Understanding
Treatment of Myeloma Bone Disease

A publication of the International Myeloma Foundation

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

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

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

**Table of contents**

<table>
<thead>
<tr>
<th>Topic</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>What you will learn from this booklet</td>
<td>4</td>
</tr>
<tr>
<td>About myeloma bone disease</td>
<td>4</td>
</tr>
<tr>
<td>What are bisphosphonates?</td>
<td>5</td>
</tr>
<tr>
<td>Are bisphosphonates a type of chemotherapy?</td>
<td>5</td>
</tr>
<tr>
<td>Who benefits from bisphosphonates?</td>
<td>6</td>
</tr>
<tr>
<td>What are the different types of bisphosphonates?</td>
<td>6</td>
</tr>
<tr>
<td>How are bisphosphonates given?</td>
<td>7</td>
</tr>
<tr>
<td>What are the possible side effects of bone-modifying agents?</td>
<td>9</td>
</tr>
<tr>
<td>Can BMAs be combined with other therapies?</td>
<td>13</td>
</tr>
<tr>
<td>Will insurance cover the costs of BMAs?</td>
<td>13</td>
</tr>
<tr>
<td>What other approaches to bone care are available?</td>
<td>14</td>
</tr>
<tr>
<td>In closing</td>
<td>15</td>
</tr>
<tr>
<td>Terms and definitions</td>
<td>15</td>
</tr>
</tbody>
</table>
What you will learn from this booklet

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

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

Understanding Treatment of Myeloma Bone Disease will familiarize you with therapies given to prevent and treat myeloma bone involvement. Therapy with a bone-modifying agent (BMA) is not treatment for myeloma, but it does help to prevent skeletal complications of myeloma (known as skeletal-related events). BMAs, which include both bisphosphonates and the newly approved monoclonal antibody Xgeva® (denosumab), a RANK ligand (RANKL) inhibitor, are an essential component of supportive care for patients with myeloma.

About myeloma bone disease

Approximately 80% of patients with myeloma develop bone disease. Bone disease can cause the bones to become thinner and weaker (osteoporosis), and it can make holes appear in the bone (lytic lesions). The weakened bone is more likely to break due to minor pressures or injury (pathologic fracture). The bones most commonly affected are the axial skeleton (spine, pelvis, ribs, and skull) and the upper ends of the long bones of the arms and legs.

In the healthy skeleton, there is a balance between the breakdown of old bone tissue (performed by cells called osteoclasts) and the building of new bone tissue (formed by osteoblasts). Myeloma cells send signals to osteoclasts, causing them to break down much more bone than what is required for normal skeletal health. Myeloma cells also inhibit the formation of osteoblasts, thus preventing the repair of bone loss. In addition to giving rise to bone disease, this process of accelerated bone breakdown releases calcium from the bones into the bloodstream. If this release happens too quickly, a condition called hypercalcemia can occur. Both myeloma bone disease and hypercalcemia can be treated with a group of drugs called bisphosphonates.

What are bisphosphonates?

Bisphosphonates are small inorganic molecules that bind to a substance called hydroxyapatite on the surface of damaged bones. At the sites of bone damage, bisphosphonates inhibit and destroy osteoclasts. Since bone damage is caused by the increased numbers and activity of these osteoclasts, treatment with bisphosphonates reduces bone damage and, when the myeloma is well controlled, allows bone healing to occur.

Bisphosphonates have several beneficial effects, including:

- Preventing further bone damage,
- Reducing bone pain and the need for painkillers,
- Correcting and preventing hypercalcemia,
- Reducing the need for radiotherapy,
- Reducing pathologic fractures due to myeloma (i.e., fracture at a site where myeloma has weakened the bone),
- Improving the chances of healing and recovering bone strength,
- Improving quality of life.

Are bisphosphonates a type of chemotherapy?

Bisphosphonates are not a type of chemotherapy, nor are they a treatment for myeloma. Several clinical trials have demonstrated that bisphosphonates have no anti-myeloma effect and do not prevent progression of early myeloma.

Bisphosphonates are used to treat several types of bone disease, including osteoporosis and the bone-thinning effects of steroid treatment. Bisphosphonates were first introduced more than 20 years ago as an additive to toothpaste to reduce dental decay.
Bisphosphonates are generally safe and do not have the types of risks or side effects associated with chemotherapy, which is used to directly attack myeloma cells.

