Understanding DARZALEX® (daratumumab) injection
Founded in 1990, the International Myeloma Foundation (IMF) is the first and largest organization focusing specifically on multiple myeloma. The IMF’s reach extends to more than 525,000 members in 140 countries worldwide. The IMF is dedicated to improving the quality of life of myeloma patients while working toward prevention and a cure through our four founding principles: Research, Education, Support, and Advocacy.

**RESEARCH** The signature project of the IMF’s Research division is the Black Swan Research Initiative®, a groundbreaking and collaborative effort to develop the first definitive cure for myeloma. Each year, the IMF also awards Brian D. Novis Grants, which promote research for better myeloma treatments, management, and practices in the field. In addition, more than 200 leading myeloma researchers comprise the IMF’s International Myeloma Working Group (IMWG), a research body that has developed myeloma guidelines that are followed around the world. Finally, the IMF’s Nurse Leadership Board (NLB), comprised of nurses from leading myeloma treatment centers, develops recommendations for the nursing care of myeloma patients.

**EDUCATION** The IMF Patient & Family Seminars and Regional Community Workshops are held around the world to provide up-to-date information presented by leading myeloma specialists and researchers directly to patients and their families. The IMF’s library of more than 100 publications, for patients and caregivers as well as for healthcare professionals, is updated annually and available free of charge. Publications are available in more than 20 languages.

**SUPPORT** The IMF’s InfoLine is staffed by information specialists who answer myeloma-related questions and provide support via phone and email to thousands of families each year. In addition, the IMF sustains a network of more than 150 myeloma support groups and offers training for the hundreds of dedicated patients, caregivers, and nurses who volunteer to lead these groups in their communities.

**ADVOCACY** The IMF’s Advocacy team has educated and empowered thousands of individuals who make a positive impact each year on issues critical to the myeloma community. Working in the US at both federal and state levels, we lead coalitions to advocate for parity in insurance coverage. We also represent the myeloma community’s interests before the US Congress and agencies such as the National Institutes of Health, the Food and Drug Administration, the Centers for Medicare and Medicaid Services, and the Veterans Administration. Outside the US, the IMF’s Global Myeloma Action Network (GMAN) works to help patients gain access to treatment.

Learn more about the ways the IMF is helping to improve the quality of life of myeloma patients while working toward prevention and a cure. Contact us at 818.487.7455 or 800.452.CURE, or visit myeloma.org.

Improving Lives Finding the Cure®
Table of contents

What you will learn from this booklet 4
What is Darzalex? 4
How does Darzalex work? 5
Who is a candidate for Darzalex? 6
How is Darzalex given? 6
What are the dose and schedule of Darzalex? 7
Ongoing clinical trials 7
Warnings and precautions 8
What are the possible side effects of Darzalex, and how are they managed? 8
Access to Darzalex and other resources 12
In closing 13
Terms and definitions 13
What you will learn from this booklet

The IMF’s Understanding series of booklets is designed to acquaint you with treatments and supportive care measures for multiple myeloma (which we refer to simply as “myeloma”). Words in bold+blue type are explained in the “Terms and definitions” section at the end of this booklet, as well as in a more complete compendium of myeloma-related vocabulary, the IMF’s Glossary of Myeloma Terms and Definitions, located at glossary.myeloma.org.

Myeloma is a cancer that is not known to most patients at the time of diagnosis. To be empowered to play an active role in your own medical care and to make good decisions about your care with your doctor, it is vital for you to learn as much as possible about myeloma and its treatments. The information in this booklet will help you in discussions with your healthcare team. The more information you have about resources that are available to you, the better and more fruitful those discussions will be.

This booklet discusses Darzalex® (also known by its generic drug name, daratumumab). It will familiarize you with the way Darzalex works, how it has been tested, the indications for which it is approved, how and when it is administered, its possible side effects, and how to manage those side effects.

Before reading this booklet, it may be helpful to read another IMF publication, Understanding the Immune System in Myeloma, which will provide some background on the types and functions of immune system cells, how they work together to protect us, the impact of myeloma on the immune system, and the way in which Darzalex enlists immune system cells to help attack and kill myeloma cells.

What is Darzalex?

Darzalex, a highly effective medication to treat myeloma, is a monoclonal antibody. Although antibodies are a naturally-occurring part of the immune system, Darzalex and other antibodies used to treat cancer are made in a laboratory.

