Understanding FARYDAK®
(panobinostat) capsules

A publication of the International Myeloma Foundation

12650 Riverside Drive, Suite 206
North Hollywood, CA 91607 USA

Telephone:
800-452-CURE (2873)
(USA & Canada)
818-487-7455
(worldwide)

Fax: 818-487-7454

TheIMF@myeloma.org
myeloma.org

© 2017 International Myeloma Foundation. All rights reserved.
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.
What you will learn from this booklet

If you are a patient with multiple myeloma (which we refer to simply as “myeloma”), it is vital for you to learn as much as possible about this disease and its treatments so that you are empowered to make good decisions about your care with your doctor. The Understanding series of publications by the International Myeloma Foundation (IMF) is designed to acquaint you with treatments and supportive care measures for 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.

This booklet provides information about Farydak® (also known by its generic drug name panobinostat), the first histone deacetylase (HDAC) inhibitor approved for use in treating myeloma. This booklet explains how Farydak works, how and when to take Farydak, at what point in myeloma treatment it is used most effectively, possible side effects, and how to manage those side effects. It is crucial that you understand the information in this booklet and in any other materials that your healthcare provider gives you about Farydak. The IMF InfoLine staff is here to assist you with your questions and to ensure that you have the best possible dialogue with the members of your healthcare team.

What is a histone deacetylase inhibitor?

Histones are a family of eight basic proteins that organize DNA into segments in the nuclei of cells. Deacetylases are enzymes within our cells that remove the small molecule acetyl from cellular proteins. Deacetylases enable cells to successfully produce new proteins and to eliminate waste proteins, and thus to survive and reproduce. When myeloma cells are actively reproducing, histone deacetylase is overexpressed, leading to the build-up of waste proteins, the silencing of tumor suppressor genes, and the unregulated growth of myeloma.

What is Farydak?

Farydak is an oral prescription medication taken in capsule form. Farydak is not administered at a medical clinic or doctor’s office, so it is your responsibility to take this medication as prescribed. If you are a patient taking Farydak, you must adhere to the prescribed dose and schedule of this medication, follow all safety measures, and promptly report any and all side effects to the doctors and nurses who oversee your care.

The IMF’s Understanding Adherence to Oral Cancer Therapy booklet is a helpful companion piece to this publication. In addition, since Farydak was approved in combination with the proteasome inhibitor Velcade® (bortezomib) and dexamethasone (a synthetic adrenocortical steroid), it would be helpful for you to read the IMF’s booklets entitled Understanding VELCADE® (bortezomib) for Injection and Understanding Dexamethasone and Other Steroids. These publications are available on the IMF website myeloma.org or by calling or emailing the IMF.

What is the indication for use of Farydak?

Farydak was approved by the US Food and Drug Administration (FDA) in February 2015, and by the European Medicines Agency (EMA) in September 2015, in combination with Velcade + dexamethasone for the treatment of adult patients with relapsed and/or refractory myeloma who have received at least two prior regimens including Velcade + an immunomodulatory drug. Immune modulators include Thalomid® (thalidomide), Revlimid® (lenalidomide), and Pomalyst® (pomalidomide, also known in Europe as Imnovid®).

Farydak has also been approved for use in Chile and Japan.

How does Farydak work in treating myeloma?

Farydak inhibits not only histone deacetylase, but it also has been found to be a powerful inhibitor of all deacetylases (in medical terms, a “pan-deacetylase” inhibitor). By inhibiting deacetylases, it interferes with the processes of protein waste elimination and cell reproduction, making it difficult for myeloma cells to survive and divide into new cells. Unlike most healthy cells in the body, myeloma cells are particularly vulnerable to the build-up of waste proteins. Farydak not only allows waste proteins to build up in myeloma cells via the aggresome pathway, it is also thought to re-enable the expression of tumor suppressor genes that have been turned off by deacetylation.