**Who benefits from bisphosphonates?**
Bisphosphonates are recommended for all patients with myeloma-related bone disease. The American Society of Clinical Oncology (ASCO) published updated clinical practice guidelines on bone-modifying agents in May 2018. Where they had previously only recommended ongoing use of bisphosphonates “for myeloma patients with documented bone disease who started on systemic treatment for myeloma,” they now recommend bisphosphonate therapy for myeloma patients “with active symptomatic myeloma that requires systemic therapy with or without evidence of lytic destruction of bone or compression fracture of the spine from osteopenia.”

Bisphosphonate therapy was introduced for myeloma in 1995 with FDA approval of Aredia® (pamidronate). Prior to that time, myeloma patients had few options at their disposal other than radiation therapy to control bone pain and reduce the risk of pathologic fractures. Bisphosphonates are particularly helpful for patients being treated with steroids such as prednisone or dexamethasone. Steroids reduce bone mass or density; bisphosphonate therapy improves this negative effect on bones.

**What are the different types of bisphosphonates?**
Several bisphosphonates are commercially available, and more potent products have been developed over the years in an effort to achieve more effective bone healing. Thus far, the various products approved and available have produced “equivalent” major benefits. However, these products are associated with several important differences in:

- Administration (e.g., intravenous versus oral delivery and the length of intravenous infusion time).
- Potential side effects (e.g., fever, possible kidney toxicity, or bone disease in the jaw).

**Pamidronate**
Approved by the FDA in 1995, pamidronate by monthly intravenous (IV) infusion became the standard of care for myeloma patients. It has become established as a safe, helpful drug for the treatment of myeloma bone disease.

**Zoledronic acid**
Zometa® (zoledronate or zoledronic acid) was approved by the FDA in 2001 based on study results comparing it with pamidronate. Zoledronic acid produces more rapid and prolonged reduction in elevated blood calcium than pamidronate when elevated levels are present. However, results evaluating effects on bone disease showed that zoledronic acid and pamidronate affect SREs equivalently. The major difference between zoledronic acid and pamidronate is the infusion time, as discussed below.

**Clodronate**
Clodronate is approved for use in Canada, the EU, Australia, and other countries. It is taken orally rather than administered intravenously, like pamidronate and zoledronic acid.

**How are bisphosphonates given?**
Both pamidronate and zoledronic acid are given intravenously on a monthly basis. A 90 mg dose of pamidronate is given over two to four hours by IV infusion, and premedication with one or two 325-mg acetaminophen tablets can be helpful. A 4 mg dose of zoledronic acid is given over 15 to 45 minutes by IV infusion, and premedication may be beneficial as well.

Toxicities associated with both medications, especially potential renal (kidney) toxicities, are related to dosage, duration of infusion, and frequency of infusion. If kidney toxicity is a concern, the infusion time of pamidronate can be increased to four hours, and the infusion time of zoledronic acid can be increased from 15 minutes to 30 or 45 minutes.

The small Z-MARK study (121 myeloma patients) published by Raje et al. in 2015 showed that dosing of Zometa (zoledronic acid) every 12 weeks over two years “maintains a low SRE rate and can be safely administered for up to 4 years.” A randomized trial comparing Zometa given every 4 weeks to Zometa given every 12 weeks for 2 years was conducted on 1,822 patients with metastatic breast cancer, metastatic prostate cancer,
or myeloma, and was published in 2017. The trial found that among these patients, “the use of zoledronic acid every 12 weeks compared with every 4 weeks did not result in an increased risk of skeletal events over 2 years.” The updated ASCO guidelines state that “for patients without active myeloma who are receiving maintenance therapy, receiving bisphosphonates every 3 months, rather than monthly, is an option.” The new guidelines note that “there are insufficient data to recommend a specific duration of bisphosphonate therapy” beyond two years. Monthly treatment is to be resumed “upon relapse with new-onset SREs.”

Occasionally, patients can benefit from oral bisphosphonates, especially patients who are intolerant of intravenous infusion, have nephrotoxicity (kidney disease), and/or are using steroids, which can cause bone loss. If a patient experiences difficulty with intravenous bisphosphonates, oral bisphosphonates can be considered.

