What is ONJ?

ONJ is a rare condition in which one or more parts of the jawbone become exposed to the inside of the mouth.

The word ‘osteonecrosis’ derives from ‘osteo’, which means bone and ‘necrosis’, which means cell death. Exposed bone has no blood supply and can therefore die (become necrotic). In the jaw the bone is only covered by a thin layer of tissue, so it can quite easily become exposed. This means the bones of the jaw are particularly prone to osteonecrosis, particularly at the site of invasive dental procedures.

Exposed, necrotic bone that does not heal within eight weeks after identification by a dentist or doctor is known as ONJ.
ONJ has occurred in myeloma, breast cancer and prostate cancer patients.

What is the link between ONJ and myeloma?

The causes of ONJ are not entirely clear. Long-term treatment with drugs known as bisphosphonates appears to cause increased risk of ONJ, particularly the intravenous (into the vein) type. Bisphosphonate drugs are recommended for all patients with active myeloma.

The incidence of ONJ in myeloma patients on intravenous (IV) bisphosphonates is still to be accurately determined, but research has suggested that between 3 and 4 out of every 100 myeloma patients (3 to 4%) having the bisphosphonate zoledronic acid (often known as Zometa®) will develop ONJ.

Risk factors for ONJ

The risk of ONJ occurring in myeloma seems to be closely associated with:

- **Type of bisphosphonate** – ONJ is more likely to occur with the use of IV bisphosphonates. Zoledronic acid appears to carry the highest risk

- **Duration of treatment** – ONJ appears to be much more likely to occur in patients who have been on bisphosphonate treatment for 3 to 4 years than in patients who have had treatment for less than a year

- **Dental treatment** – most ONJ cases arise after invasive dental treatments or oral surgery. This includes treatments such as dental extractions, implant placement and periodontal surgery, but not routine dental work such as fillings

ONJ is also more common in older people, those with a history of gum disease, mouth infections and in those who wear dentures. Other factors that may contribute to the risk of ONJ include a history of smoking and poor oral hygiene.

There is also evidence of possible genetic risk factors but further research is needed before a link can be definitively established.

About bisphosphonates

Bisphosphonates are drugs used in myeloma to strengthen and protect patients’ bones.

Studies have shown that regular treatment with bisphosphonates can help to reduce fractures, relieve pain and improve quality of life.
Bisphosphonates currently prescribed in the UK for myeloma are:

<table>
<thead>
<tr>
<th>Type</th>
<th>Examples</th>
<th>Method of administration</th>
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<tbody>
<tr>
<td>Sodium clodronate</td>
<td>Bonefos® and Loron®</td>
<td>Oral tablets, taken once or twice per day</td>
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<tr>
<td>Disodium pamidronate</td>
<td>Aredia®</td>
<td>Intravenous infusion over 90 - 120 minutes, once a month</td>
</tr>
<tr>
<td>Zoledronic acid</td>
<td>Zometa®</td>
<td>Intravenous infusion over 15 - 30 minutes, once a month</td>
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</table>

Current national guidelines on the diagnosis, treatment and management of myeloma recommend the use of bisphosphonates in all patients with active myeloma, whether or not they have evidence of myeloma bone disease.

In a large clinical study, zoledronic acid was shown to have certain benefits over Bonefos in newly diagnosed patients. This included data suggesting zoledronic acid may have an anti-myeloma effect in addition to preventing myeloma bone disease.

Based on these results, national guidelines now recommend all newly diagnosed patients be given zoledronic acid. However, when discussing the different bisphosphonate options, you and your doctor may consider that an alternative one is more appropriate depending on your situation and preferences.

For more information see the Myeloma Bone Disease and Bisphosphonates Infoguide from Myeloma UK.

**Why are bisphosphonates linked to ONJ?**

The exact reasons why ONJ is linked to long-term use of some bisphosphonates are not fully understood. It has been suggested that ONJ occurs because bisphosphonate drugs disrupt normal bone remodelling, and affect the healing process after any trauma.

Bisphosphonates may also increase the risk of ONJ by reducing the blood supply to the bone.
What are the signs and symptoms of ONJ?