A laboratory-made antibody (or immunoglobulin, as an antibody is known in scientific language) is designed to function like a naturally occurring antibody and to target a specific single protein on the surface of cancer cells. It is therefore also called a “targeted therapy.” Of the four therapies for myeloma approved by the US Food and Drug Administration (FDA) in 2015, only Darzalex has single-agent activity and was approved based on its superiority to existing treatments for myeloma.
How does Darzalex work?

Darzalex targets CD38, a **glycoprotein**. “CD” in CD38 stands for “cluster of differentiation,” a system for identifying the various **molecules** that serve as binding sites, or **antigens**, to which antibodies bind on the surface of cells. CD38 is widely expressed on the surface of myeloma cells, but is only expressed at low levels on other cells in the **bone marrow**, making it easier for them to recover after therapy.

When Darzalex binds to CD38, it causes myeloma cell death in multiple ways:

- It kills myeloma cells directly.
- It recruits immune system cells called **macrophages**, which bind to the Darzalex-CD38 complex and then engulf and destroy myeloma cells.
- It attracts **natural killer (NK) cells**, which target and kill myeloma cells.
- It recruits **complement proteins** that boost the killing power of antibodies and punch holes in the targeted myeloma cells.
- It modulates the immune response by decreasing immune system suppression.
- It inhibits CD38 from functioning as an **enzyme** that regulates calcium flux in the cell. Blocking the transfer of calcium ions is toxic to cancer cells but spares normal cells.

*Figure 1. Daratumumab (DARA) mechanisms of action*
Who is a candidate for Darzalex?

In the United States, Darzalex is indicated for the treatment of adult patients with myeloma:

- In combination with Revlimid® (lenalidomide) + dexamethasone (Rd) in newly diagnosed patients who are ineligible for autologous stem cell transplant (ASCT) and in patients with relapsed or refractory myeloma who have received at least one prior therapy,
- In combination with Velcade® (bortezomib) + melphalan + prednisone (VMP) in newly diagnosed patients who are ineligible for ASCT,
- In combination with Velcade + thalidomide + dexamethasone (VTd) in newly diagnosed patients who are eligible for ASCT,
- In combination with Velcade + dexamethasone (Vd) in patients who have received at least one prior therapy,
- In combination with Pomalyst® (pomalidomide) + dexamethasone (Pd) in patients who have received at least two prior therapies including Revlimid + a proteasome inhibitor (Kyprolis® [carfilzomib], Ninlaro® [ixazomib], or Velcade),
- As monotherapy in patients who have received at least three prior lines of therapy including a proteasome inhibitor + an immunomodulatory drug (Pomalyst, Revlimid, or thalidomide), or who are double-refractory to a proteasome inhibitor and an immunomodulatory agent.

In Europe:

- Darzalex as a single agent is approved for monotherapy of adult patients with relapsed and refractory myeloma, whose prior therapy included a proteasome inhibitor and an immunomodulatory drug, and who have demonstrated disease progression on their last therapy.
- Darzalex is approved in combination with Revlimid + dexamethasone or Velcade + dexamethasone for the treatment of patients with myeloma who have received at least one prior therapy.
- Darzalex is approved in combination with Velcade + melphalan + prednisone (VMP) for the treatment of adult patients with newly diagnosed myeloma who are ineligible for autologous stem cell transplant.

How is Darzalex given?

Darzalex is administered as an intravenous (IV, into the vein) infusion at a doctor’s office or a hospital clinic.
What are the dose and schedule of Darzalex?

Especially with the first dose of Darzalex, the infusion rate is very slow. The slower the rate of infusion, the less likely it is that a severe infusion reaction will occur. The first dose is usually given over a period of up to 8 hours. If it is well tolerated, subsequent doses may be given more rapidly at your doctor’s discretion. Medications are given before and after each Darzalex infusion to help prevent a reaction.

A split-dosing regimen, the option to split the first infusion of Darzalex over two consecutive days is approved in both the US and Europe. The concentration of Darzalex in the body was found to be comparable regardless of whether the first dose was administered as a split infusion or as a single first infusion.

