Understanding NINLARO® (ixazomib) capsules

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About the International Myeloma Foundation

Founded in 1990, the International Myeloma Foundation (IMF) is the oldest and largest myeloma-specific charity in the world. With more than 350,000 members in 140 countries, the IMF serves myeloma patients, family members, and the medical community. The IMF provides a wide range of programs in the areas of Research, Education, Support, and Advocacy:

**RESEARCH** The IMF is the leader in globally collaborative myeloma research. The IMF supports lab-based research and has awarded over 100 grants to top junior and senior researchers since 1995. In addition, the IMF brings together the world’s leading experts in the most successful and unique way through the International Myeloma Working Group (IMWG), which is publishing in prestigious medical journals, charting the course to a cure, mentoring the next generation of innovative investigators, and improving lives through better care.

**EDUCATION** The IMF’s educational Patient & Family Seminars, Medical Center Workshops, and Regional Community Workshops are held around the world. These meetings provide up-to-date information presented by leading myeloma specialists and researchers directly to myeloma patients and their families. Our 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** Our toll-free InfoLine at 800-452-CURE (2873) is staffed by coordinators 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 Advocacy program trains and supports concerned individuals to advocate on health issues that affect the myeloma community. Working both at the state and federal level, the IMF leads two coalitions to advocate for parity in insurance coverage. Thousands of IMF-trained advocates make a positive impact each year on issues critical to the myeloma community.

Learn more about the way the IMF is helping to improve the quality of life of myeloma patients while working toward prevention and a cure.

Contact us at 800-452-CURE (2873) or 818-487-7455, or visit myeloma.org.

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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 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.

You will learn about the drug Ninlaro® (also known by its generic drug name, ixazomib). Ninlaro is an oral medication taken in capsule form rather than an intravenous drug that is administered at a clinic or doctor’s office.

Given that Ninlaro is taken as a pill, the responsibility for taking this medication as directed by your doctor falls on you. It is crucial that you read and understand the information in this booklet and in any other materials that your healthcare team provides to you.

Ninlaro is approved by the US Food and Drug Administration (FDA) for use in combination with the immunomodulatory drug Revlimid® (lenalidomide) and dexamethasone (a corticosteroid). Therefore, there are three additional IMF publications that are helpful companions to this booklet. We recommend that you read the following:

- Understanding Adherence to Oral Cancer Therapy
- Understanding Dexamethasone and Other Steroids
- Understanding REVLIMID® (lenalidomide)

The IMF provides these and other booklets free of charge: please visit myeloma.org or contact the IMF.

What is Ninlaro?

Ninlaro is an oral medication to treat myeloma. It is the first oral proteasome inhibitor approved by the FDA to treat myeloma. Proteasome inhibitors are a class of drugs. Proteasome inhibitors have been approved as an effective method of treating myeloma since 2003. Ninlaro is the third proteasome inhibitor approved for the treatment of myeloma.

How does Ninlaro work?

Proteasomes, enzyme complexes found in the nucleus of every cell in the body, including cancer cells, are often likened to protein garbage disposers. Proteasomes break down, or degrade, unneeded or damaged proteins into smaller components. Proteasomes also carry out the regulated breakdown of undamaged proteins in the cell, a process that is necessary for the control of many critical cellular functions. These smaller components of degraded proteins are used to create new proteins required by the cell. Proteasomes can thus be thought of as crucial to the cell’s “recycling” of proteins.

If the proteasome is stopped, or inhibited, then the damaged and unneeded cellular proteins build up in the cell’s nucleus and cytoplasm and cause it to die. Myeloma cells are particularly sensitive to proteasome inhibition (more so than healthy cells), so proteasome inhibitors are effective treatments for myeloma.

What is the indication for use of Ninlaro?

