



*Understanding*  
**DARZALEX<sup>®</sup>**  
(daratumumab) injection



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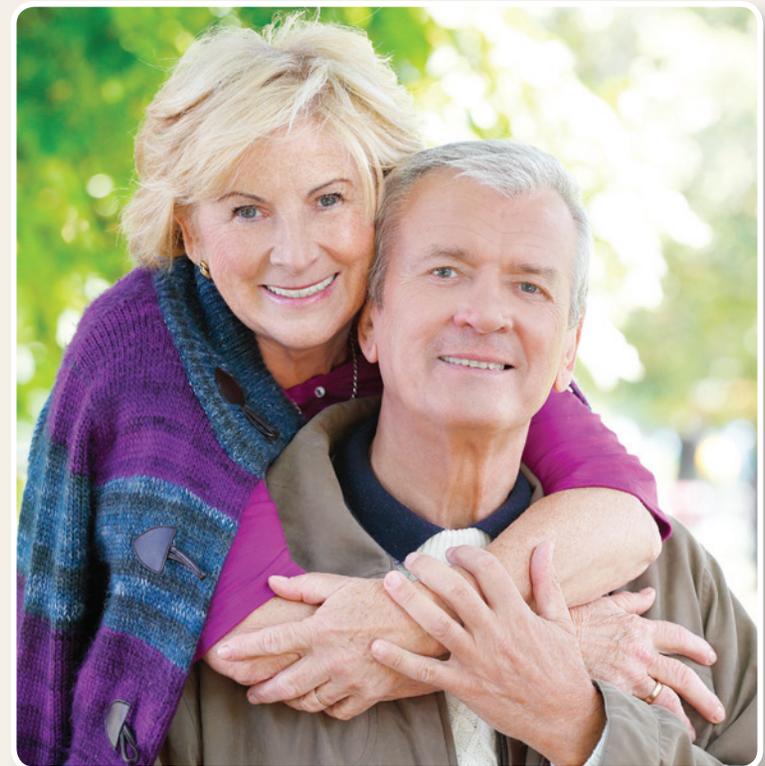
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**Founded in 1990, the International Myeloma Foundation (IMF) is the first and largest organization focusing specifically on multiple myeloma. The IMF's reach extends to more than 525,000 members in 140 countries worldwide. The IMF is dedicated to 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 trained specialists who answer questions and provide support and information via phone and email to thousands of families each year. The IMF sustains a network of more than 150 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**®

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## 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](http://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 that discussion 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 the myeloma cell.
- 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.

## What were the results with Darzalex in clinical trials?

In May 2013, based on preliminary clinical trial evidence, Darzalex was granted "breakthrough" designation by the US Food and Drug Administration (FDA), suggesting that this new drug might offer a substantial improvement over available therapies. Darzalex also received priority review and **orphan drug** designations by the FDA.

In November 2015, Darzalex was granted accelerated approval by the FDA based upon the efficacy and safety data from two non-randomized studies, MMY2002 and GEN501.

In the MMY2002 study, 106 participants with **relapsed/refractory** myeloma received single-agent Darzalex. Patients in the study had myeloma for a median of 4.8 years following diagnosis. They were heavily pretreated, with a median of five prior lines of therapy. Almost all of the trial patients were refractory to their last treatment, including **proteasome inhibitors** like Velcade® (bortezomib) and Kyprolis®

(carfilzomib) and **immunomodulatory drugs** like Revlimid® (lenalidomide) and Pomalyst® (pomalidomide). **Overall survival (OS)** in this study was 65% after the first year of follow-up. The 42-patient GEN501 study with single-agent Darzalex for relapsed/refractory myeloma had a one-year OS rate of 77%. Although patients in these clinical trials received Darzalex as a single agent (alone, without dexamethasone or any other drug), some patients responded very deeply to the treatment, with no sign of myeloma in the blood, bone marrow, or urine. These responses and the high rates of OS at one year after the patients had completed therapy on the trial were exceptional in this heavily pretreated population of patients. The results of these two trials led to the early approval of Darzalex, before randomized phase III studies were completed.

