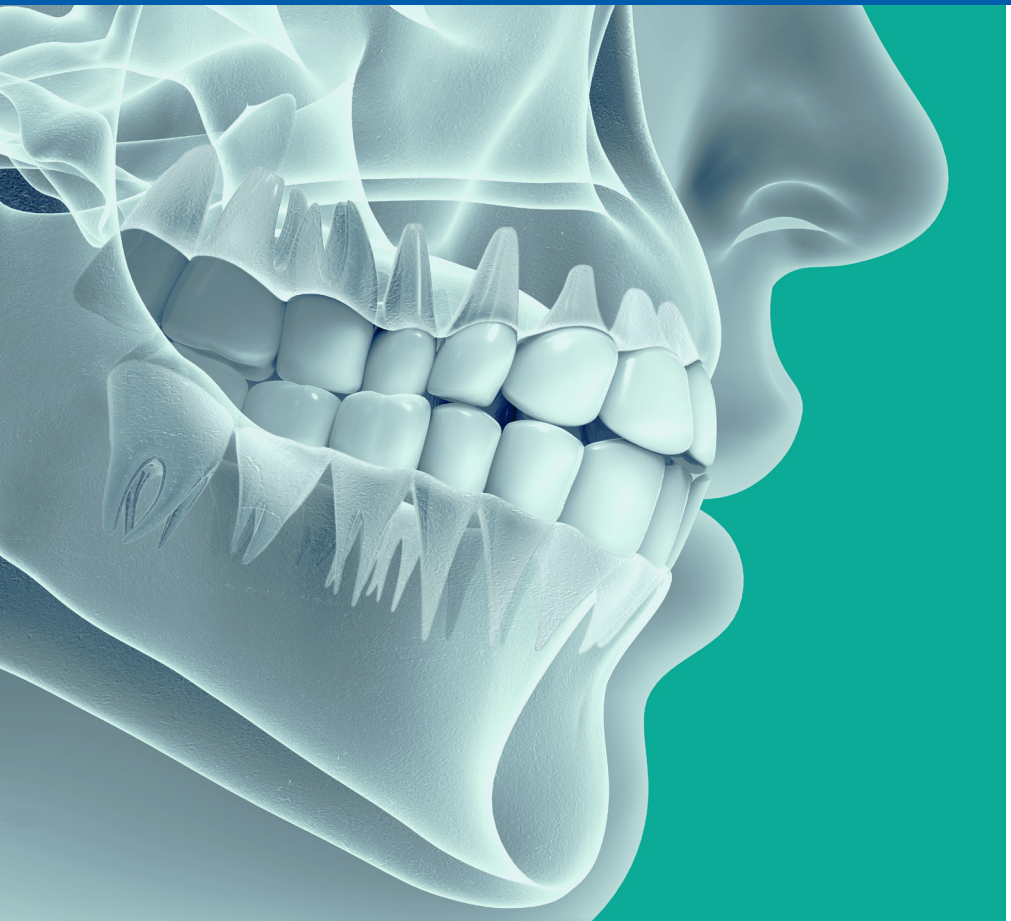

Osteonecrosis of the jaw

A guide for healthcare professionals and patients

Purpose of the guidance

- Bone-protective therapy (bisphosphonates or denosumab) is important for maintaining bone health in:[1,2]
  - patients with bone metastases (cancer that has spread to the bone)
  - patients with bone lesions as a result of multiple myeloma.
- Bone-protective therapy can also be used to:[3,4]
  - treat osteoporosis in men and postmenopausal women who have an increased risk of fracture
  - treat or prevent bone loss associated with adjuvant cancer treatment or long-term systemic glucocorticoid therapy.
- However, in a minority of patients, bone-protective treatment can be associated with a complication known as osteonecrosis of the jaw (ONJ).[1–6]
- Prevention and management of ONJ should be coordinated by a multidisciplinary healthcare team that includes an oral healthcare team.[7,8]
- This guide provides an introduction to ONJ, including information on signs and symptoms, prevention and management. It should be a helpful aid when discussing ONJ with your patients.
- **To help your patients keep their oral healthcare team informed about the risk of ONJ, it is recommended that they be given an alert card to show at every dental visit.**

What is ONJ?