In the US, oral bisphosphonates Fosamax® (alendronate) and Actonel® (risedronate) are not approved specifically for myeloma by the FDA. Outside the US, myeloma patients can be treated with clodronate if there are problems with intravenous bisphosphonates. A large randomized trial conducted in the UK, however, demonstrated that zoledronic acid is more effective than clodronate.

**Treatment with Xgeva**

Xgeva was approved in early 2018 in the US and the EU for the prevention of skeletal-related events in patients with myeloma. The approvals were based upon Xgeva’s proven non-inferiority to Zometa in a pivotal, 1,1718-patient, phase III ‘482 clinical trial.

Xgeva is a monoclonal antibody that binds to the cytokine RANKL, an essential factor in initiating bone breakdown by osteoclasts. Like the bisphosphonates, Xgeva is an osteoclast inhibitor, but its mechanism of action (the way it works), the way it is metabolized by the body, and its route of administration all differ from the bisphosphonates.

- Bisphosphonates bind to bone mineral tissue, where they are absorbed by mature osteoclasts, causing osteoclasts to die. Xgeva does not become imbedded in bone tissue; it affects immature osteoclasts, blocking their ability to mature, function, and survive.

- While bisphosphonates are excreted via the kidneys, and can cause kidney toxicity, Xgeva is not cleared by the kidneys, and produces a low level of kidney-related side effects as compared to the bisphosphonates. The ASCO guidelines indicate that Xgeva may be preferable to bisphosphonates in patients with kidney damage.

- While bisphosphonates approved for myeloma are given as an intravenous infusion, Xgeva is given as a subcutaneous injection.

**What are the most common side effects of Xgeva?**

The most common side effects of Xgeva are diarrhea, nausea, low red blood cells, low blood platelets and calcium levels, back pain, swelling of the lower legs or hands, upper respiratory tract infection, rash, and headache.

The most common serious adverse reaction in the ‘482 trial was pneumonia, which occurred in 8% of patients in both the Xgeva and Zometa arms of the study.

Physicians are also advised to counsel their female patients that Xgeva can cause embryo-fetal harm (harm to an unborn baby if the mother takes Xgeva while pregnant).

Other important precautions with Xgeva are the risk of osteonecrosis of the jaw and atypical thigh bone fractures (see below), both of which occur with bisphosphonate therapy as well.

**What are the possible side effects of bone-modifying agents?**

Generally, BMAs are tolerated well. The most common side effects are:

**Fever**

Fever may occur as an infusion reaction to Zometa or pamidronate. Fever associated with bisphosphonates is typically mild (i.e., 100°F to 101°F), and occurs a few hours after the intravenous infusion and lasting for a few hours at most. It typically occurs with the first or second infusion, and less frequently – if at all – thereafter. Fever is usually easily treated or prevented by pretreating with one or two 325-mg acetaminophen tablets. Occasionally, patients have severe recurrent fever and cannot tolerate intravenous bisphosphonates. Oral bisphosphonates are an option for such patients (see above).
Vein irritation
With IV bisphosphonates, vein irritation (mild phlebitis) can occur at the site of the infusion. It is usually mild, and patients typically recover within 1 to 2 days. Careful infusion is recommended to avoid any leakage of medication around the vein. Also, a short infusion of saline at the end of the bisphosphonate infusion is recommended to clear the pamidronate or zoledronic acid from the area and reduce the chance of phlebitis.

General aches and pains
These effects sometimes occur briefly, along with fever, with infused bisphosphonates. Back pain has been reported in patients who are receiving therapy with Xgeva.

Kidney dysfunction
A main concern with bisphosphonate therapy relates to kidney side effects. All bisphosphonates are potential toxins for the kidneys. Since myeloma itself can impact kidney function (through damage caused by myeloma light chain protein and/or by elevated blood calcium), the possibility of kidney-related side effects is of particular concern.