Ninlaro is indicated in combination with Revlimid® (generic name lenalidomide) and dexamethasone for patients with myeloma who have received at least one prior therapy. In November 2015, Ninlaro was approved by the FDA for this indication based on the results of a large, phase III randomized clinical trial. Ninlaro was approved for the same indication by the European Commission in November 2016, becoming the first and only oral proteasome inhibitor approved for use across the European Economic Area, which includes the 28 member states of the European Union (EU) plus Norway, Liechtenstein, and Iceland.

What is the clinical trial experience with Ninlaro?

Ninlaro was approved by the FDA and the European Commission based upon the data from the TOURMALINE study, an international phase III clinical trial of Ninlaro + Revlimid + dexamethasone versus placebo + Revlimid + dexamethasone in 722 patients with relapsed and/or refractory myeloma who had received at least one prior line of therapy. Patients whose myeloma did not respond to prior treatment with Revlimid or proteasome inhibitors were not eligible to participate in the study. Patients in both the experimental arm (which included Ninlaro) and the control arm (which substituted a placebo for Ninlaro) were treated until their myeloma progressed or they were unable to tolerate the treatment.

The efficacy of Ninlaro was evaluated by the median duration of progression-free survival (PFS) in the two arms of the study. The median PFS in the experimental arm was 20.6 months, while the median PFS in the control arm was 14.7 months, as measured from the time that patients who were randomized to one treatment arm or the other. The median time to respond to therapy was 1.1 months for the Ninlaro regimen, and 1.9 months for the regimen using a placebo. The overall response rate (ORR) was 78% in the Ninlaro arm, and 72% in the placebo arm.
Patients in the study were given a blood thinner to prevent blood clots, as recommended for all patients taking Revlimid and dexamethasone. Other medications were given as necessary at the physicians’ discretion to improve patients’ tolerance of the drugs. For more information, please read the section on Supportive Care.

Currently, Ninlaro is being studied in clinical trials in combination with many agents in addition to Revlimid and dexamethasone, and in various disease settings, including smoldering myeloma and newly diagnosed myeloma. There are several clinical trials evaluating Ninlaro as maintenance therapy in the non-transplant setting as well as following autologous or allogeneic transplant. For further information about these and other clinical trials, visit the IMF’s Myeloma Matrix 2.0: Smart Search at myeloma.org/matrix.

What are the dose and schedule of Ninlaro + Revlimid + dexamethasone?

Ninlaro is taken in 4-week (28-day) cycles. The recommended starting dose of Ninlaro is one 4 mg capsule taken orally on Days 1, 8, and 15 of a 28-day treatment cycle. Thus, one capsule of Ninlaro is taken once a week for the first three weeks of every 4-week (28-day) cycle. No Ninlaro is taken during the fourth week of each cycle.

Ninlaro also comes in 3 mg and 2.3 mg capsules, and your doctor can reduce the dose of Ninlaro depending upon your medical status and side effects. If you have moderate or severe liver or kidney dysfunction at the time you start treatment with Ninlaro, your dose of Ninlaro should be lowered. The starting dose for patients with moderate to severe liver or kidney impairment is 3 mg. For patients with kidney disease requiring dialysis, Ninlaro is not dialyzable, and therefore can be administered without regard to the timing of dialysis.

The recommended starting dose of Revlimid is 25 mg taken orally on Days 1 through 21 of a 28-day treatment cycle.

The recommended starting dose of dexamethasone is 40 mg taken orally on Days 1, 8, 15, and 22 of a 28-day treatment cycle.

If necessary, your doses of Revlimid and dexamethasone can be lowered by your doctor.

Be sure to report any new health-related problems you’re having to a member of your healthcare team.

Important instructions for taking Ninlaro safely

Read these safety instructions carefully BEFORE you take Ninlaro:

- Take the Ninlaro + Revlimid + dexamethasone combination therapy exactly as your healthcare provider instructs.
- Take Ninlaro on the same day each week. This is important for efficacy and safety, and will help you establish a routine for remembering to take your medication.
- Take Ninlaro at about the same time of day each week.
- Take Ninlaro at least 1 hour before, or at least 2 hours after, eating (i.e., on an empty stomach).
- DO NOT take Ninlaro at the same time you take dexamethasone, because dexamethasone should be taken with food, and Ninlaro should not be taken with food.
- Store Ninlaro capsules at room temperature in their original packaging. Do not remove the capsule from the packaging until just before you take it.
- Swallow the whole Ninlaro capsule with a full glass of water.