- ONJ is a condition that occurs when the jawbone is damaged (usually following an infection or dental procedure), causing delayed healing and leading to the jawbone being exposed for longer than would normally be expected.[9]
- Some types of treatment can lead to an increased risk of ONJ, these include:[1–5,10,11]
  - high-dose bone protective therapy, used to prevent bone complications in patients with bone metastases or bone lesions
  - low-dose bone protective therapy, used to treat osteoporosis in men and postmenopausal women who have an increased risk of fracture, and to treat or prevent bone loss associated with adjuvant cancer treatment or long-term systemic glucocorticoid therapy
  - some cancer therapies that work by blocking blood vessel growth.
- The risk of developing ONJ is different with high or low doses of bone-protective therapy.
- It is not fully understood what exactly triggers the development of ONJ, but there is ongoing scientific research to understand this better.
- **ONJ needs to be managed by a specialist experienced in managing ONJ.**

It is important to discuss with patients whether they may be at an increased risk of ONJ

Who is at risk of ONJ?

The main risk factor for developing ONJ is using bone-protective therapy. The risk of ONJ increases with more frequent and higher dosing, and longer treatment duration; therefore, patients receiving high-dose bone-protective therapy have an increased risk of ONJ compared with those receiving low-dose therapy.[7] Some other cancer therapies that work by blocking blood vessel growth are also associated with ONJ.[11]

Various other factors are associated with an increased risk of ONJ in patients receiving bone-protective therapy.[1–4,6,7,10,12–16]

Patients who are at a higher risk of ONJ include:

those with dental disease or poor dental hygiene (e.g. people who are unable to perform oral care or those with ill-fitting dentures)

those undergoing invasive dental treatments (e.g. tooth extraction [mainly due to pre-existing gum disease], insertion of dental implants or surgery in the region of the mouth)

Who is at risk of ONJ? (continued)

those receiving or who have received certain cancer therapies (e.g. radiotherapy in the region of the head and neck, chemotherapy, corticosteroid therapy, or previous treatment with bisphosphonates or inhibitors of blood vessel growth)

patients with other diseases or disorders (e.g. cancer, anaemia, infections, diabetes mellitus, immunosuppression or renal failure)

smokers

elderly patients (over 60 years old).

How can patients reduce their risk of ONJ?

- ✓ Patients should have a dental appointment for a full dental assessment and to ensure good positioning of any false teeth.
- ✓ Any required dental surgery, tooth extractions or treatment of pressure points from false teeth should have been completed before bone-protective treatment is started.
- ✓ It is recommended that patients maintain good oral hygiene. Patients should:[7,8,15–17]
  - brush their teeth and tongue using a soft bristle toothbrush and a fluoride toothpaste two to four times a day
  - rinse their mouth and gargle with a saline or saltwater solution at least four times a day
  - clean between their teeth every day (e.g. with interdental brushes).

All patients should have a dental assessment and complete any necessary invasive dental procedures, with full healing of extraction site wounds, before starting bone-protective therapy[1–4,11,17]

How can patients reduce their risk of ONJ? (continued)

To reduce the risk of ONJ further during treatment with bone-protective therapy, patients need to:[1–4,6–9,15–17]

- ✓ have routine dental check-ups at least every 6 months and dental treatments as needed (prophylactic dental cleaning, tooth fillings, non-traumatic treatments or prosthetic insertions without bone anchoring may be performed)
- ✓ seek smoking cessation advice
- ✓ tell their healthcare team, including their oral healthcare provider, about any problems with their mouth or teeth (e.g. loose teeth, pain, swelling, non-healing sores, discharge or pus) or any planned dental treatments as soon as possible
- ✓ tell their oral healthcare provider if they are having any problems with the fit of dentures, if worn.