- The dose of Darzalex, whether alone or in combination with Revlimid + dexamethasone, is 16 mg/kg of body weight. It is given weekly for weeks 1–8, every 2 weeks for weeks 9–24, and every 4 weeks for weeks 25 onward until disease progression.
- In combination with Velcade + dexamethasone, Darzalex is given at the standard dose, but is given weekly for weeks 1–9, every 3 weeks for weeks 10–24, and every 4 weeks for weeks 25 onward until disease progression.

Ongoing clinical trials

Many clinical trials are studying Darzalex for newly diagnosed myeloma or in new combinations, including:

- Darzalex + Velcade + Revlimid + dexamethasone (D-VRd) vs VRd in the frontline setting.
- Darzalex + Velcade + cyclophosphamide + dexamethasone (D-VCd) vs VCd in the frontline setting.
- Darzalex + Ninlaro + Revlimid + dexamethasone (D-IRd) in the frontline setting.
- Darzalex + Kyprolis + Revlimid + dexamethasone (D-KRd) in the frontline setting.
- Darzalex + Kyprolis + Revlimid + dexamethasone (D-KRd) in high-risk smoldering multiple myeloma (SMM).
- Darzalex + Revlimid as post-ASCT maintenance therapy in minimal residual disease (MRD) positive patients.
- Darzalex + Kyprolis + dexamethasone (D-Kd) in relapsed/refractory myeloma.
- Darzalex + Ninlaro + Revlimid + dexamethasone (D-IRd) in relapsed/refractory myeloma.
- Darzalex in subcutaneous administration in relapsed/refractory myeloma.

**Warnings and precautions**

**Interference with blood tests**
- Darzalex binds to the CD38 cell surface antigen on red blood cells and interferes with blood compatibility testing, including antibody screening and cross-matching done prior to blood transfusions. Your doctor should type and screen your blood before you start treatment with Darzalex in case you need a blood transfusion subsequently.
- Darzalex has been known to interfere with the results of serum protein electrophoresis (SPEP) and immunofixation electrophoresis (IFE) tests used to monitor myeloma. This led to false positive test results for patients with IgG kappa myeloma protein, leading to inaccuracies in detecting complete response and disease progression. In January 2018, the FDA approved a new assay for evaluating monoclonal protein in serum by IFE for myeloma patients treated with Darzalex.

**Risk of herpes zoster infection**
A small percentage of patients in clinical trials with Darzalex developed reactivation of the herpes zoster virus. The current package insert for Darzalex stipulates that all patients should receive preventive treatment with an antiviral medication, such as acyclovir or valacyclovir, within one week after starting Darzalex and continuing for three months following treatment. Before starting treatment with Darzalex, please discuss preventive antiviral treatment with your doctor.

**Pregnancy**
There are no human data to inform a risk with use of Darzalex during pregnancy, but anti-cancer agents and monoclonal antibodies may cause fetal harm in general. To avoid exposure to the fetus, women of reproductive potential should use effective contraception during treatment and for 3 months after stopping Darzalex treatment.

**What are the possible side effects of Darzalex, and how are they managed?**
Side effects that occurred in 20% or more of the patients in the Darzalex registration clinical trials (registration trials are clinical trials that are evaluated by the FDA before a drug is approved) were infusion reactions, fatigue, nausea, back pain, fever, cough, and upper respiratory tract
infection. In addition to these side effects, Darzalex may also cause blood cell counts to drop, with significant numbers of patients experiencing low red blood cell counts (anemia), low platelet counts (thrombocytopenia), and low white blood cell counts (neutropenia and lymphopenia). Blood counts are carefully monitored during treatment with Darzalex. If they are too low, your doctor will either hold your dose of Darzalex until your counts improve or will provide you with supportive care in the form of transfusions or medications that stimulate the formation of new blood cells.

Infusion reactions

Infusion reactions can occur with many intravenously-administered cancer therapies. Infusion reactions to monoclonal antibodies are caused by the release of cytokines and are sometimes referred to as “cytokine-release syndrome.” Cytokines are small proteins that are released by cells in order to affect the behavior of other cells. Infusion reactions result from the release of cytokines from cells targeted by the monoclonal antibody as well as from immune system cells that are recruited to the targeted area. Reactions are often flu-like, and include nasal congestion, fever, chills, cough, throat irritation, difficulty breathing, low blood pressure, nausea, and rash.