- Do not crush, chew, or open the Ninlaro capsule.
- Avoid direct contact with the contents of the Ninlaro capsule. If you accidentally get powder from inside the capsule on your skin, wash the area well with soap and water. If you get it in your eyes, flush your eyes well with water.

- If you miss or delay a dose of Ninlaro, take the dose as long as the next scheduled dose is more than 3 days (72 hours) away. DO NOT take a missed dose of Ninlaro if it is within 3 days (72 hours) of your next scheduled dose.

- If you vomit after taking a dose of Ninlaro, DO NOT repeat the dose. Just take your next dose of Ninlaro on the next scheduled day at the usual time.

- If you take more Ninlaro than your healthcare provider has prescribed, call your provider immediately, or go to the nearest hospital emergency room.

- Tell your doctor about all other medications and supplements that you’re taking before you take your first dose of Ninlaro.

- Tell your doctor about all of your medical conditions. Special precautions must be taken with your dosing if you have liver or kidney problems or diabetes.

- Tell your doctor if you are pregnant, or plan to become pregnant. You should not become pregnant while taking Ninlaro, which can harm your unborn baby.

- Tell your doctor if you are breastfeeding or plan to breastfeed while taking Ninlaro. You should not breastfeed while taking Ninlaro.

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What are the possible side effects, and how are they managed?

Careful records of all drug-related and possibly drug-related side effects are maintained during clinical trials. All the side effects experienced by patients in both arms of the TOURMALINE clinical trial were recorded for evaluation prior to the approval of Ninlaro in combination with Revlimid and dexamethasone. The below side effects occurred most commonly among the patients enrolled in the TOURMALINE trial, but other, less common side effects occurred as well. In addition, serious side effects outside of clinical trials have been reported to the regulatory agencies. If you are a patient in the US, you and/or your doctor should report side effects to the FDA at fda.gov or by calling 800-332-1088.

In addition to the most common side effects listed below, back pain is also common while taking Ninlaro. You should promptly report any changes in your health to your healthcare providers while you are taking Ninlaro + Revlimid + dexamethasone. Some side effects can be life-threatening if not managed promptly and effectively.

**Thrombocytopenia (low platelet count)**

Thrombocytopenia is a lowered level of platelets in the blood. Platelets help blood to clot; fewer platelets can lead to bruising, bleeding, and slower healing. Both Ninlaro and Revlimid can cause platelet counts to drop. During treatment with Ninlaro + Revlimid + dexamethasone, the platelet count reaches its lowest point on days 14–21 of each 28-day cycle, but usually recovers to baseline by the beginning of the next cycle. (That is why there is no Ninlaro dose during week four of each cycle.) 78% of the patients in the Ninlaro arm of the TOURMALINE trial had thrombocytopenia, some of it severe enough to be life-threatening.

**Prevention and treatment of thrombocytopenia**

Your doctor should monitor your complete blood count (CBC) throughout your treatment with Ninlaro + Revlimid + dexamethasone. You should inform the members of your healthcare team if you experience excessive bruising or bleeding. Management of thrombocytopenia may include holding your Ninlaro and Revlimid treatment until your platelet count recovers and then lowering your Ninlaro and Revlimid doses. Some patients with persistent low platelet counts may require platelet transfusions.

**Diarrhea**

In the TOURMALINE trial, 42% of the patients in the Ninlaro + Revlimid + dexamethasone arm and 36% in the placebo arm (Revlimid + dexamethasone without Ninlaro) experienced diarrhea. While no patient on the trial had diarrhea that was life-threatening, 6% of the cases in the Ninlaro arm and 2% of the cases in the placebo arm were severe.