Two pivotal phase III clinical trials led to expanded approval for Darzalex. The first study was the 490-patient phase III CASTOR trial, in which Velcade + low-dose dexamethasone was compared to Darzalex + Velcade + low-dose dexamethasone for relapsed/refractory myeloma. The CASTOR trial was halted in March 2016 when the interim data indicated that the inclusion of Darzalex with Velcade + dexamethasone improved **progression-free survival (PFS)**. Patients randomized to receive Velcade + dexamethasone without Darzalex were allowed to cross over at disease progression into the Darzalex arm of the study. The results of this study were published in the *New England Journal of Medicine* in August 2016.

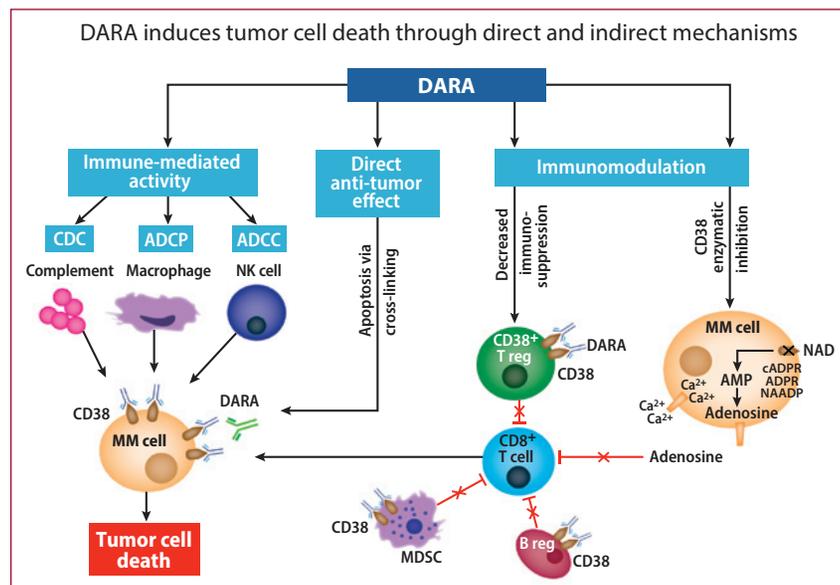
The second of the two pivotal phase III trials was the 569-patient POLLUX study, in which Darzalex with Revlimid + low-dose dexamethasone was compared to Revlimid + low-dose dexamethasone for patients with relapsed or refractory myeloma who had had at least one prior line of therapy. In addition to meeting the primary end-point of improved PFS, the **overall response rate (ORR)** was significantly improved with the addition of Darzalex, and the rate of complete responses was doubled in the Darzalex arm. Based on these results, the data were unblinded, and patients on the Revlimid + dexamethasone study arm were allowed to cross over at disease progression to the Darzalex arm of the study. The results of this study were published in the *New England Journal of Medicine* in October 2016.

In August 2016, Janssen Pharmaceuticals submitted the data from the twin CASTOR and POLLUX studies to the FDA and the European Medicines Agency (EMA) to request that they broaden their approved indications for use of Darzalex in combination with Revlimid + dexamethasone or Velcade + dexamethasone as a treatment for patients with myeloma following at least one prior therapy.

In November 2016, the FDA granted this expanded approval. In April 2017, expanded approval was granted by the European Commission. In June 2017, the FDA approved Darzalex in combination with Pomalyst + dexamethasone for the treatment of patients with myeloma who have received at least two prior therapies including Revlimid and a proteasome inhibitor (such as Velcade, Kyprolis, or Ninlaro). This indication for Darzalex is supported by data from the phase 1b EQUULEUS study, which showed that the combination of Darzalex + pomalidomide + dexamethasone resulted in an ORR of 59.2%, with very good partial response (VGPR) achieved in 28.2% of patients. Complete response (CR) was achieved in 5.8% of patients, stringent CR (sCR) was achieved in 7.8% of patients, and partial response (PR) was achieved in 17.5% of patients. The median time to response was one month, and the median duration of response was 13.6 months.