Infusion reactions occurred in 46% of the patients in the registration trials for Darzalex, most of them mild to moderate, and most occurring during or within four hours after the first infusion. Infusion reactions occurred in 5% of the patients with the second infusion and in 4% with subsequent infusions. Infusion reactions that were severe enough to require hospitalization occurred in 3% of patients. There were no life-threatening infusion reactions.

Prevention and treatment of infusion reactions

Medications are given both before and after Darzalex infusions to minimize the risk of infusion reactions.

Approximately one hour before every infusion of Darzalex, all patients receive:

- An intravenously administered corticosteroid, such as methylprednisolone.
- An oral medication to reduce/prevent fever, such as acetaminophen.
- An oral or intravenous (IV) antihistamine, such as diphenhydramine.

All patients receive post-infusion medication to reduce the risk of delayed infusion reactions. An oral corticosteroid (as above) is given to the patient on the day of and the day after each Darzalex infusion.
If a reaction of any kind occurs during the administration of Darzalex, the infusion will be stopped.

**Fatigue**

Fatigue is commonly associated with cancer and with cancer therapy. 39% of the patients in the registration trials for Darzalex experienced fatigue, all but 2% of which was mild to moderate and did not limit the patients’ ability to care for themselves. Caution is advised if you are operating machinery, including automobiles. For more detailed information, please see the IMF publication *Understanding Fatigue*.

**Prevention and treatment of fatigue**

The effects of fatigue may be minimized by maintaining:

- A moderate level of activity.
- A healthy diet and proper fluid intake.
- A consistent sleeping schedule with enough rest.
- Regularly scheduled visits with your doctor or healthcare provider to discuss issues that may contribute to your fatigue.
- A careful review of the side effects of any other supplements and medications you are taking to ensure that they are not contributing to your fatigue.

**Nausea**

Approximately one quarter of the patients in the registration trials had mild to moderate nausea. There were no cases of severe nausea.

**Prevention and treatment of nausea**

For patients who have been treated with Darzalex in clinical trials, nausea was most likely to be a short-lived infusion-related reaction rather than an ongoing side effect. Pre- and post-infusion medications help to reduce the occurrence and severity of nausea. Your doctor may order an anti-nausea drug such as ondansetron or granisetron prior to your Darzalex infusion.

**Back pain**

Treatment-related (rather than myeloma-related) back pain can occur as a result of inflammatory cytokines released in reaction to the monoclonal antibody or may occur because a patient receiving Darzalex has low levels of **white blood cells (WBC)** and develops an infection along with body aches and pains. Of the 25% of patients who experienced back pain in the Darzalex registration trials, only 2% experienced back pain that was severe enough to limit their ability to care for themselves.
**Prevention and treatment of back pain**

As with any infusion reaction, pre- and post-infusion medications can reduce or prevent infusion-related back pain. If back pain is the result of a flu infection, you should consult your doctor, who will treat you with appropriate medication.

**Fever**

Fever is defined as an oral temperature greater than 38°C or 100.4°F. When the white blood cell count is low, the body’s ability to defend itself against infections is compromised, and fever needs to be further evaluated immediately. Fever can also be a sign of the interaction of the monoclonal antibody with the immune system, as it may be a flu-like symptom caused by the release of cytokines in an infusion reaction.

**Prevention and treatment of fever**

You can minimize the effects of fever in the following ways:

- Notify your healthcare team immediately if you have a fever greater than 38°C or 100.4°F.
- If your doctor’s office is closed and you are not able to reach a covering physician, go to an urgent care facility or emergency room to have the fever worked up.
- Check your temperature twice a day if you feel warm.
- To avoid dehydration, drink a lot of non-alcoholic and non-caffeinated liquids.
- Take medications to control the fever as indicated.

Your treating physician may also do the following to control fever and treat its cause:

- Tell you to use over-the-counter medications (medications that you can buy without a prescription) such as acetaminophen to treat fever related to flu-like syndrome. Do not take more than the recommended amount of acetaminophen in a 24-hour time frame. There are other drugs used to reduce fever that may be an option, but you should not take any medications without first consulting a doctor familiar with your medical history.
- If you have a fever as a result of an infection, the doctor will prescribe antibiotics, or you may need to receive intravenous antibiotics in the hospital. You may also be given a drug that helps to boost the white cell count (a “colony-stimulating factor”).
Cough
Infusion reactions to Darzalex have included a range of respiratory symptoms such as cough, wheezing, throat tightness and irritation, swelling of the throat and lungs, nasal congestion, and allergic rhinitis (irritation and inflammation of the mucus membranes inside the nose). Cough was reported in 21% of the patients enrolled in the registration trials for Darzalex, all of it mild to moderate.