**Prevention and treatment of diarrhea**

Antidiarrheal medications such as Imodium® (loperamide) can help control diarrhea. If you have diarrhea, take precautions to prevent dehydration by drinking a sufficient amount of water, and call the doctor’s office or clinic where you’re being treated. Your doctor should monitor your electrolytes (potassium, in particular) and correct electrolyte abnormalities if they’re detected. Call for immediate medical advice if you experience dizziness, light-headedness, or fainting. Your physician may hold or reduce your Ninlaro and Revlimid doses or administer antidiarrheal medication or intravenous hydration, as required.

**Constipation**

Prevention is the key to managing constipation, which is defined as having fewer than three bowel movements a week. Chronic constipation is defined as infrequent bowel movements or difficult passage of stools that persists for several weeks or longer.

While 34% of the patients in the Ninlaro arm, and 25% in the placebo arm of the TOURMALINE trial experienced constipation, less than 1% of cases in either arm were considered serious. Sometimes constipation is the flip side of diarrhea, with patients cycling back and forth between these two uncomfortable states. Talk to your healthcare providers about strategies to regulate your bowel health.

**Prevention and treatment of constipation**

There are several strategies that may help alleviate constipation:

- Drink at least eight 8-ounce glasses of fluid daily.
- Add plenty of dietary fiber every morning, such as prune juice, apple juice, or bran.
- Get some exercise daily, even if it’s just walking. Moving your body increases peristalsis, the rhythmic contractions that move food through the digestive system.
- Report the problem to a member of your healthcare team, who may recommend a stool softener or laxative.
Nausea and vomiting
Nausea affected 26% and 21% of the patients in the Ninlaro and placebo arms of the TOURMALINE trial, respectively, and vomiting occurred in 22% and 11%, respectively. None of these episodes was life-threatening.

Prevention and treatment of nausea
You should be premedicated with drugs to help prevent nausea and vomiting prior to each dose of Ninlaro. Precautions should be taken to prevent dehydration caused by vomiting. You should drink a sufficient amount of water and other fluids and seek medical advice if you experience dizziness, lightheadedness, or fainting. Your physician may administer anti-emetic medication (to prevent vomiting) or intravenous hydration, as required.

Peripheral neuropathy
Peripheral neuropathy (PN) is a serious condition in which treatment affects nerves in the hands, feet, legs, and/or arms. Symptoms of PN include numbness, tingling, cramping, burning, weakness, or pain in the hands, feet, legs, and/or arms. Some patients may have experienced PN from the effects of the myeloma itself and/or from previous treatments for myeloma. If you begin taking Ninlaro with peripheral neuropathy as a pre-existing condition, it is especially important that you pay attention to any increase in your discomfort. Report a worsening of your condition to your doctor immediately. If detected and managed appropriately, your neuropathy should not become worse. If these signs and symptoms are new to you, dealing with them promptly may prevent them from becoming a long-term problem.

28% of the patients on the Ninlaro arm of the TOURMALINE study reported PN, 18% of it mild enough not to cause pain or affect the activities of daily living (grade 1 on a scale of 1–4). In the Revlimid + dexamethasone + placebo arm, 21% reported PN, of which 14% was grade 1. Only 2% of patients in either arm of the study reported PN that caused severe pain, weakness, or numbness that interfered with the activities of daily living.

Prevention and treatment of peripheral neuropathy
The best approach to treating PN is to prevent it from occurring or worsening. By promptly reporting any signs of numbness or tingling to your doctor, you can avoid potentially painful or disabling neuropathy.

Your doctor will withhold or lower the dose of Ninlaro and Revlimid until your symptoms improve. If you develop more serious neuropathy, the doctor may prescribe a medication to help, may refer you to a neurologist or a physical therapist, and/or may discontinue your treatment regimen.