In the laboratory, Farydak worked well against myeloma cell lines as a single agent, but was found to have greater effect when combined with another class of anti-myeloma drugs, known as proteasome inhibitors. Like deacetylase inhibitors, proteasome inhibitors also cause myeloma cell death by interfering with the removal of waste proteins from cells. As is often the case, the combination of these two drugs, when boosted by the added synergy of the corticosteroid dexamethasone, is more powerful and effective than any of the drugs alone.

What are the doses and scheduling of Farydak + Velcade + dexamethasone?

Farydak was approved in combination with Velcade + dexamethasone at a starting dose of one 20 mg capsule taken on days 1, 3, 5, 8, 10, and 12 of a 3-week (21-day) treatment cycle. An easy way to remember the dosing of Farydak is 3-2-1: take it 3 times a week, for 2 weeks in a row, and then take 1 week off.

What you should know before taking Farydak:

- Drug interactions can occur with Farydak. Before starting Farydak treatment, your doctor needs to know about all the medicines you take, including prescription and over-the-counter (OTC) medications, vitamins, and herbal supplements. You should
keep a list of them to show your healthcare provider and pharmacist each time you get a new medication.

While taking Farydak, avoid eating star fruit, pomegranate, and grapefruit, and avoid drinking pomegranate juice or grapefruit juice. These fruits and juices may affect the amount of Farydak in the blood.

No Farydak is taken on days 13–21 of the treatment cycle.

Farydak should be swallowed with a cup of water at about the same time of day on each day it is taken.

The capsules should be swallowed whole and not opened, crushed, or chewed.

Farydak can be taken either with or without food.

Farydak also comes in 15 mg and 10 mg capsules. Dosing of Farydak can be modified to reduce side effects and improve tolerance of the drug, as can the doses of Velcade and dexamethasone.

If you miss a dose of Farydak, take it as soon as possible, and within 12 hours after your scheduled dose.

If you take too much Farydak, call your doctor.

Velcade is administered as a subcutaneous injection (a shot) or an intravenous (IV) infusion at the standard dose of 1.3 mg per square meter of body mass on days 1, 2, 4, 8, and 9 of each cycle.

The recommended starting dose of dexamethasone in this combination therapy is 20 mg taken orally on days 1, 2, 4, 5, 8, 9, 11, and 12 of each 3-week cycle.

Dexamethasone should be taken on a full stomach.

This regimen can be continued for up to 8 cycles, and may be continued after 8 cycles if the patient is benefiting from the therapy and tolerating it. If the combination therapy is continued after 8 cycles, Farydak is taken on the same days as approved, but Velcade should be given only once weekly, on days 1 and 8 of each cycle, and dexamethasone twice weekly, on days 1, 2, 8, and 9 of each cycle.

What is the clinical trial experience with Farydak?

Farydak was approved based on the results of “PANORAMA-1,” a large, phase III, randomized clinical trial comparing Farydak + Velcade + dexamethasone (FVD) to placebo + Velcade + dexamethasone (VD). The study included 768 patients with relapsed/refractory myeloma who had received 1 to 3 prior therapies and were enrolled at 215 clinical trial sites around the world.

Of those 768 patients, 193 had been treated previously with both Velcade and an immunomodulatory drug, and these patients benefited most from the triplet therapy of FVD. The data from this subgroup of patients were submitted for approval of Farydak in combination with Velcade + dexamethasone. The median progression-free survival (PFS) of patients in the FVD arm of this study subgroup was 10.6 months, compared to 5.8 months in the placebo arm. The overall response rate (ORR) among the Farydak-treated patients in this subgroup was 58.5%, 22.3% of whom had a complete response (CR) or near-complete response (nCNR). Among the patients who were treated with VD, the ORR was 41.4%, with 9.1% achieving a CR or nCNR.