Prevention and treatment of cough
As with the other infusion reaction-related events listed in these pages, cough can be best managed proactively with pre- and post-infusion medications. If you develop a cough as a result of an upper respiratory infection, your doctor will recommend medications, if appropriate, to treat the infection. In general, maintaining good hydration, drinking hot liquids, taking lozenges, avoiding irritants in the air, and breathing warm steam from a shower or humidifier will help relieve your symptoms.

Upper respiratory tract infection (URI)
Upper respiratory tract infection is a bacterial or viral infection of the nose, throat, sinuses, or larynx. 20% of the patients in the registration trials for Darzalex had a URI; all but 1% were mild to moderate.

Prevention and treatment of upper respiratory tract infection
As with fever and cough above, you must report your symptoms to a member of your healthcare team right away. You will be treated with medications if necessary. If your infection is serious and your white blood cell count is low, the doctor may hold your Darzalex infusion until you recover or support you with medications to stimulate the production of new white blood cells.

Access to Darzalex and other resources
Janssens Pharmaceuticals has a CarePath program to help support patients who are receiving treatment with Darzalex. Visit darzalex.com or call 844.553.2792. CarePath case coordinators can help you with:

- Access to nurse educators.
- Referrals to independent organizations that provide assistance with costs associated with travel to and from treatment.
- A tool that connects patients and caregivers to national and/or state advocacy groups that offer resources relevant to their needs.
- Personalized, live appointment reminders.
In closing

While a diagnosis of cancer is something you cannot control, gaining knowledge that will improve your interaction with your doctors and nurses is something you can control, and it will have a significant impact on how well you do throughout the disease course.

This booklet is not meant to replace the advice of your doctors and nurses who are best able to answer questions about your specific healthcare management plan. The IMF intends only to provide you with information that will guide you in discussions with your healthcare team. To help ensure effective treatment with good quality of life, you must play an active role in your own medical care.

We encourage you to visit myeloma.org for more information about myeloma and to contact the IMF InfoLine with your myeloma-related questions and concerns. The IMF InfoLine consistently provides callers with the most up-to-date and accurate information about myeloma in a caring and compassionate manner. IMF InfoLine specialists can be reached at InfoLine@myeloma.org or 800.452.CURE or 818.487.7455.

Terms and definitions

Anemia: A decrease in hemoglobin, a protein which is contained in red blood cells and carries oxygen to the body’s tissues and organs. Anemia is usually defined as hemoglobin below 10 g/dL, and/or as a decrease of ≥ 2 g/dL from the normal level for an individual. Over 13–14 g/dL is considered normal.

Antibody: A protein produced by plasma cells in response to an antigen that enters the body. Also see “Immunoglobulin.”

Antigen: Any foreign substance (such as bacteria, a virus, toxin, or tumor) that causes the immune system to produce natural antibodies.

Antihistamine: A drug that acts against histamine, a powerful and highly irritant agent released in the body after contact with certain allergens.

Bone marrow: The soft, spongy tissue in the center of bones that produces white blood cells, red blood cells, and platelets. This is the tissue within which abnormal plasma cells build up when myeloma is growing.

Calcium: A mineral found mainly in the hard part of bone matrix (hydroxyapatite). If produced or released in excess, it can build up in the bloodstream. See “Hypercalcemia.”

Cancer: A term for diseases in which malignant cells divide without control. Cancer cells can invade nearby tissues and spread through the bloodstream and lymphatic system to other parts of the body.
Clinical trial: A research study of new treatment that involves patients. Each study is designed to find better ways to prevent, detect, diagnose, or treat cancer and to answer scientific questions.