Peripheral edema
Peripheral edema is accumulation of fluid that causes swelling, usually in the ankles, feet, and legs. This swelling is the result of the accumulation of excess fluid under the skin in the spaces within the tissues, or “interstitial” spaces. Peripheral edema can be a side effect of long-term use of anti-inflammatory medications (such as the corticosteroid dexamethasone), which increase fluid pressure from sodium and water retention, and thereby upset the balance of inflow and drainage of interstitial fluid. Peripheral edema can also result from many other causes, including immobility, obesity, varicose veins, cardiac, kidney, or liver dysfunction, gastrointestinal disorders, medications for diabetes such as insulin and pioglitazone, and non-steroidal anti-inflammatories such as ibuprofen and naproxen.

Usually peripheral edema affects both legs/ankles/feet. If you have swelling in one leg only, you should tell your healthcare team immediately, as it might signal the presence of a blood clot.

Peripheral edema affected 25% and 18% of patients in the Ninlaro and placebo regimens of the TOURMALINE trial, respectively. The majority of the cases of peripheral edema were mild, and none were life-threatening.

Prevention and treatment of peripheral edema
Patients should be evaluated for underlying causes of peripheral edema and provided supportive care, as necessary. A reduction in dietary salt intake may be required. The dose of dexamethasone may be modified, and if the edema is severe, the dose of Ninlaro should also be adjusted.

Rash
Rash was reported in 19% of patients in the Ninlaro regimen and 11% of the patients in the placebo regimen in the TOURMALINE trial. The majority of these cases were mild, and fewer than 1% of the patients in either arm discontinued one or more of the three drugs because of a skin reaction. However, rash can be a serious concern. It is potentially dangerous, as a rash may be mild initially and then escalate in severity. Drug rashes vary in severity from mild redness with tiny bumps over a small area to peeling of the entire skin. Rashes may appear suddenly within minutes after a person takes a drug, or they may be delayed for hours or days.

Prevention and treatment of rash
Notify your doctor right away if you experience a rash. Proper evaluation of a skin rash requires a visit to a doctor or other healthcare professional. If detected and managed appropriately, a rash is reversible. The dose of Revlimid should be held until the rash recovers, and then Revlimid...
should be given at a lower dose. If the rash appears again, the doses of both Ninlaro and Revlimid should be modified. For a life-threatening rash, the treatment regimen should be discontinued altogether.

Liver toxicity (hepatotoxicity)
Drug-induced liver injury was reported in 6% of patients treated with Ninlaro and 5% of the patients treated with placebo in the TOURMALINE study. Signs of liver toxicity include yellowing of your skin or the whites of your eyes and/or pain in your right upper-stomach area.

Prevention and treatment of hepatotoxicity
Your doctor will monitor your liver enzymes with regular blood tests while you are being treated with Ninlaro + Revlimid + dexamethasone. If you have moderate to severe liver impairment, your dose of Ninlaro should be reduced.

Eye disorders
Eye disorders are readily detectable, so reporting and seeking remedy for them can and should be done as soon as you experience a problem. Members of your healthcare team may provide supportive care or refer you to an eye specialist.

Fetal harm
Based on findings with animals, Ninlaro can cause fetal harm when administered to a pregnant woman. There are no adequate or well-controlled studies in pregnant women, but studies in rats and rabbits that were exposed to the medication at slightly higher levels than those observed in patients caused embryo-fetal toxicity. Women of childbearing potential should not become pregnant while taking Ninlaro. Animal studies indicated that there were no effects due to Ninlaro on male or female reproductive organs.

Prevention of fetal harm
Both male and female patients of childbearing potential should use effective contraceptive measures during treatment with Ninlaro and for 90 days following the final dose.