- Pamidronate has been used widely for over two decades, including the initial trials period. The type of kidney toxicity that has emerged is an excess of a serum protein, called albumin, in the urine (known as albuminuria or nephrotic syndrome). This toxicity has occurred predominantly with uses of higher than recommended doses (e.g., 180 mg versus 90 mg) and/or more frequent than recommended dosing schedules (e.g., every two weeks versus once per month). This side effect is usually reversible with dose and/or schedule adjustments or, in occasional severe cases, by discontinuing pamidronate. Very rarely has irreversible damage occurred. Periodic monitoring (e.g., every three to six months) of urine protein levels with 24-hour urine collection is recommended to prevent any significant kidney damage.

Dosing of pamidronate
In 2010, the Nordic Myeloma Study Group published a randomized, double-blind, phase III clinical trial in Lancet Oncology that compared 30 mg versus the standard dose of 90 mg of pamidronate in patients with newly diagnosed myeloma. Their aim was to find the lowest effective dose of pamidronate, given the toxicities associated with long-term bisphosphonate treatment. The study concluded that “monthly infusion of pamidronate 30 mg should be the recommended dose for prevention of bone disease in patients with multiple myeloma.” If you do require a dose adjustment of pamidronate, you can discuss this option with your oncologist knowing that a large study validated the efficacy of one third of the standard dose.

- Zoledronic acid was approved in January, 2002, and has been in use for approximately 20 years, including the clinical trial period. The major kidney toxicity-related concern that has emerged with zoledronic acid is an increase in serum creatinine, which is an indication of kidney dysfunction. Reports of both increased creatinine, and occasionally more severe kidney damage (acute tubular necrosis), have raised concerns that this much more potent bisphosphonate must be used more cautiously with respect to kidney function. To minimize the potential for kidney-related problems, your doctor should follow several recommendations:
  - Your doctor should be especially cautious with the use of zoledronic acid if there is concern about kidney dysfunction (i.e., with Bence Jones myeloma, diabetes, long-standing high blood pressure, or in elderly or frail patients). Zoledronic acid should not be used in patients with known kidney deterioration as determined by creatinine level over 3 mg/dL.
  - Your doctor should check your serum creatinine level before each dose of zoledronic acid.
  - If the serum creatinine value has increased by 0.5 mg/dL in a patient who had normal renal function at the outset, the doctor should hold the next dose of zoledronic acid until the creatinine value returns to within 10% of baseline.
  - If the serum creatinine value has increased by 1.0 mg/dL in a patient with abnormal renal function at the outset, the doctor should hold the next dose until the value returns to within 10% of baseline.
  - In a patient who has experienced a mild elevation in serum creatinine value that has returned to 10% of baseline, the doctor may consider adjustments to the treatment schedule. Adjustments may include increasing the time of infusion from 15 to 30 minutes or more, using a larger volume of diluting fluids, or delaying the administration of the next dose. The doctor should use his or her judgment to determine which option is most appropriate for an individual patient.
Your doctor should be aware that certain medications with the potential to affect kidney function may be more likely to do so if they are given at the same time as bisphosphonates. Some examples of these medications are certain antibiotics, thalidomide, and nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin, ibuprofen, and Celebrex® (celecoxib).

**Osteonecrosis of the jaw**

Osteonecrosis of the jaw (ONJ) is a problem that occurs in 3%–4% of patients with myeloma or other cancers who have been treated with both bisphosphonates and with Xgeva. This condition is often preceded by inflammation or an infection in the mouth, and produces pain, swelling, and bone damage around the tooth sockets in the jaws. There is bone necrosis or loss of bone, which can lead to loose teeth, sharp edges of exposed bone, bone spurs, and the breaking loose of small bone spicules or dead bone. Symptoms may not be obvious at first, or may include pain, swelling, numbness, a “heavy jaw” feeling, or loosening of a tooth.