- **Control group** – The arm of a randomized clinical trial that receives the standard treatment or placebo (no treatment).
- **Experimental group** – The arm of a randomized trial that gets the new treatment.
- **Randomized clinical trial** – A research study in which subjects are randomly assigned to receive a particular treatment or not.
- **Arm** – One of the treatment groups of a randomized trial. The majority of randomized trials have two, but some have more.
- **End point** – The goal of the trial; what a clinical trial is trying to measure or find out. Typical end points include measurements of toxicity, response rate, and survival.
- **Double blind** – Aspect of a randomized trial in which neither the participant nor the investigator knows the arm of the trial to which the patient is assigned. The purpose is to eliminate any bias in the reporting of results.
- **Phase I trial** – A trial designed to determine the maximum-tolerated dose (MTD) of a new drug or a new combination of drugs. It is usually the first human testing of a new treatment, although in phase I trials of combination therapies, the individual elements may already have been well tested. Patients in phase I trials generally have advanced cancer that is refractory to all standard treatment. In a typical phase I trial, successive groups (“cohorts”) of 3 to 6 patients are given the treatment. All patients in a cohort get the same dose. The first cohort typically gets a very low dose, and the dose is raised in each subsequent cohort until a set number of patients experience dose-limiting toxicity (DLT). The dose level used for the previous cohort is then taken to be the MTD. This dose is then used in a phase II trial.
- **Phase II trial** – A trial designed to determine the response rate of a new therapy that has already been tested in phase I trials. Typically, 14 to 50 patients with one type of cancer are treated to see how many have a response. Patients are usually required to have advanced cancer that is refractory to any standard treatment. In addition, patients must have measurable disease. If results from a phase II trial are promising enough, the treatment may then be tested in a phase III trial. If the results are obviously much better than the standard treatment, then it may not be necessary to do a phase III trial, and the treatment may be approved based on phase II trial results.
- **Phase III trial** – A trial designed to compare two or more treatments for a given type and stage of cancer. The end point of a phase III trial is usually survival or disease-free survival. Phase III trials are usually randomized, so patients don’t choose which treatment they receive.
A typical phase III trial has 50 to thousands of patients. Some phase III trials compare a new treatment that has had good results in phase II trials with an older, well known, standard treatment. Other phase III trials compare treatments that are already in common use. Some treatments in phase III trials may be available outside the clinical trial setting.

• **Phase IV trial** – Even after a drug has been approved by the United States Food and Drug Administration (FDA) for use in a particular indication, there may be need for additional studies. Phase IV clinical trials may be required by regulatory authorities or may be undertaken by the sponsoring company for a variety of reasons. For example, safety surveillance is designed to detect any rare or long-term side effects over a larger patient population and longer time period than was possible during the phase I–III clinical trials.

**Complement proteins:** A complex system of more than 30 proteins that act in concert to help eliminate infectious microorganisms. The complement system causes the lysis (bursting) of foreign and infected cells, the phagocytosis (ingestion) of foreign particles and cell debris, and the inflammation of surrounding tissue.

**Cytokine:** Cytokines are proteins secreted by cells which can stimulate or inhibit growth/activity in other cells. Cytokines are produced locally (for myeloma, in the bone marrow) and circulate in the bloodstream. Cytokines are normally released in response to infection.

**Electrophoresis:** A laboratory test in which a patient’s serum (blood) or urine proteins are subjected to separation according to their size and electrical charge. For myeloma patients, electrophoresis of the blood or urine allows both the calculation of the amount of myeloma protein via serum or urine electrophoresis (SPEP or UPEP), as well as the identification of the type of M-spike for each patient (immunoelectrophoresis, IFE). Electrophoresis is used as a tool both for diagnosis and for monitoring.

**Enzyme:** A protein molecule manufactured by a cell. An enzyme acts as a catalyst that increases the rate of a specific biochemical reaction in the body.

**Frontline therapy:** A general term for the initial treatment used in an effort to achieve response in a newly diagnosed myeloma patient. See “**Induction therapy**” and “**Response.**”

**Generic drug name:** A generic drug name refers to the chemical makeup of a drug rather than its brand name. A generic name is given to a drug before it is approved and given a brand name. After a drug goes off patent, other manufacturers may make generic versions of the drug. For example: ibuprofen is the generic name for drugs brand-named Advil® and Motrin®.

**Glycoproteins:** Proteins on the outer surface of cells that have sugars (carbohydrates) attached to them. They function as receptor sites where other molecules may attach to the cell.
**Herpes zoster:** The virus that causes chicken pox. When reactivated, the herpes zoster infection frequently affects nerves. This condition is also called “Shingles.”