Supportive care
Patients taking Ninlaro + Revlimid + dexamethasone are at an increased risk for herpes zoster viral infection (shingles), venous thromboembolic (VTE) events, and peripheral neuropathy (PN). The IMF’s Nurse Leadership Board recommends the following supportive care measures for patients on this regimen:

- All patients should be given preventative treatment with an anti-viral medication to prevent shingles, a reactivation of the herpes zoster virus. All patients taking a proteasome inhibitor are at risk for reactivation of the herpes zoster virus.
- All patients should receive preventative treatment with a blood thinner (anti-coagulant) to prevent a possible VTE.
- Watch for the signs and symptoms of PN listed above so that you can report the onset or worsening of symptoms immediately.
- Get regular physical activity, which will help combat muscle weakness (a possible dexamethasone side effect), prevent blood clots, and improve your mood.

Access to Ninlaro and other resources
Takeda Oncology, the company that developed Ninlaro, has established the website ninlaro.com and the “NINLARO Empower” program. Complete the Empower enrollment form at ninlaro.com/empower or call 844-617-6468 (select option 2) to learn about comprehensive programs that can assist with the financial burden and other day-to-day needs associated with your Ninlaro treatment. “NINLARO Empower” services include the following:

- Helping you understand your insurance coverage for Ninlaro;
- Providing information about specialty pharmacies that supply Ninlaro;
- Assisting eligible patients with out-of-pocket costs;
- Helping you start your medication as quickly as possible, as directed by your doctor;
- Connecting you with additional resources, such as legal services, counseling and support programs, emotional support, and transportation assistance.

Eligible patients could pay as little as $25 per prescription of Ninlaro.

For a list of other organizations that may be able to assist with drug access and reimbursement, please visit resources.myeloma.org.

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 up-to-date information about myeloma, and to contact the IMF InfoLine with your myeloma-related questions and concerns. The IMF InfoLine consistently provides callers with the best information about myeloma in a caring and compassionate manner. IMF InfoLine specialists can be reached at InfoLine@myeloma.org, or 800-452-CURE (2873) or 818-487-7455.

Terms and definitions

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 gets 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, and in addition, they 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 become standard-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.

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.

Cytoplasm: The jellylike material that makes up much of a human cell inside the cell membrane, and surrounds the nucleus.

Deep vein thrombosis (DVT): A condition that occurs when a blood clot (thrombus) forms in one or more of the deep veins in the body, usually in the legs. Deep vein thrombosis can cause leg pain or swelling, but may occur without any symptoms.
Electrolytes: Minerals in your blood and other body fluids that carry an electrical charge and are essential for life. Electrolytes include sodium, potassium, calcium, magnesium, chloride, and phosphorus. They affect the amount of water in the body, the acidity of the blood (pH), nerve and muscle function (including the heart), and other important processes.

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®.

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

Median: The middle number in a series of numbers. Thus, median progression-free survival means that half the patients had remissions that were shorter than the median PFS, and half the patients had remissions that were longer than the median PFS.

Multiple myeloma: A cancer arising from the plasma cells in the bone marrow. The cancerous plasma cells are called myeloma cells.

Nucleus: The nucleus of the cell in advanced organisms is the control center of the cell. It serves two functions: it stores all the genetic material (DNA) of the cell, and it coordinates the cell’s activities, which include growth, intermediary metabolism, protein synthesis, and reproduction (cell division).

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

Placebo: An inert (inactive) substance often used in clinical trials for comparison with an experimental drug. No clinical trial for cancer patients in the United States can ethically or legally randomize patients to receive a placebo alone when they require treatment. In the placebo arm of a cancer treatment trial, patients receive treatment with approved therapy plus a placebo.

Progression-free survival (PFS): The improved survival of a patient that can be directly attributed to the treatment given for the myeloma. The time period during which the patient survives, and the myeloma does not regrow or relapse. See “Progressive disease.”

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

Proteasome: A joined group (or complex) of enzymes that destroy damaged or unwanted proteins and undamaged proteins that require degradation in the cell. This turnover or “recycling” of proteins is important to maintain balance within the cell and helps to regulate several functions including cell growth.

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.

Pulmonary embolism (PE): A condition that occurs when a blood clot in the vein (deep vein thrombosis, or DVT) breaks loose, travels through the bloodstream, and lodges in a lung, blocking blood flow.