At the time of Farydak’s approval by the FDA, overall survival (OS) data were not available for the PANORAMA-1 study. However, Dr. Jesús San Miguel (University of Navarra, Spain) presented a final analysis of overall survival data from the PANORAMA-1 clinical trial at the American Society of Hematology (ASH) meeting in December 2015. The data demonstrated that there was no statistically significant overall survival benefit to FVD over VD. An ongoing clinical trial, PANORAMA-3, is looking at three variations of the FVD regimen with an eye to maximizing the safety and efficacy of this combination. It is now known that if patients are taking a combination of Velcade and Farydak, the regimen is much better tolerated with a subcutaneous injection of Velcade rather than with intravenously infused Velcade.

Farydak is being studied in a number of clinical trials:

- In combination with Kyprolis® (carfilzomib) + dexamethasone in relapsed/refractory myeloma;
- In combination with Revlimid + Velcade + dexamethasone (RVD) in both relapsed/refractory and newly diagnosed myeloma;
- In combination with Ninlaro® (ixazomib) + dexamethasone in relapsed/refractory myeloma;
- As a single agent in post-autologous transplant maintenance therapy;
- As consolidation therapy for patients who have less than a complete response (CR) following frontline autologous transplant;
- As part of a conditioning regimen including gemcitabine, busulfan, and melphalan prior to autologous transplant.

To be treated with FVD, you should have had at least a partial response (PR) to prior Velcade treatment with manageable toxicity, and then relapsed after a fixed number of Velcade cycles. (Retreatment with Velcade + dexamethasone at least six months after a prior response is an FDA-approved indication.) The patient should have had progressive disease on an immunomodulatory drug, and may have become refractory to the immunomodulatory drug.

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

There are certain potential side effects of Farydak that are serious enough to require an FDA-mandated “Boxed Warning” on the package insert. A Boxed Warning is the strictest warning put in the labeling of prescription drugs when there is reasonable evidence of an association with a
serious hazard from the drug. The Boxed Warning for Farydak includes severe diarrhea and severe cardiac toxicities (heart problems).

Severe diarrhea (defined as 7 or more stools per day requiring treatment with intravenous fluids or hospitalization) occurred in 25% of Farydak-treated patients in the PANORAMA-1 study. Heart problems included severe and fatal cardiac ischemic events, severe arrhythmias, and ECG (electrocardiogram) changes. Electrolyte abnormalities, which can be caused by fluid loss through diarrhea or vomiting, may make an irregular heart rhythm worse.

Because of these potentially life-threatening side effects, the FDA required that a Risk Evaluation and Mitigation Strategy (REMS) be put into effect for Farydak. Physicians who prescribe Farydak receive special information and education about risk mitigation and management for these Boxed Warnings, and are encouraged to report all adverse reactions of Farydak to the FDA’s MedWatch.

Side effects are reported in two categories: those related to blood cell counts (“hematologic” side effects) and those that are not related to blood cell counts (“non-hematologic” side effects). While Farydak can lower the number of all three types of blood cells – platelets (thrombocytes), red blood cells (RBC), and white blood cells (WBC) – very low levels of thrombocytes were the most common hematologic side effect, occurring in 67% of patients in the PANORAMA-1 clinical trial. The most common non-hematologic side effect was diarrhea, while other common adverse reactions of Farydak that occurred in at least 20% of patients treated in clinical trials were fatigue, nausea, peripheral edema, decreased appetite, fever, and vomiting. The most common non-blood-related laboratory abnormalities were electrolyte abnormalities and increased creatinine, which indicates kidney dysfunction.

Diarrhea
Diarrhea (defined as three or more loose stools per day) is common with Farydak and may be severe. In the PANORAMA-1 study, diarrhea occurred in 68% of patients treated with Farydak + Velcade + dexamethasone compared to 42% treated with placebo + Velcade + dexamethasone. As mentioned earlier in this booklet, severe diarrhea (defined as 7 or more stools per day requiring treatment with intravenous fluids or hospitalization) occurred in 25% of Farydak-treated patients in the PANORAMA-1 study. Tell your healthcare provider right away if you have stomach cramps, loose stools, frequent bowel movements, or if you feel like you’re becoming dehydrated. Thirst and dark-colored urine are early symptoms of dehydration.