**Hypercalcemia:** A higher than normal level of calcium in the blood. In myeloma patients, it usually results from bone breakdown with release of calcium from the bone into the bloodstream. This condition can cause a number of symptoms, including loss of appetite, nausea, thirst, fatigue, muscle weakness, restlessness, and confusion. See “Calcium.”

**Immune system:** The body’s defense system from pathogens and foreign substances that destroys infected and malignant cells and removes cellular debris. The immune system includes white blood cells and organs and tissues of the lymphatic system.

**Immunofixation electrophoresis (IFE):** An immunologic test of the serum or urine used to identify proteins. For myeloma patients, it enables the doctor to identify the M-protein type (IgG, IgA, kappa, or lambda). The most sensitive routine immunostaining technique, it identifies the exact heavy- and light-chain type of M-protein.

**Immunoglobulin (Ig):** A protein produced by plasma cells; an essential part of the body’s immune system. Immunoglobulins attach to foreign substances (antigens) and assist in destroying them. The classes (isotypes) of immunoglobulins are IgG, IgA, IgD, IgE, and IgM. Also see “Antibody.”

**Immunomodulatory drug:** An agent that affects, enhances, or suppresses the immune system. Sometimes called an IMiD® compound.

**Induction therapy:** A specific term used for the initial treatment given to a patient in preparation for an autologous stem cell transplant (ASCT). See “Frontline therapy” and “Line of therapy.”

**Infusion reaction:** An allergic or cytokine-related response to an intravenously administered cancer treatment.

**Line of therapy:** A term used to calculate the number of therapies a patient has received. Induction therapy + an autologous stem cell transplant (ASCT) is considered a single line of therapy. See “Induction therapy.”

**Lymphopenia:** Low levels of B cells, T cells, and natural killer (NK) cells. Also called “lymphocytopenia.”

**Macrophage:** A macrophage is an immune system cell whose job it is to engulf and devour any cell (including a cancer cell) that does not have proteins on its surface that identify it as a healthy body cell.

**Minimal residual disease (MRD):** The presence of residual tumor cells after treatment has been completed and complete remission (CR) has been attained. Even patients who have attained a stringent complete response (sCR) may have MRD. Very sensitive new testing methods are now able to detect 1 myeloma cell among 1,000,000 sampled cells in blood or bone marrow. See “MRD-negative.”
Molecule: The smallest particle of a substance that retains all the properties of the substance. A molecule is an electrically neutral group composed of two or more atoms held together by chemical bonds.

Monoclonal antibody: An antibody manufactured in a lab rather than produced in the human body. Monoclonal antibodies are specifically designed to find and bind to cancer cells and/or immune system cells for diagnostic or treatment purposes. Monoclonal antibodies can be used alone, or they can be used to deliver drugs, toxins, or radioactive material directly to tumor cells.

MRD-negative: Minimal residual disease-negative; not even one myeloma cell found in 100,000 or 1,000,000 bone marrow plasma cells sampled (depending on the test). See “Minimal residual disease.”

Multiple myeloma: A cancer of the bone marrow plasma cells, white blood cells that make antibodies. The cancerous plasma cells are called myeloma cells.

Natural killer (NK) cell: A lymphocyte (type of white blood cell) that is a component of the innate immune system. NK cells are responsible for tumor surveillance and are able to induce strong responses against tumors through the release of cytokines.

Neutropenia: A reduced level of neutrophils, a type of white blood cell necessary to combat bacterial infection.

Progressive disease: Myeloma that is becoming worse or relapsing, as documented by tests. Defined as an increase of $\geq 25\%$ from the lowest confirmed response value in the myeloma protein level and/or new evidence of disease.

Proteasome inhibitor: Any drug that interferes with the normal function of the proteasome, an enzyme complex responsible for breaking down and recycling unwanted proteins in both normal cells and cancer cells.

Proteins: Substances composed of amino acids. Proteins are an essential part of all living organisms, especially as structural components of body tissues such as muscle, hair, collagen, etc., as well as enzymes and antibodies.

Refractory: Disease that is no longer responsive to standard treatments. Patients with refractory myeloma have had progressive disease either during treatment or within 60 days following treatment. Most clinical trials for advanced disease are for patients with relapsed and/or refractory myeloma.

Relapse: The reappearance of signs and symptoms of a disease after a period of improvement. Patients with relapsed disease have been treated, then developed signs and symptoms of myeloma at least 60 days after treatment ended. Most clinical trials for advanced disease are for patients with relapsed and/or refractory myeloma.
Response or remission: Complete or partial disappearance of the signs and symptoms of cancer. Remission and response are interchangeable terms.