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.

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.

Transplant (transplantation): There are several different types of transplantation.

- Peripheral blood stem cell (PBSC) transplant – Doctors remove healthy stem cells from a patient’s circulating blood system (not from the bone marrow) and store them before the patient receives high-dose chemotherapy to destroy the cancer cells. The stem cells are then returned to the patient, where they can produce new blood cells to replace cells destroyed by the treatment. Using PBSC for autologous transplantation allows for easier and safer collection of stem cells and faster recovery after the transplant than bone marrow transplant.

- Autologous transplant – A procedure in which stem cells are removed from a patient’s blood and then are given back to the patient following intensive treatment.

- Bone marrow transplant – This term refers to the process of collecting stem cells from the bone marrow and infusing them into a patient. This term is used less frequently today in myeloma as stem cells are now collected from the peripheral or circulating blood.

- Allogeneic (allograft) transplant – The infusion of bone marrow or stem cells from one individual (donor) to another (recipient). A patient receives bone marrow or stem cells from a compatible, though not genetically identical, donor. An HLA blood test is done to determine if a patient has a potential donor match. A donor may be a family member or may be obtained through a donor registry such as the National Marrow Donor Program (NMDP). Rarely, donor cells may be obtained from an umbilical cord blood bank.

- Reduced-intensity conditioning (RIC) allo transplant – A newer and, for myeloma, safer technique than an allogeneic transplant. RIC is a non-myeloablative, reduced-intensity “mini-allo” transplant performed within 180 days after a standard autologous transplant.
• **Tandem transplant** – A term used to indicate two transplants. This may be two autologous transplants or an autologous transplant followed by an allogeneic (donor) transplant. Tandem transplants are usually planned with 3 to 6-month intervals between transplants. Tandem transplantation has become less common in the era of effective novel therapies.

• **Matched unrelated donor (MUD) transplant** – Refers to a stem cell transplantation procedure in which the patient and the stem cells are genetically matched but are not from family members. This procedure is not recommended for myeloma patients because it carries an unacceptably high mortality rate.

• **Syngeneic transplant** – The infusion of bone marrow or stem cells from one identical twin into another.

• **Umbilical cord blood transplant** – Stem cells obtained from the umbilical cords of newborns. These are frozen and stored in cord blood banks.

**Venous thromboembolism (VTE):**
A condition that includes both deep vein thrombosis (DVT) and pulmonary embolism (PE). Nearly two thirds of VTE events result from hospitalization. Risk factors include infection, age > 75, cancer, and a history of VTE. See “Deep vein thrombosis (DVT)” and “Pulmonary embolism (PE).”

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**10 STEPS TO BETTER CARE**
A UNIQUE TOOL FOR DIAGNOSTIC AND TREATMENT INFORMATION

One of the most daunting aspects of being diagnosed with multiple myeloma is learning about – and understanding – an unfamiliar disease that is quite complicated. From diagnosis to long-term survival, the 10 Steps to Better Care® will guide you through the myeloma journey:

1. Know what you’re dealing with. Get the correct diagnosis.
2. Tests you really need.
3. Initial treatment options.
4. Supportive care and how to get it.
5. Transplant: Do you need one?
6. Response Assessment: Is treatment working?
7. Consolidation and/or maintenance.
9. Relapse: Do you need a change in treatment?

Visit [10steps.myeloma.org](http://10steps.myeloma.org) to gain a better understanding of the disease and diagnosis, and proceed through the steps to learn the best tests, treatments, supportive care, and clinical trials currently available.

As always, the International Myeloma Foundation (IMF) urges you to discuss all medical issues thoroughly with your doctor. The IMF is here to equip you with the tools to understand and better manage your myeloma. Visit the IMF website at myeloma.org or call the IMF InfoLine at 800-452-CURE (2873) or 818-487-7455 to speak with our trained information specialists about your questions or concerns. The IMF is here to help.