

Myeloma Bone Disease and Bisphosphonates

What is Myeloma Bone Disease?

Approximately 70% of myeloma patients will have bone disease at the time of diagnosis and approximately 90% of patients will experience bone disease while living with myeloma.

This is due to the myeloma cells producing chemicals that upset the natural equilibrium of bone remodeling. The body relies on osteoclasts to breakdown bones at the same rate as osteoblasts rebuild. The chemicals produced by the myeloma cells cause the osteoclasts to work faster and inhibit the normal functioning osteoblasts. This can result in lytic lesions or 'holes' in the bones, fractures, osteoporosis and/or pain. This process can also release calcium into the blood. If this happens too quickly, the calcium levels in the blood can rise, the medical term being 'hypercalcaemia'.

The bones most commonly affected are those in the spine, pelvis, ribs and skull and the upper ends of the long bones of the arms and legs. The bones in the hands and feet are usually not affected.

Both myeloma bone disease and hypercalcaemia are treated with a group of drugs called bisphosphonates which are explained on the next page.

How is Bone Disease Monitored?

There are numerous radiological techniques used to investigate and monitor myeloma bone disease. The type of scanning technique used will be determined by the presenting symptoms of each case. The most common technique used is the **skeletal survey**. This is a series of x-rays of the skull, spine, ribs, pelvis and long bones of the arms and legs to detect any lytic lesions or osteoporosis.

If pain is reported but no fractures or lesions are detected on x-rays a more sensitive scan may be required. A **computerised tomography (CT)** scan or **magnetic resonance imaging (MRI)** scan provides a three dimensional picture to evaluate the soft tissue as well as the bones.

Less commonly used are **fluro-deoxyglucose positron emission tomography (FDG/PET)** and **sestamibi scans**. FDG/PET scanning involves injecting a radioactive drug that highlights areas of rapid cell growth as 'hot spots' such as tumours. A sestamibi uses an injected radiolabelled isotope that may find myeloma deposits not detected on other scans. It may also be necessary to have a bone **mineral density (BMD)** test if osteoporosis is detected.

Those with nonsecretory myeloma, where there is no detectable paraprotein in the blood or urine, may rely on imaging to monitor the progress of their myeloma.

The medical team will recommend the type of scan that is required for each particular case. Investigations are carried out at the time of diagnosis and may be repeated after treatment, at follow up or with any new bone symptom.

What are Bisphosphonates?

Bisphosphonates are a group of drugs that inhibit the over activity of the osteoclast cells that break down bone. Since bone damage is caused by increased numbers and activity of these osteoclast bone cells, bisphosphonates reduce new bone damage and allow an opportunity for bone healing to occur. Bisphosphonates are also used to treat bone symptoms in some other cancers.

Bisphosphonates have several beneficial effects, including:

- Preventing further bone damage
- Reducing bone pain and the need for pain killers
- Correcting and preventing hypercalcaemia (high levels of calcium in the blood)
- Reducing the need for radiotherapy
- Reducing pathological fractures due to myeloma
- Improving quality of life, particularly by decreasing pain and maintaining mobility
- Improving the chance of healing and recovering the strength of the bone
- Some evidence has emerged that the inclusion of an intravenous bisphosphonate to treatments for myeloma can have a direct anti myeloma effect and improve the survival rate.

Who Benefits From Bisphosphonates?

Bisphosphonates are recommended for all patients with symptomatic myeloma (that is myeloma requiring treatment) especially if there is related bone disease. The time frame for continuation of treatment will vary between patients but most doctors will prescribe the bisphosphonate for two years and then reassess the schedule.

Are There Different Types of Bisphosphonates?

There are three bisphosphonates available to treat myeloma bone disease and these are tabled below. Differences are associated with the route of administration and potential side effects.

Type	Other Names	Administered
Zoledronic Acid	Zometa	IV infusion over a minimum of 15 minutes every month
Pamidronate	Aredia, APD	IV infusion over 90-120 minutes, every month
Clodronate	Bonefos	Tablets taken once or twice daily

What Are The Possible Side Effects of Bisphosphonates?

Bisphosphonates are generally well tolerated. Any side effects are usually mild with the most common being fever, vein irritation and general aches and pains. A potentially more serious side effect is that of kidney dysfunction

Fever and flu-like symptoms can occur shortly after the intravenous infusion. They are typically mild and last only for two to three hours. The effects are easily treated with paracetamol.

Vein irritation may occur at the site of the infusion. Again, it is usually mild and patients recover within one to two days.

General bone aches and pains sometimes occur and are mostly linked to the onset of fever and / or flu-like symptoms. They can persist for a day or two after each infusion and can be managed with simple analgesics (painkillers) such as paracetamol.

Nausea that is mild and short lasting is quite common with oral bisphosphonates.

Kidney dysfunction is the most important potential side effect. All three bisphosphonates can potentially harm kidney function. Since myeloma can affect kidney function (e.g. due to paraprotein damage or hypercalcaemia) the possibility of kidney related side effects is of particular concern. The doctor will check kidney function regularly by a simple blood test.

To ensure the safety and effectiveness of bisphosphonate drugs and to help protect the kidneys, it is important to stay well hydrated. Drinking two to three litres of water a day is ideal.

Be aware that certain medications can increase the risk of kidney dysfunction when given with bisphosphonates. Non steroidal anti inflammatory drugs, especially drugs that include Ibuprofen (Nurofen), should be avoided. Examples of other drugs that cause problems are thalidomide and some antibiotics. The doctor or nurse should be informed of any new medication taken.

If kidney dysfunction occurs the doctor may temporarily discontinue the bisphosphonate, reduce the dose or increase the time frame between doses.

Osteonecrosis of the Jaw (ONJ) is a breakdown of the jawbone which is painful and very slow healing. It is a rare complication of intravenous bisphosphonate treatment that is usually caused by an invasive dental procedure such as a tooth extraction. However, it may also occur spontaneously.

In an effort to reduce the incidence of ONJ in people with myeloma, it is recommended that those having bisphosphonate treatments have a thorough dental examination before commencing the drug and let their dentist know they will be receiving a bisphosphonate. It is important to maintain good oral health for the duration of the treatment by ensuring teeth are regularly brushed and flossed and that dentures are correctly fitted and don't rub. Any, jaw pain should be reported to the doctor and the treating team must be advised about any required invasive dental procedures. Smoking increases the risk of ONJ substantially and should be avoided at all costs.

If left untreated bone disease can have a great impact on the quality of life in those with myeloma. In some circumstances the doctor may recommend vitamin D and/or calcium supplements to help maintain bone strength.

There are many ways to minimise and manage bone pain. Communicating any new pain or symptom with the doctor will ensure every effort is made to maintain comfort and control bone disease.

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The information in this fact sheet is not intended to replace medical care or the advice of a physician. Your doctor should always be consulted regarding diagnosis and treatment.

For further information please contact one of our Myeloma Support Nurses
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1800 MYELOMA (1800 693 566)
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