Patients receiving high-dose bone-protective therapy should be referred to a specialist experienced in managing ONJ if they require invasive dental treatment or develop tooth or gum disease that doesn't respond to treatment within a few weeks.

During treatment, patients should be encouraged to maintain good oral hygiene and have regular dental check-ups[1–4,7,15]

Identifying ONJ

- At each consultation, the signs and symptoms of ONJ should be considered, and the importance of patients maintaining their oral health should be discussed.
- Patients should inform their healthcare team if they are experiencing any problems with their oral health at each consultation, and should be encouraged to have regular check-ups (at least every 6 months) with their oral healthcare provider.[9]
- The signs and symptoms are also associated with many other common clinical conditions, which need to be ruled out before ONJ can be diagnosed.[11]

Oral signs and symptoms to be aware of include:[6,13,15,16,18]

- an area of exposed bone in the mouth
- pain, numbness or tingling in the region of the jaw
- loosening of teeth
- holes in the tissue of the mouth
- swelling of the jaws or gums
- discharge or pus in the mouth
- soft tissue infection
- bad breath.

If a patient presents with any concerning symptoms, it is important to seek specialist advice immediately.

Identification

Identifying ONJ (continued)

- ONJ is characterised by three main features:[7,11]

an area of exposed jawbone or necrotic bone that can be probed through a small opening in the gums

8

no healing of the affected area for more than 8 weeks

no previous radiation to the jaw.

Before treatment: exposed necrotic bone within the gum

After treatment

ONJ is treatable

Image used with permission, courtesy of Tim Van den Wyngaert

Managing ONJ

If ONJ is suspected, patients should be referred to a specialist experienced in managing ONJ.

Identification of ONJ by an oral healthcare professional at an early stage means that the majority of patients can experience improvements in symptoms and be managed using the following measures:[6,7,10,11,15]

- ✓ maintenance of optimal oral hygiene
- ✓ treatment of active dental and gum disease
- ✓ use of antibacterial mouth rinses
- ✓ treatment with antibiotics.

This approach will resolve the majority of early-stage cases or provide long-term symptomatic relief.[10,19,20] For non-responsive ONJ lesions, consultation by an oral health specialist is required in order to assess if surgery (debridement and/or resection) may be effective.[10,21,22]

Bone-protective therapy in patients with ONJ

- If ONJ develops, bone-protective therapy may be stopped until the jaw has healed; however, the advantages of stopping treatment should be balanced against the risk of bone problems if therapy is discontinued.[11,23] This decision will be made by the treating doctor in agreement with the dental specialist team.[1–4,7]

The majority of cases of ONJ can be managed to improve symptoms and to encourage healing. Patients and their healthcare providers may decide to stop bone-protective therapy temporarily until the jawbone has healed.[11]