In January 2018, the FDA granted a priority review designation to Darzalex in combination with Velcade + melphalan + prednisone (VMP) for the treatment of patients with newly diagnosed myeloma who are ineligible for autologous stem cell transplant (ASCT). The designation was based on findings from the European phase III ALCYONE study of Darzalex + VMP vs. VMP in newly diagnosed myeloma patients. Study results demonstrated that Darzalex + VMP elicited an 18-month PFS rate of 71.6% compared with 50.2% for VMP alone – a 50% reduction in the risk of progression or death. The overall survival analysis is ongoing.

**Figure 1. Daratumumab (DARA) mechanisms of action**



Umami SZ et al. Clinical Efficacy of Daratumumab Monotherapy in Patients with Heavily Pretreated Relapsed or Refractory Multiple Myeloma. Abstract #29. Oral presentation at American Society of Hematology (ASH) 2015.

In May 2018, the FDA approved Darzalex in combination with Velcade + melphalan + prednisone (VMP) for the treatment of patients with newly diagnosed myeloma who are ineligible for autologous stem cell transplant (ASCT). The designation was based on findings from the European phase III ALCYONE clinical trial of VMP vs. Darzalex + VMP in newly diagnosed myeloma patients that was published in the *New England Journal of Medicine*. Study results thus far demonstrate that response rates are higher with Darzalex + VMP than with VMP alone, and that median PFS has not yet been reached in the Darzalex + VMP arm, while the median PFS for VMP alone is 18.1 months. The analysis of overall survival is ongoing. This is the first approval of Darzalex in the newly diagnosed setting.

Many trials evaluating Darzalex in new disease settings or new combinations are ongoing, including:

- A clinical trial evaluating subcutaneous rather than intravenous administration of Darzalex to patients with relapsed/refractory myeloma.
- A clinical trial evaluating Darzalex in patients with **smoldering multiple myeloma (SMM)**.
- A clinical trial of Darzalex in combination with Ninlaro + dexamethasone in patients with relapsed/refractory myeloma.

## Who is a candidate for Darzalex?

In the United States:

- Darzalex as a single agent is indicated for patients with myeloma who have received at least three prior lines of therapy including a proteasome inhibitor and an immunomodulatory drug, or who are double-refractory to a proteasome inhibitor and an immunomodulatory drug.
- 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 Pomalyst + dexamethasone for the treatment of patients with myeloma who have received at least two prior therapies including Revlimid and a proteasome inhibitor.
- Darzalex is approved in combination with Velcade + melphalan + prednisone (VMP) for the treatment of patients with newly diagnosed myeloma who are ineligible for autologous stem cell transplant (ASCT).

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.

## 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?

- 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.

*Especially with the first dose, the infusion rate for Darzalex 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 will be given more rapidly at your doctor's discretion. Medications are given before and after each Darzalex infusion to help prevent a reaction.*

## 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.

Because Darzalex can cause reactivation of **herpes zoster**, all patients should receive preventive treatment with an antiviral medication such as acyclovir or valacyclovir.

## 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 37.5°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.

## 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 the need for antiviral prophylaxis to prevent herpes

zoster reactivation within one week after starting Darzalex and continuing for three months following treatment. Please discuss an antiviral medication, such as acyclovir or valacyclovir, with your doctor before starting treatment with Darzalex.

## 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.

## Access to Darzalex and other resources

Janssen Pharmaceuticals has a CarePath program to help support patients who are receiving treatment with Darzalex. Visit [darzalex.com](http://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](http://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](mailto:InfoLine@myeloma.org) or 800-452-CURE or 818-487-7455.