Prevention and treatment of diarrhea
Anti-diarrheal medications such as Imodium® (loperamide HCl) can help control diarrhea. Your healthcare provider will make sure you have some anti-diarrheal medication on hand when you start Farydak. You should take anti-diarrheal medicine at the first sign of stomach cramping or loose stools. If you have diarrhea, take precautions to prevent dehydration by drinking water, and call your doctor 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 Farydak and Velcade doses or administer anti-diarrheal medication or intravenous hydration, as required.

Heart problems
Farydak can cause severe heart problems, which can lead to death. Your risk of heart problems may be increased if you have a pre-existing condition called “long QT syndrome,” a heart rhythm condition that can potentially cause fast, chaotic heartbeats, or if you have other heart problems.

Prevention and treatment of heart problems
Your healthcare provider will order blood tests to check your electrolyte levels (which help control heart rhythm) and an electrocardiogram (ECG) before and during treatment with Farydak. You should not start Farydak if you have recently had a heart attack, if you have unstable angina, if you have long QT syndrome, or if your ECG is abnormal. Call your doctor and get emergency medical help right away if you experience chest pain, faster or slower heartbeat, a racing heart, lightheadedness or faintness, dizziness, blue-colored lips, shortness of breath, or swelling in your legs after taking Farydak.

Severe bleeding from low platelet count (thrombocytopenia)
Farydak can cause severe bleeding (hemorrhage), which can lead to death. In the PANORAMA-1 clinical trial, severe bleeding occurred in the gastrointestinal tract or the lungs of 4% of the patients treated with Farydak and in 2% of the patients in the control arm. It may take longer than normal to stop bleeding while you are taking Farydak. A low platelet level was common among patients in the PANORAMA-1 study, occurring in 97% of patients in the Farydak + Velcade + dexamethasone arm and 83% of the patients in the placebo + Velcade + dexamethasone arm.

Prevention and treatment of bleeding
Your doctor will carefully monitor your platelet levels weekly throughout your treatment with Farydak + Velcade + dexamethasone. If your platelet count is low and you experience bleeding, your doctor will hold your Farydak and Velcade doses and give you a platelet transfusion, if needed. Tell your healthcare provider immediately if you have any of the following signs or symptoms of bleeding:

- Blood in your stools or tarry, black stools;
- Pink or brown urine;
- Unexpected bleeding, or bleeding that is severe and that you cannot control;
- Vomiting blood or vomit that looks like coffee grounds;
Fatigue may be minimized by maintaining:
- Prevention and treatment of fatigue
- 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 fatigue issues;
- A careful review of the side effects of all the other supplements and medications you are taking in addition to FVD (to ensure that they are not contributing to your fatigue).

Nausea and vomiting
In the PANORAMA-1 clinical trial, 36% of Farydak patients experienced nausea (6% of which was serious enough to require hospitalization), while 26% of patients experienced vomiting (7% of which was serious enough to require hospitalization or urgent intervention).

Prevention and treatment of nausea and vomiting
Precautions should be taken to prevent dehydrating caused by vomiting. Your doctor will establish your baseline electrolyte values, including potassium, magnesium, and phosphate, and will correct them before starting you on FVD. Your hydration status and electrolytes will be evaluated weekly (or more often, if necessary) throughout treatment. 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 (IV fluids), as required, or may hold or lower your dose of Farydak.

If you vomit after taking Farydak, do not take another capsule. Stay on your schedule, and take your next dose as usual.

Peripheral edema
Peripheral edema is an accumulation of excess fluid under the skin in the spaces within the tissues, or “interstitial” spaces, often resulting in swollen ankles, feet, and legs. Peripheral edema can be a side effect of long-term use of anti-inflammatory medications (such as 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-inflammatory drugs (NSAIDs) such as ibuprofen and naproxen.