Management

References

1. European Medicines Agency. Zometa® (zoledronic acid) summary of product characteristics. 2020. Available from: www.ema.europa.eu/documents/product-information/zometa-epar-product-information_en.pdf (Accessed 28 September 2020).
2. European Medicines Agency. XGEVA® (denosumab) summary of product characteristics. 2020. Available from: https://www.ema.europa.eu/documents/product-information/xgeva-epar-product-information_en.pdf (Accessed 28 September 2020).
3. European Medicines Agency. Prolia® (denosumab) summary of product characteristics. 2020. Available from: https://www.ema.europa.eu/en/documents/product-information/prolia-epar-product-information_en.pdf (Accessed 28 September 2020).
4. European Medicines Agency. Aclasta® (zoledronic acid) summary of product characteristics. 2020. Available from: https://www.ema.europa.eu/en/ documents/product-information/aclasta-epar-product-information_en.pdf (Accessed 28 September 2020).
5. European Medicines Agency. Further measures to minimize risk of osteonecrosis of the jaw with bisphosphonate medicine. 2015. Available from: https://www.ema.europa.eu/en/news/further-measures-minimise-risk-osteonecrosis-jaw-bisphosphonate-medicine (Accessed 28 September 2020).
6. Myeloma UK. Osteonecrosis of the jaw (ONJ). Available from: https://www.myeloma.org.uk/documents/osteonecrosis-of-the-jaw-infosheet/ (Accessed 28 September 2020).
7. Yarom N *et al.* Medication-Related Osteonecrosis of the Jaw: MASCC/ISOO/ASCO Clinical Practice Guideline. *J Clin Oncol* 2019;37:2270–90.
8. European Oral Care in Cancer Group. Oral Care Guidance and Support. 2017. Available from: http://www.eocc.co.uk/wp-content/uploads/2018/01/EOCC-Guidance-English.pdf (Accessed 28 September 2020).
9. Royal Osteoporosis Society. Osteonecrosis of the jaw (ONJ) and drug treatments for osteoporosis. Available from: https://theros.org.uk/information-and-support/osteoporosis/treatment/health-risks/osteonecrosis-of-the-jaw/ (Accessed 28 September 2020).
10. Khan AA *et al.* Diagnosis and management of osteonecrosis of the jaw: a systematic review and international consensus. *J Bone Miner Res* 2015;30:3–23.
11. American Association of Oral and Maxillofacial Surgeons. Medication-related osteonecrosis of the jaw – 2014 update. 2014. Available from: http://www.aaoms.org/docs/govt_affairs/advocacy_white_papers/mronj_position_paper.pdf (Accessed 28 September 2020).
12. Saad F *et al.* Incidence, risk factors, and outcomes of osteonecrosis of the jaw: integrated analysis from three blinded active-controlled phase III trials in cancer patients with bone metastases. *Ann Oncol* 2012;23:1341–7.
13. Yamashita J, McCauley LK. Antiresorptives and osteonecrosis of the jaw. *J Evid Based Dent Pract* 2012;12:233–47.
14. Barasch A *et al.* Risk factors for osteonecrosis of the jaws: a case-control study from the CONDOR dental PBRN. *J Dent Res* 2011;90:439–44.
15. Nicolatou-Galitis O *et al.* Medication-related osteonecrosis of the jaw: definition and best practice for prevention, diagnosis, and treatment. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2019;127:117–35.
16. Nicolatou-Galitis O *et al.* Alveolar bone histological necrosis observed prior to extractions in patients, who received bone-targeting agents. *Oral Dis* 2020;26:955–66.
17. Otto S *et al.* Medication-related osteonecrosis of the jaw: prevention, diagnosis and management in patients with cancer and bone metastases. *Cancer Treat Rev* 2018;69:177–87.
18. Ficarra G, Beninati F. Bisphosphonate – related osteonecrosis of the jaws: the point of view of the oral pathologist. *Clin Cases Miner Bone Metab* 2007;4:53–7.

References

References (continued)

19. Bodem JP *et al.* Value of nonsurgical therapeutic management of stage I bisphosphonate-related osteonecrosis of the jaw. *J Craniomaxillofac Surg* 2015;43:1139–43.
20. Moretti F *et al.* A prospective clinical trial for assessing the efficacy of a minimally invasive protocol in patients with bisphosphonate-associated osteonecrosis of the jaws. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2011;112:777–82.
21. Lopes RN *et al.* Surgical therapy for bisphosphonate-related osteonecrosis of the jaw: six-year experience of a single institution. *J Oral Maxillofac Surg* 2015;73:1288–95.
22. Ristow O *et al.* Treatment perspectives for medication-related osteonecrosis of the jaw (MRONJ). *J Craniomaxillofac Surg* 2015;43:290–3.
23. Gallego L, Junquera L. Consequence of therapy discontinuation in bisphosphonate-associated osteonecrosis of the jaws. *Br J Oral Maxillofac Surg* 2009;47:67–8.

ADEE
ADVANCING EDUCATION AND ORAL HEALTH

This document was reviewed by an ADEE panel in September 2020.

For further information, please visit https://adee.org/partners/adeeamgen-onj

Amgen (Europe) GmbH
6343 Risch-Rotkreuz
Switzerland

www.amgen.com

Job code: SC-EU-AMG162-00625
Date of preparation: October 2020

References