## Terms and definitions

**Anemia:** A decrease in hemoglobin, 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  $\geq 2$  g/dL from the normal level for an individual. Over 13–14 g/dL is considered normal.

**Antibody:** A protein produced by white blood cells called plasma cells in response to, and to counteract, an antigen that enters the body. The medical term for antibody is "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.

**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.

**Corticosteroid:** A group of natural and synthetic analogues of the hormones secreted by the pituitary gland. These include the glucocorticoids used in the treatment of myeloma such as dexamethasone, prednisone, and methylprednisolone. Glucocorticoids have multiple effects, and are used for a large number of conditions.

**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. They 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 (immuno-electrophoresis, 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.

**Generic drug name:** A generic drug name refers to the chemical makeup of a drug rather than to 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, which, when reactivated, 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 which 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 (also called isotypes) of immunoglobulins are IgG, IgA, IgD, IgE, and IgM. The non-medical word for immunoglobulin is “antibody.”

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

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

**Lymphopenia:** Low levels of B cells, T cells, and natural killer (NK) cells.

**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.

**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 artificially manufactured antibody (that is, made in a lab rather than in the human body) that is 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.

**Multiple myeloma:** A cancer of the bone marrow plasma cells, the 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.

**Orphan drug:** The orphan drug designation is granted by the US Food and Drug Administration (FDA) to provide incentives such as tax credits, user fee waivers, and eligibility for orphan drug exclusivity to assist and encourage the development of drugs for rare diseases.

**Overall response rate (ORR):** The percentage of patients in a clinical trial whose monoclonal protein decreased by at least 50% in response to treatment.

**Overall survival (OS):** The median number of individuals in a group who are alive after a particular duration of time. OS is often used as a measure of treatment efficacy in clinical trials. The lengthening duration of OS in myeloma trials makes it a difficult endpoint to use, leading to the effort to validate minimal residual disease status as a new endpoint.

**Progression-free survival (PFS):** The length of time during and after the treatment of a disease, such as cancer, that a patient lives with the disease but it does not get worse. In a clinical trial, measuring the progression-free survival is one way to see how well a new treatment works. Also called PFS. See “**Progressive disease**.”

**Progressive disease:** Myeloma that is becoming worse or relapsing, as documented by tests. Defined as an increase of  $\geq 25\%$  from 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.

**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.

**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 the 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's library of educational publications will help arm you with one of the most important weapons in the fight against myeloma: INFORMATION. The IMF publications listed below are available in English, and selected titles are also available in other languages. All IMF publications are free of charge and can be viewed, downloaded, or ordered at [publications.myeloma.org](http://publications.myeloma.org)

- *Patient Handbook*
- *Concise Review of the Disease and Treatment Options*
- *Understanding Clinical Trials*
- *Understanding Dexamethasone and Other Steroids*
- *Understanding DARZALEX® (daratumumab)*
- *Understanding EMPLICITI® (elotuzumab)*
- *Understanding Fatigue*
- *Understanding High-Dose Therapy with Stem Cell Rescue*
- *Understanding the Immune System in Myeloma*
- *Understanding KYPROLIS® (carfilzomib)*
- *Understanding MGUS and Smoldering Multiple Myeloma*
- *Understanding NINLARO® (ixazomib) capsules*
- *Understanding POMALYST® (pomalidomide)*
- *Understanding REVLIMID® (lenalidomide)*
- *Understanding Treatment of Myeloma Bone Disease*
- *Understanding Treatment of Myeloma-Induced Vertebral Compression Fractures*
- *Understanding VELCADE® (bortezomib)*
- *Understanding Your Test Results*

In addition, the IMF produces an array of **Tip Cards**, concise reference tools on a variety of topics of interest, as well as periodicals such as the quarterly journal **Myeloma Today**, the weekly e-newsletter **Myeloma Minute**. Subscriptions to all IMF periodicals are free of charge at [subscribe.myeloma.org](http://subscribe.myeloma.org)

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

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