Usually, peripheral edema affects both of the legs, ankles, and/or 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. In the Farydak arm of the PANORAMA-1 study, 29% of the patients had peripheral edema compared to 19% of those in the placebo arm.

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. If the edema is severe, the dose of Farydak should be adjusted.

Decreased appetite
There are many causes for loss of appetite during treatment with FVD, including other side effects of treatment such as diarrhea and nausea. Lack of exercise, anxiety, depression, and pain can also contribute to the problem. Good communication with your healthcare team members will help them understand how you’re feeling physically and mentally, and will help determine the source of your appetite loss.

Prevention and treatment of decreased appetite
- Managing your gastrointestinal health and controlling diarrhea and nausea while on FVD is an important step in maintaining your appetite.
- Your doctor will order liver function tests to rule out liver toxicity.
- If you are losing weight, your doctor or nurse may refer you to a nutritionist or suggest a nutritional supplement to provide more calories.

Fever
Fever can be the sign of a bacterial or viral infection, an adverse reaction to a drug or, in rare cases, an aggressive myeloma relapse. Since fever could indicate a life-threatening condition, you should report it to your healthcare provider immediately.

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 100.4°F (38.5°C).
- 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.
- 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 (OTC) medications that you can buy without a prescription, such as acetaminophen (Tylenol®) 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, prescribe antibiotics or give you intravenous antibiotics in the hospital. You may also be given a colony-stimulating factor (CSF), a drug that helps boost the white blood cell count.
- Withhold or reduce the dose of your medications.

**Low WBC count**

White blood cells constitute the immune system, the body’s defense against infection. When the WBC count is low, the body’s normal defenses against viral, bacterial, and fungal infections are reduced. Both Farydak and Velcade can lower the WBC count, while dexamethasone prevents the remaining white cells from reaching the sites of infected tissues. Each of these drugs can contribute to an increased risk of infection. The addition of Farydak to Velcade and dexamethasone caused almost twice as much reduction in WBC count in the PANORAMA-1 clinical trial than occurred in the control arm of the study.

**Prevention and treatment of low WBC count**

Your doctor will withhold your doses of Farydak and Velcade if your WBC count becomes too low and you develop a fever. You may also receive a colony-stimulating factor (CSF) to stimulate production of more white blood cells in your bone marrow. If your WBC count does not improve after treatment with a CSF, or you develop a severe infection, treatment with Farydak will be discontinued.

**Low RBC count**

Red blood cells contain hemoglobin, a protein that contains iron and transports oxygen from the lungs to the body’s organs and tissues. When you have anemia, the result is low levels of oxygen in the body, which may cause shortness of breath, paleness, and feelings of exhaustion. In the Farydak arm of the PANORAMA-1 study, 62% of the patients developed anemia, as compared to 52% in the placebo arm.

**Prevention and treatment of low RBC count**

Your doctor will assess you for anemia before and throughout therapy with FVD.

The following are options for treatment of anemia:

- If your hemoglobin is < 8 grams per deciliter, (g/dL), your doctor will hold your dose of Farydak until your hemoglobin is ≥ 10 g/dL, and then resume treatment at a lower dose.
- Transfusions of red blood cells can help reverse low RBC counts.

**Electrolyte abnormalities**

Electrolytes (which include sodium, potassium, calcium, magnesium, chloride, and phosphorus) are electrically charged substances in the blood and other fluids that are involved in such important functions as regulating the amount of water in the body, the acidity of the blood, nerve and muscle function (including the heart muscle), and other important processes. Electrolyte abnormalities can be caused by poor intake of fluid or nutrition (loss of appetite), by loss of body fluid (vomiting or diarrhea), or by kidney dysfunction (as evidenced by increasing creatinine levels).

