Osteonecrosis of the jaw (ONJ)

Symptoms and complications Infosheet

This Infosheet explains what osteonecrosis of the jaw (ONJ) is, its link to long-term treatment with drugs known as bisphosphonates, and the symptoms and managements of ONJ.

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’ comes 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, especially at the site of invasive dental procedures (such as having teeth removed).

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 patients and in patients with breast cancer and prostate cancer.
What is the link between ONJ and myeloma?
ONJ can occur as an infrequent side effect of a group of drugs called bisphosphonates, particularly ones given intravenously (into the vein) and given for prolonged periods. Bisphosphonates are given to myeloma patients to treat myeloma bone disease.

What is the risk that myeloma patients will develop ONJ?
The incidence of ONJ in myeloma patients on intravenous (IV) bisphosphonates has not been accurately determined. Research has suggested that between three and 11 of every 100 patients (3 to 11%) receiving the bisphosphonate zoledronic acid (Zometa®) might develop ONJ. However, more recently, myeloma patients have been advised to take precautions, such as avoiding invasive dentistry (e.g. tooth extractions) during treatment, and this is likely to greatly reduce the incidence of 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 more likely to occur in patients who have been on bisphosphonate treatment for prolonged periods

- **Dental treatment** – many ONJ cases arise after invasive dental treatments or oral surgery. This includes treatments such as tooth removal, insertion of tooth implants and periodontal surgery, but not routine dental work such as fillings

ONJ is also more common in people with a history of gum disease or 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>
</tr>
<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>
</tr>
</tbody>
</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.

A large clinical trial (Myeloma IX) provided evidence of a significant anti-myeloma effect of zoledronic acid, in comparison with the oral bisphosphonate sodium clodronate. National guidelines now recommend that myeloma patients are given zoledronic acid unless it is unsuitable for them. Your doctor will discuss the best option for you.

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. They should give you advice about what you can do to reduce the risks
- 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
- 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 and control infections as needed, such as antiseptic mouth wash, painkillers and antibiotics.

In more serious cases of ONJ, an oral surgeon may remove some of the dead tissue or bone from the area with a small operation called debridement. More major surgery of the jaw is usually avoided as this has not been reliably shown to help. A less invasive form of surgery using low-level lasers to remove necrotic cells has also been used, but more research 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 an uncommon 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.

There is currently no firm consensus on how long bisphosphonate treatment should be continued. 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 loosening of your teeth

If you are on a bisphosphonate you should report any such symptoms to your doctor or nurse

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.

For a list of references used to develop our resources, visit myeloma.org.uk/references

To give feedback about this publication, email myelomauk@myeloma.org.uk or fill in a short survey at myeloma.org.uk/pifeedback

Other information available from Myeloma UK

Myeloma UK has a range of publications available covering all areas of myeloma, its treatment and management. Download or order them from myeloma.org.uk/publications

To talk to one of our Myeloma Information Specialists about any aspect of myeloma, call our Myeloma Infoline on 0800 980 3332 or 1800 937 773 from Ireland.

The 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 myeloma.org.uk
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