Signs and symptoms of ONJ include:

- Non-healing of a tooth socket after extraction
- An area of exposed bone in the mouth
- Swelling of gums
- A heavy or numb feeling in the jaw
- Pain
- Loosening of teeth
- Discharge of pus

It is important to note that having these signs and symptoms does not necessarily mean you have ONJ - they can be also due to other, more common conditions. However, you should contact your doctor or dentist for advice if you experience any of the signs and symptoms above, particularly if you are currently on bisphosphonate treatment.

Management of ONJ

The Medicines and Healthcare products Regulatory Agency (MHRA) recommend prevention as the best approach to the management of this complication. The following points are important in preventing or reducing the risk of ONJ occurring:

- Your doctor should tell you about ONJ and its signs and symptoms before starting you on regular bisphosphonate treatment
- You should have a routine dental examination, X-ray and any necessary invasive dental work carried out before starting on treatment with bisphosphonates
- If you wear dentures, you should make sure these fit properly before starting treatment with bisphosphonates
- You should be informed about how you, as a patient, can help to reduce the risk of ONJ occurring
- Once on bisphosphonates, you should maintain good mouth hygiene and have regular dental check-ups
Invasive dental procedures should be avoided if possible when on bisphosphonates. If invasive treatment is absolutely necessary, this should be done in collaboration with an experienced oral and maxillofacial surgeon. Some doctors may recommend you stop bisphosphonate treatment before dental treatment and re-start once healing is complete.

Treatment of ONJ
If you do develop ONJ, your doctor will prescribe treatment to help relieve symptoms, such as antibiotics, antiseptic mouth wash and pain-killers. As well as relieving symptoms such as infection and pain, these treatments may prevent further bone from becoming exposed, therefore slowing or stopping the progression of ONJ.

Aggressive surgery is usually avoided, as this has not been reliably shown to help and may result in further exposure of bone. An oral surgeon may, however, need to remove some of the dead tissue or bone from the area with a small operation (debridement). A less invasive form of surgery using low-level lasers to remove necrotic cells has proven popular in recent years. However, more research into low-level laser therapy is needed before this treatment becomes more widely available.

Putting ONJ into perspective

It is essential to remember how important bisphosphonates are in the management of myeloma bone disease, and to bear in mind that ONJ is a rare complication. As always, if you have any concerns about your treatment or any side-effects, you should discuss them with your doctor or nurse. You should never stop any of your treatments without first seeking their advice.

The complication of ONJ has increased the debate among myeloma doctors about how long patients should stay on bisphosphonate treatment. There is currently no firm consensus but some guidelines recommend that doctors consider stopping bisphosphonates after two years. This will depend on a number of factors, for example if you are in remission and have no active bone disease. In patients who do stop bisphosphonate treatment after two years, doctors may advise re-starting at the time of relapse.
Self-care tips

Below are some things you can do to help reduce the risk of ONJ occurring:

- Maintain good mouth care - brush your teeth regularly and use any mouthwashes prescribed
- Make sure dentures fit properly and don’t rub
- Visit your dentist regularly for check-ups
- Make sure your dentist knows you are on a bisphosphonate treatment
- Tell your doctor or nurse about any dental work you may need
- Look out for any symptoms in your mouth such as pain, numbness or sore areas
- If you are on a bisphosphonate you should report any such symptoms to your doctor or nurse

Future directions

ONJ is a potentially unpleasant but rare complication linked to bisphosphonate treatment in myeloma.

Current guidelines on the diagnosis and management of myeloma patients issued by the National Institute for Health and Care Excellence (NICE) have highlighted that the optimal frequency and duration of bisphosphonate treatment is an area of medicine requiring further research. The more doctors understand about the links between bisphosphonate use and ONJ, the better able they will be to minimise the risk of ONJ, or prevent it altogether.
About this Infosheet
The information in this Infosheet is not meant to replace the advice of your medical team. They are the people to ask if you have questions about your individual situation. All Myeloma UK publications are extensively reviewed by patients and healthcare professionals prior to publication.

Other information available from Myeloma UK
Myeloma UK has a range of Essential Guides, Infoguides and Infosheets available covering many areas of myeloma, its treatment and management.

To order your free copies or to talk to one of our Myeloma Information Specialists about any aspect of myeloma, call the Myeloma Infoline: 0800 980 3332 or 1800 937 773 from Ireland

The Myeloma Infoline is open from Monday to Friday, 9am to 5pm and is free to phone from anywhere in the UK and Ireland.

Information and support about myeloma is also available around the clock at www.myeloma.org.uk

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