**Prevention and treatment of electrolyte abnormalities**

Your doctor can manage electrolyte abnormalities by evaluating and treating the underlying causes: too little intake of electrolytes via food and liquids, loss of electrolytes via diarrhea and vomiting, and poor kidney function.

In addition to treating the underlying source of the abnormalities, your doctor may need to supplement your diet to increase low levels of certain electrolytes lost through diarrhea and vomiting. If your kidneys are functioning poorly, your diet may need to be structured to reduce high levels of phosphorus, potassium, and magnesium and to increase levels of sodium and calcium.

**Increased creatinine**

Creatinine is a substance that is normally secreted by the kidneys into the urine. When the kidney is impaired, the amount of creatinine in the blood increases. The kidneys may function poorly because of myeloma light chain deposits in the tubules of the kidney, or because of the effects of treatment related to hydration, or both. In the PANORAMA-1 study, 41% of the patients in the Farydak arm had increased creatinine, as opposed to 23% in the placebo arm. However, only one Farydak-treated patient had a serious increase in creatinine, as opposed to two in the placebo arm. Among the treatment-related reasons for increased creatinine are other side effects such as loose watery stool, vomiting, loss of appetite, and dehydration.

**Treatment for increased creatinine**

As is true for treating electrolyte abnormalities, managing increased creatinine requires evaluation and management of the possible underlying causes, including the myeloma itself, diarrhea, vomiting, loss of appetite, and dehydration.

**Other precautions for patients**

- There is an increased risk of infection while taking Farydak. If you have any of the following symptoms of infection you should contact the doctor immediately or go to the emergency room: fever, night sweats or chills, cough, body aches, shortness of breath, blood in the phlegm, sores on the body, warm or painful areas on the body, or feelings of unusually extreme tiredness.
Liver toxicity (hepatotoxicity) has occurred in patients treated with Farydak. Your doctor should monitor your liver with appropriate blood tests prior to treatment and regularly during treatment with Farydak. If abnormal liver function tests are observed, your doctor may need to hold or adjust your dose of Farydak until they normalize again. Call your doctor right away if you have any of the following symptoms of liver problems:
- Tiredness or weakness;
- Loss of appetite;
- Dark amber-colored urine;
- Upper stomach pain;
- Yellowing of your skin or the whites of your eyes (jaundice).

Before taking Farydak, tell your doctor:
- If you have diarrhea.
- If you have heart problems.
- If you have a history of bleeding problems.
- If you have an infection. You should not take Farydak if you have an infection.
- If you have liver problems.
- If you are pregnant or plan to become pregnant. Farydak can harm an unborn baby. You should not become pregnant while taking Farydak. If you think you may be pregnant, tell your doctor. Women who are breastfeeding should not take Farydak because it is not known if it will pass into the breast milk. You and your healthcare provider should decide if you will take Farydak or breastfeed.

Access to Farydak and patient resources
Regardless of insurance coverage, all patients have access to a free 21-day (one cycle) supply of Farydak capsules. Patients may have commercial insurance or may have federal or state-funded insurance (such as Medicare, Medicaid, or other programs). Expedited overnight delivery is available, but only for patients who need to start therapy the following day.

To fill your Farydak prescription, there is a network of designated specialty pharmacies. Your doctor may complete a Service Request Form and fax it to one of the designated pharmacies. Only pharmacies in the network can dispense Farydak; visit us.farydak.com for a list of designated pharmacies. Most of the time, a network pharmacy will mail your prescription to you or to your doctor’s office.

Some doctors’ offices, especially those that are part of a hospital or treatment center, will have a pharmacy on site that can fill your Farydak prescription. With these pharmacies, you can walk in and pick up your prescription.

A $0 co-pay program is available for eligible patients with commercial insurance (not Medicare, Medicaid, or other federal or state-funded programs). Your pharmacy will work directly with your insurance carrier when your prescription is filled; you do not need a co-pay card.

