be shared with the treatment team so that assistance can be provided. Communication will help lead to the active management of side effects, minimize symptoms, and help alleviate fears and concerns during treatment. Involvement in personal care will ultimately lead to confidence and a sense of control regarding treatment choices.



About the IMF

*"One person can make a difference,
Two can make a miracle."*

Brian D. Novis
IMF Founder

Myeloma is a little-known, complex, and often misdiagnosed bone marrow cancer that attacks and destroys bone. Myeloma affects approximately 75,000 to 100,000 people in the United States, with more than 14,500 new cases diagnosed each year. While there is presently no known cure for myeloma, doctors have many approaches to help myeloma patients live better and longer.

The International Myeloma Foundation (IMF) was founded in 1990 by Brian and Susie Novis shortly after Brian's myeloma diagnosis at the age of 33. It was Brian's dream that future patients would have easy access to medical information and emotional support throughout their battle with myeloma. He established the IMF with the 3 goals of treatment, education, and research. He sought to provide a broad spectrum of services for patients, their families, friends, and health care providers. Although Brian died 4 years after his initial diagnosis, his dream didn't. Today the IMF reaches out to an international membership of more than 100,000. The IMF was the first organization dedicated solely to myeloma, and today it remains the largest.

The IMF provides programs and services to aid in the research, diagnosis, treatment, and management of myeloma. The IMF ensures that no one must brave the myeloma battle alone.

We care for patients today, while working toward tomorrow's cure.

How Can the IMF Help You?

PATIENT EDUCATION

INFORMATION PACKAGE

Our free IMF InfoPack provides comprehensive information about myeloma, treatment options, disease management, and IMF services. It includes our acclaimed *Patient Handbook*.

INTERNET ACCESS

Log on to www.myeloma.org for 24-hour access to information about myeloma, the IMF, education, and support programs.

ONLINE MYELOMA FORUM

Join the IMF Internet Discussion Group at www.myeloma.org/listserve.html to share your thoughts and experiences.

MYELOMA MINUTE

Subscribe to this free weekly email newsletter for up-to-the-minute information about myeloma.

PATIENT & FAMILY SEMINARS

Meet with leading experts in myeloma treatment to learn more about recent advances in therapy and research.

MYELOMA MATRIX

New to our website and in print, this program is a comprehensive guide to drugs in development for myeloma.

MYELOMA TODAY NEWSLETTER

Our bimonthly newsletter is available free of charge by subscription.

SUPPORT

MYELOMA HOTLINE: 800-452-CURE

Toll-free throughout the United States and Canada, the IMF Hotline is staffed by specialists trained at the National Cancer Institute (NCI).

SUPPORT GROUPS

A worldwide network of more than 90 myeloma support groups hold regular meetings for members of the myeloma community. The IMF conducts annual retreats for myeloma support group leaders.

RESEARCH

BANK ON A CURE™

This DNA bank will provide genetic data research in new drug development.

THE INTERNATIONAL PROGNOSTIC INDEX (IPI)

This updated staging system for myeloma will enhance physicians' ability to select the most appropriate treatment for each patient.

RESEARCH GRANTS

Leading the world in collaborative research and achieving extraordinary results, the IMF Grant Program supports both junior and senior researchers working on a broad spectrum of projects. The IMF has attracted many young investigators into the field of myeloma, and they have remained in the field and are actively pursuing a cure for this disease.

Glossary

Cells: The smallest unit of living organisms. Many cells together make up a tissue, and organized tissues make up the organs of the human body.

Chemotherapy: Drugs that are used to kill cancer cells.

Clinical trial: Study in which the effectiveness of a drug is tested in a group of patients using a specific treatment protocol.

Complete response: When a tumor regresses to such an extent that it is undetectable. For myeloma, a complete response means that the myeloma protein can no longer be detected in the blood and/or urine and that the bone marrow shows no evidence of myeloma.

Disease stabilization: When a tumor stops progressing and remains the same size.

Erythema nodosum leprosum: A condition that affects some patients with leprosy, in which areas of the skin become reddened when small blood vessels become congested.

Immunomodulatory agent: A drug that affects the level of an immune response against invading tumor cells such as myeloma.

Inflammatory: Pertaining to a protective response of the body against injury or disease.

Leukopenia: A low level of white blood cells.

Myeloma: A cancer of bone marrow plasma cells. Cancerous plasma cells are called myeloma cells.

Partial response: When a tumor regresses at least by half but does not disappear completely (in myeloma, a 25% to <50% decrease in paraprotein levels).

Peripheral neuropathy: Tingling or numbness in the hands, arms, legs, and/or feet.

Side effects: Unwanted effects caused by a drug.

S.T.E.P.S.[®] (System for Thalidomide Education and Prescribing Safety) program: A program designed for doctors, nurses, pharmacists, and patients to ensure that developing fetuses are not exposed to thalidomide.

White blood cells: Blood cells that help the body fight infection.

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