

Managing Myeloma Bone disease: Bisphosphonates

What is myeloma bone disease (MBD)?

Normal bone strength of the skeleton is maintained by a fine balance between bone breakdown (by osteoclast cells) and bone formation for repair (by osteoblast cells). In myeloma, the balance is disrupted, bone breakdown increases, and bone repair slows. Factors released by increased bone breakdown promote myeloma cell growth leading to progressive damage or holes (lytic lesions) in the bones. Myeloma bone disease occurs in more than 80% of people during the course of their myeloma.

How is myeloma bone disease monitored and diagnosed?

- **Blood tests:** increased calcium levels indicate abnormal bone destruction with release of calcium into the bloodstream. Follow up with radiology examinations is needed.
- **Skeletal Survey:** (plain x-rays of skull, spine, ribs, pelvis and long bones of the arms and legs) can only show bone disease of greater than 10mm, and 50% of bone strength lost (thinning or osteopenia). Skeletal survey is not sensitive enough to determine if there is no MBD; body structures can also obscure a larger lesion from view. A negative skeletal survey and persistent pain needs follow up with more sensitive imaging. Skeletal survey is a quick test to determine presence of extensive MBD.
- **CT** (Computerised Tomography) or **MRI** (Magnetic Resonance Imaging) are more sensitive scans, they provide three dimensional pictures to evaluate the soft tissue as well as the bones. MRI of the spine and pelvis detects approximately 90% of myeloma bone disease and areas of bone marrow infiltration by myeloma cells.
- **PET** (Positron Emission Tomography) or **SESTAMBI** scans involve 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. They both show increased bone cell activity, but are not enough alone to diagnose lytic lesions in the bones. Their role in myeloma bone disease diagnosis is still unclear, and is not currently recommended as standard of care.

Myeloma bone disease is defined as "one or more lytic lesions, seen on plain xray, CT, or CT/PET" greater than 5mm. Positive PET scans without the presence of a bone lesion is not enough information for diagnosis.

How is MBD managed?

MBD is managed and prevented using a class of drugs called bisphosphonates.

What are bisphosphonates (BP)?

BP drugs coat the bone surface, helping protect it from erosion by the over activity of myeloma stimulated osteoclast cells. BPs reduce new bone damage and allow an opportunity for some bone healing to occur.

Who should receive BP treatment?

BP therapy should be commenced on everyone with myeloma that needs treatment, whether MBD has been diagnosed or not. Clinical studies show those diagnosed with myeloma needing treatment, who get BP therapy, have increased survival over those not receiving it. There is not enough evidence to recommend BP use for anyone with asymptomatic or smouldering myeloma, MGUS or isolated plasmacytoma.

BP types in Australia

There are three BP drugs reimbursed by the Pharmaceutical Benefits Scheme for use in myeloma.

- **Zoledronic Acid** (*Zometa*®) given intravenously over 15-30 minutes.
- **Pamidronate** (*APD, Aredia*®) given intravenously over 90-120 minutes.
- **Clodronate** (*Bonefos*) is a tablet taken once or twice a day.

Intravenous (IV) BPs are preferred as they contribute to a better MBD management and overall survival than that seen with oral. In some people the risk of side effects from IV BPs or the necessity to travel to hospital to receive the infusion outweighs the benefit and oral BP is recommended.

How is BP treatment given?

IV bisphosphonates are infused every four weeks initially at the hospital day ward. Some clinics are able to offer a treatment at home service for bisphosphonate and other therapies.

What is the treatment duration?

After 1 – 2 years, the risk of bone related damage will be re-assessed by the doctor.

- If there are few bone lesions (<4) and no generalised bone thinning with a very good disease response to myeloma therapy, treatment may stop until disease returns.
- If the bone disease is widespread, but the myeloma is stable and no new bone lesions have appeared for >4 months, a 3 monthly IV maintenance program is an option.
- With progressive disease and a risk of elevated blood calcium levels, IV treatment will continue every 4 weeks.

What side effects are there with BP treatment?

Mild side effects include

- Fever following infusion: should only last for a few hours.
- Cold and flu like symptoms: should last no longer than the day of infusion.
- General bone aches and pains: should pass within a few days, and be treated easily with simple painkillers like paracetamol.
- Nausea and gastrointestinal upset: mild, common with oral BP treatment.

Serious side effects include

- Lowered levels of electrolytes in the blood. Serum calcium, phosphate and magnesium are measured regularly on blood test. Calcium and vitamin D supplementation may need to be ordered by your doctor.
- Damage to kidneys, especially if there is impaired kidney function caused by myeloma or pre-existing conditions such as diabetes. Kidney function is tested before each dose of BP, the infusion may be delayed until the kidneys improve (over days or weeks) or given at a reduced dose. Keeping a good fluid intake is important. Also avoid non-steroidal anti-inflammatory drugs, (e.g. ibuprofen) which significantly increases the risk of kidney damage.
- Osteonecrosis of the Jaw (ONJ): an uncommon but serious complication of all BPs. Localised death of bone tissue occurs in the jaw bones causing pain and an exposed area of bone through an unhealed ulcer. Before starting BP treatment, a full dental assessment and any invasive dental work (e.g. tooth extraction) is done. If further invasive dental work is needed whilst on BP then doses are stopped for 2-3 months prior and withheld until complete oral healing has occurred. Good oral hygiene is essential and the best way to avoid problems.

What other measures help bone health?

- All people are encouraged to exercise to help with general well-being, manage weight and help prevent health issues associated with a sedentary lifestyle.
- Staying active within your limitations. Regular exercise helps strengthen muscles and bones, reducing the risk of bone thinning (osteoporosis) that can worsen the effects of myeloma bone disease. Please refer to the Myeloma Australia information sheet on exercise.
- Looking after oral hygiene
- Staying hydrated
- Getting planned blood tests
- Working with the haematologist and dentist

In conclusion:

- MBD is likely to occur in almost all people with myeloma.
- When untreated it can result in bone damage, compound renal problems, increased pain, and negatively impact quality of life.
- Carefully monitored bisphosphonate treatment alongside myeloma treatment, is a safe way of preventing and treating myeloma bone damage.

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

**For further information please contact one of our Myeloma Support Nurses on our Support Line:
1800 MYELOMA (1800 693 566)
or visit our website: www.myeloma.org.au**