Eligible patients may receive other types of financial support. For further information, visit oncologyaccessnow.com or call the Patient Assistance Now (Oncology) access program at 1-800-282-7630.

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
Adrenocortical steroid: Any of the steroidal hormones produced by the adrenal cortex (the outer part of the adrenal gland) or their synthetic (man-made) equivalents. Also known as adrenocorticoids, glucocorticosteroids, or corticosteroids.

Aggresome: A collection (aggregation) of misfolded proteins in the cell, formed when the protein-degradation system of the cell is overwhelmed. Protein folding occurs when a chain of randomly coiled polypeptides (amino acids that are bonded together) folds into a characteristic three-dimensional structure. The sequence of amino acids in the peptide chain determines its final structure. Unchecked misfolding of proteins results in such diseases as Alzheimer’s, Parkinson’s, and amyloidosis.

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

Arrhythmia: An arrhythmia is a problem with the rate or rhythm of the heartbeat. It means that the heart beats too quickly, too slowly, or with an irregular pattern. Arrhythmias are caused by problems with the heart’s electrical conduction system.

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.

818-487-7455 worldwide  •  800-452-CURE (2873) toll-free in US & Canada

myeloma.org
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.

Colony-stimulating factor (CSF): Proteins that stimulate the development and growth of blood cells. Neupogen® (filgrastim), Neulasta® (pegfilgrastim), and Leukine® (sargramostim) are colony-stimulating factors that are used to mobilize stem cells from the bone marrow into the bloodstream prior toapheresis. These may also be used after the transplant to hasten blood count recovery.

Conditioning: A treatment regimen given to a patient to destroy cancer cells prior to stem cell transplant. The most common conditioning regimen given to myeloma patients is 200 mg of melphalan per square meter of body mass.

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.

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.

Frontline: See “Induction therapy.”

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.

Induction therapy: The initial treatment used in an effort to achieve remission in a newly diagnosed myeloma patient. Sometimes called “frontline” therapy.

Ischemic events: An event caused by an inadequate supply of blood to an organ or tissues, such as from an obstructed blood flow. Myocardial ischemia occurs when blood supply to the heart is reduced, preventing it from receiving enough oxygen. This can cause damage to the heart muscle.

Non-steroidal anti-inflammatory drug (NSAID): A drug used to reduce fever, swelling, pain, and redness.

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): For a group of individuals suffering from a cancer, this term denotes the chances of staying alive. It denotes the median number of individuals in the group who are likely to be alive after a particular duration of time. At a basic level, OS is representative of cure rates. OS is often used as a measure of treatment efficacy in clinical trials.

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.

Platelets: One of the three major blood elements, others being the red blood cells and white blood cells. Platelets plug up breaks in the blood vessel walls and release substances that stimulate blood clot formation. Platelets are the major defense against bleeding. Also called thrombocytes.

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 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, and so forth, as well as enzymes and antibodies.

Red blood cells (RBC, erythrocytes): Cells in the blood that contain hemoglobin and deliver oxygen to and take carbon dioxide from all parts of the body. Red cell production is stimulated by a hormone (erythropoietin) produced by the kidneys. Myeloma patients with damaged kidneys don’t produce enough erythropoietin and can become anemic. Myeloma patients can also become anemic because of myeloma cells’ effect on the ability of the bone marrow to make new red blood cells.

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. VGPS 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).

Tumor suppressor gene: Also called an anti-oncogene. A gene that protects a cell from one step on the path to cancer. When this gene mutates to cause a loss or reduction in its function, the cell can progress to cancer, usually in combination with other genetic changes.

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, granulocytes, lymphocytes, and monocytes.

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. VGPS 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).

Tumor suppressor gene: Also called an anti-oncogene. A gene that protects a cell from one step on the path to cancer. When this gene mutates to cause a loss or reduction in its function, the cell can progress to cancer, usually in combination with other genetic changes.

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, granulocytes, lymphocytes, and monocytes.