- Consultation with an oral surgeon or dental oncologist familiar with osteonecrosis is strongly recommended for patients who suspect that they may have ONJ. Management without surgery is recommended as a first step. A protective mouth guard may also be helpful. Minor dental work to reduce sharp edges or remove injured tissue may be required.
- Antibiotic treatment is recommended if there is infection. The type of therapy selected depends upon the type of infection that is documented. Oral rinses can also be used.
- If problems persist and/or if healing is slow, consideration can be given to stopping bisphosphonate therapy for two to four months to facilitate recovery. Although study results are lacking, there are anecdotal reports of benefit with brief interruption of pamidronate or zoledronic acid treatment.
- If dental surgery is absolutely required, interruption of bisphosphonate therapy is strongly recommended. Current data indicate very poor healing with continued bisphosphonates in this setting.
- Dentures can be worn, but many need adjustment. Placement of dental implants appears to be contraindicated. Use of hyperbaric oxygen does not appear to be helpful.
- Careful monitoring and follow-up are required.
- Prevention can help patients avoid or reduce the scope of the problem. Inform your dentist about this potential risk for patients before you start therapy with a bisphosphonate or Xgeva; maintain excellent oral hygiene, and make sure that you visit the dentist regularly. Avoid tooth extraction and/or any elective jaw surgery if at all possible. If there is an opportunity, proceed with careful dental evaluation and any required preventive dental care before starting bisphosphonate therapy.
- The incidence of ONJ appears to have decreased dramatically, probably due to increased awareness and proactive dental practice.

**Atypical thigh fractures**

Rare atypical fractures of the femur (thigh bone) known as subtrochanteric and diaphyseal femur fractures have been seen after five or more years of bisphosphonate treatment and have been reported in patients who are receiving treatment with Xgeva. The FDA has included the risk of these fractures to the Warnings and Precautions section of the labels of all approved bisphosphonate drugs, as well as to the Xgeva label (package insert).

Atypical femoral fractures may occur in one or both thighs and usually present as a dull aching pain weeks to months before a complete fracture occurs. Many patients who are also receiving therapy with a glucocorticoid (such as dexamethasone) report these fractures. Report any new or unusual thigh, hip, or groin pain to a member of your healthcare team right away.

**Can BMAs be combined with other therapies?**

In general, BMAs can be safely combined with most other therapies. Your doctor may decide not to give these therapies on or close to the same day as administration of intravenous chemotherapy. Caution about potential kidney toxicity with bisphosphonates has been noted above, so the addition of another drug that can harm the kidneys should be avoided.

**Will insurance cover the costs of BMAs?**

In the US, Medicare and most insurance programs reimburse for bisphosphonate therapy. Any problems with reimbursement should be brought to the attention of your doctor. It is important to note that Aredia is off patent and is available as a generic drug in the US and abroad, and Zometa is off patent
in several countries (but not yet in the United States). Xgeva is significantly more expensive than generic pamidronate or Zometa, so unless there are medical reasons for which a patient cannot receive bisphosphonate therapy (such as kidney disease), there may be insurance issues with receiving reimbursement for Xgeva.

Since hospitals and clinics set up contracts for one product versus another, it’s important to double-check which agent, from which source, is being administered to you. Some patients may experience a new side effect or be intolerant of the vehicle – the solution into which the active ingredients are added – in a generic medicine they haven’t had before. If this happens to you, be sure to find out what drug you received and which company manufactured it, and report your side effects to your doctor.

What other approaches to bone care are available?

**Kyphoplasty** provides a tool that may have an impact on bone care for myeloma patients. This procedure involves the injection of liquid cement using the balloon technique in an attempt to provide acute pain relief and improvement in the structural integrity of collapsed vertebrae or other damaged bones. The results of the CAFE study, a randomized clinical trial of kyphoplasty versus non-surgical intervention, concluded that patients randomized to have kyphoplasty had improved pain relief, back function, and quality of life. For more information on this topic, read the IMF’s *Understanding Treatment of Myeloma-Induced Vertebral Compression Fractures* booklet.

General measures to improve bone health are recommended, including:

- Adequate pain control to allow for movement and exercise.
- Radiation therapy and/or orthopedic surgery to restore structural integrity of bones and recovery of full mobility. Radiation therapy should be used sparingly for acute problems such as spinal cord compression, severe refractory pain, and treatment or prevention of pathologic fracture. Since radiation therapy can impair local bone healing, many doctors prefer to use systemic steroids and/or other anti-myeloma therapies. Orthopedic surgery should be used as necessary.

- Exercise, especially walking and/or swimming, to enhance bone strength, flexibility, and endurance.
- Avoidance of risky activities (e.g., bicycling, skiing, skating, climbing ladders), which can increase the likelihood of falls and/or fractures.
- Regular re-evaluation and follow-up testing to rule out new bone disease and assess the impact of treatment.