- **Stringent complete response (sCR)** – sCR is CR (as defined below) plus normal FLC ratio and absence of clonal cells in bone marrow by immunohistochemistry or immunofluorescence.

- **Complete response (CR)** – For myeloma, CR is negative immunofixation on serum (blood) and urine, and disappearance of any soft tissue plasmacytomas, and ≤ 5% plasma cells in bone marrow. CR is not the same as a cure.

- **Very good partial response (VGPR)** – VGPR is less than CR. VGPR is serum M-protein and urine M-protein detectable by immunofixation but not on electrophoresis, or 90% or greater reduction in serum M-protein, plus urine M-protein less than 100 mg per 24 hours.

- **Partial response (PR)** – PR is a level of response in which there is at least a 50% reduction in M-protein, and reduction in 24-hour urinary M-protein by at least 90% (or to less than 200 mg per 24 hours).

Side effect: Unwanted effect caused by a drug. Also known as “adverse reaction” or “adverse event (AE).”

Smoldering multiple myeloma (SMM): SMM is a higher level of disease than MGUS, but is still not active myeloma with CRAB features indicating organ damage. Patients with standard-risk SMM do not require treatment, but should be observed at regular intervals by a hematologist-oncologist. Patients with high-risk SMM may choose to participate in a clinical trial.

Subcutaneous injection or “shot”: A method of administering medication under the skin by a short needle that injects a drug into the tissue layer between skin and muscle.

Thrombocytopenia: A low number of platelets in the blood. “Normal” levels vary from laboratory to laboratory. The normal level at the Mayo Clinic is 150,000–450,000. If the platelet count is less than 50,000, bleeding problems could occur. Major bleeding is usually associated with a reduction to less than 10,000.

White blood cells (WBC): General term for a variety of cells responsible for fighting invading germs, infection, and allergy-causing agents. These cells begin their development in bone marrow and then travel to other parts of the body. Specific white blood cells include neutrophils, basophils, eosinophils, lymphocytes, and monocytes.
You are not alone. The IMF is here to help.

Myeloma is a cancer that is not known to most patients at the time of diagnosis. To be empowered to play an active role in your own medical care and to make good decisions about your care with your doctor, it is vital for you to learn as much as possible about myeloma and its treatments.

The IMF produces and maintains a library of publications to help arm you with one of the most important weapons in the fight against myeloma: INFORMATION. The following is a partial list of publications available in English, and selected titles are also available in other languages.

- Patient Handbook
- Concise Review of the Disease and Treatment Options
- Understanding Clinical Trials
- Understanding DARZALEX® (daratumumab) injection
- Understanding Dexamethasone and Other Steroids
- Understanding EMPLICITI® (elotuzumab)
- Understanding FARYDAK® (panobinostat) capsules
- Understanding Fatigue
- Understanding Freelite® and Hevylite® Tests
- Understanding High-Dose Therapy with Stem Cell Rescue
- Understanding the Immune System in Myeloma
- Understanding KYPROLIS® (carfilzomib) injection
- Understanding MGUS and Smoldering Multiple Myeloma
- Understanding NINLARO® (ixazomib) capsules
- Understanding Peripheral Neuropathy in Myeloma
- Understanding POMALYST® (pomalidomide) capsules
- Understanding REVLIMID® (lenalidomide)
- Understanding the Role of Vertebroplasty and Kyphoplasty
- Understanding Thalidomide Therapy
- Understanding Treatment of Myeloma Bone Disease
- Understanding Treatment of Myeloma-Induced Vertebral Compression Fractures
- Understanding VELCADE® (bortezomib) injection
- Understanding the VRd Regimen for Newly Diagnosed Myeloma
- Understanding XPOVIO™ (selinexor)
- Understanding Your Test Results

All IMF publications and periodicals are always free of charge. Visit publications.myeloma.org to read, download, or order printed copies. Subscribe to IMF periodicals at subscribe.myeloma.org or by contacting the IMF.

As always, the IMF urges you to discuss all medical issues with your doctor, and to contact the IMF’s InfoLine specialists with your myeloma questions and concerns.

818.487.7455        800.452.CURE        TheIMF@myeloma.org