**In closing**

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

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

We encourage you to visit myeloma.org for more information about myeloma and to contact the IMF InfoLine with your myeloma-related questions and concerns. The IMF InfoLine consistently provides callers with the most up-to-date and accurate information about myeloma in a caring and compassionate manner. IMF InfoLine specialists can be reached at InfoLine@myeloma.org or 818-487-7455 or 800-452-CURE.

**Terms and definitions**

**Acute tubular necrosis (ATN):** The death of tubular epithelial cells that form the renal tubules of the kidneys. ATN is a form of acute renal failure. Kidney function can be recovered when not all tubular cells are affected.

**Albuminuria:** The presence of an excess of serum albumin in the urine.

**Bence-Jones myeloma:** Myeloma characterized by the presence of Bence-Jones protein, an abnormal protein in urine made up of free kappa or lambda light chains.

**Bisphosphonate:** A type of drug that protects against osteoclast activity (bone breakdown) and binds to the surface of bone where it is being resorbed or destroyed.

**Bone-modifying agent (BMA):** The group of drugs that includes denosumab (Xgeva®), zoldronic acid (Zometa®), and pamidronate (Aredia®).
These agents are used to prevent bone breakdown in myeloma and some other cancers.

**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.

**Chemotherapy**: Any drugs used to kill cancer cells. “Combination chemotherapy” uses more than one drug in a cancer treatment regimen.

**Creatinine**: A small chemical compound normally excreted by the kidneys into the urine. If the kidneys are damaged, the serum level of creatinine builds up, resulting in an elevated serum creatinine. The serum creatinine test is used to measure kidney function.

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

**Hydroxyapatite**: A compound that helps form bones and gives them rigidity and strength.

**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.”

**Kyphoplasty**: The injection of liquid cement into damaged bone using a balloon technique. This procedure may provide acute pain relief and improvement in structural integrity of collapsed vertebrae or other damaged bones.

**Lytic lesion**: The damaged area of a bone that shows up as a dark spot on an X-ray when at least 30% of the healthy bone in any one area is eaten away. Lytic lesions look like holes in the bone and are evidence that the bone is being weakened.

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

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

**Nephrotic syndrome**: A group of diseases characterized by excretion of large amounts of protein (mostly albumin) into urine. Nephrotic syndrome frequently produces edema.

**Nonsteroidal anti-inflammatory drug (NSAID)**: A drug used to reduce fever, swelling, and pain.

**Osteoblast**: A bone cell associated with production of bone tissue. Osteoblasts produce osteoid, which then becomes mineralized with calcium to form new hard bone.

**Osteoclast**: A cell found at the junction between the bone marrow and the bone. It is responsible for breaking down or remodeling old bone tissue. In myeloma, the osteoclasts are overstimulated, while osteoblast activity is blocked. The combination of accelerated bone resorption and blocked new bone formation results in lytic lesions.

**Osteonecrosis of the jaw (ONJ)**: A jaw problem observed in a small percentage of patients taking bisphosphonates. The condition can cause pain, swelling, and bone damage around the tooth sockets in the jaws. Bone necrosis, or death of bone, occurs and can lead to loose teeth, sharp edges of exposed bone, bone spurs, and the breaking loose of small bone spicules or dead bone. It is defined as ≥ 3 months with non-healing exposed bone. Symptoms may not be obvious at first, or may include pain, swelling, numbness or a “heavy jaw” feeling, or loosening of a tooth.

**Osteoporosis**: A progressive bone disease that is characterized by a decrease in bone mass and density, leading to an increased risk of fracture. Diffuse involvement of bones with myeloma produces what looks like osteoporosis on X-ray and bone density measurement.

**Pathologic fracture**: A break in a bone usually caused by cancer or some disease condition. Occurs in myeloma-weakened bones, which can’t bear normal weight or stress.

**Phlebitis**: Inflammation of a vein.

**Skeletal-related event (SRE)**: Bone damage or fracture.

**Steroid**: A type of hormone. Synthetic steroids are often given to myeloma patients along with one or more anticancer drugs and typically enhance the anti-myeloma treatment benefit.

**Systemic treatment**: Treatment using substances that travel through the bloodstream to reach and affect cells in the entire body.
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

- 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

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