

Bone-protective therapy and osteonecrosis of the jaw

What is osteonecrosis of the jaw (ONJ)?

- ONJ^a 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
- Prevention and management of ONJ should be coordinated by a multidisciplinary healthcare team that includes an oral healthcare team
- ONJ needs to be managed by a specialist experienced in managing ONJ

Bone-protective therapy^b (bisphosphonates^c or denosumab) is one type of medication that can lead to the development of ONJ in a minority of patients

- Bone-protective therapy is mainly used to:^d

- 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

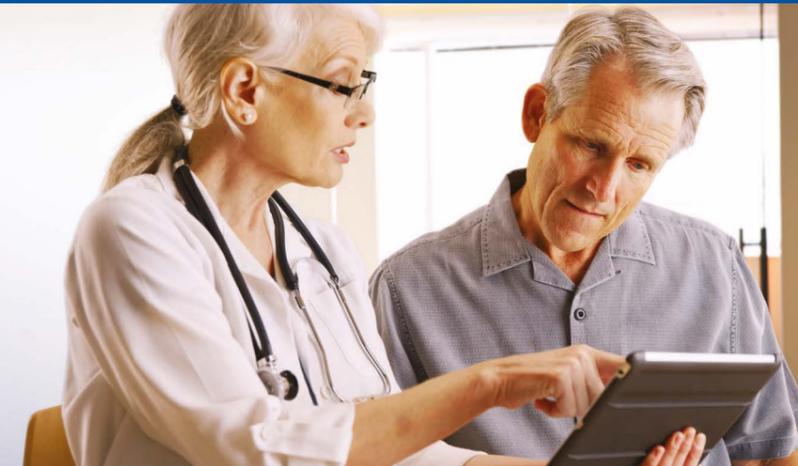


Low dose

- maintain bone health in patients with **bone metastases** or bone lesions as a result of **multiple myeloma**

High dose

- The risk of ONJ is greater in patients receiving high-dose bone-protective therapy than in those receiving low-dose therapy



Identifying ONJ

- ONJ is characterised by:



current or previous treatment with bone-protective therapies or cancer therapies that block blood vessel growth (angiogenic inhibitors)



no healing of the affected area for more than 8 weeks

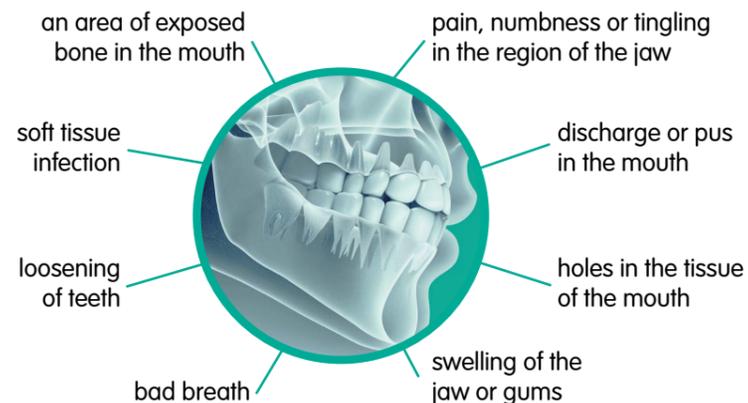


an area of exposed jawbone or necrotic bone that can be probed through a small opening (fistula) in the gums^e



no previous radiation to the jaw

- Oral signs and symptoms include:



Identifying those at risk of ONJ

- The main risk factor is the use of **high-dose bone-protective therapy**

- The risk of ONJ with **low-dose bone-protective therapy** is only slightly greater than the risk for the general population
- Some other cancer therapies that block blood vessel growth (angiogenic inhibitors) are also associated with ONJ

- Other factors that may increase the risk of ONJ include:



invasive dental treatments



cancer therapy



dental disease or poor dental hygiene



smoking



concomitant diseases (e.g. anaemia, infections, diabetes mellitus, immunosuppression or renal failure)



older age (over 60 years old)

ONJ is treatable

Help to detect ONJ earlier by considering these key questions at every routine dental visit

- Has your patient had any recent changes in medication?
- Is your patient currently undergoing treatment for cancer, osteoporosis or bone loss?
- Does your patient have any additional risk factors for ONJ?

Managing ONJ

- When identified early, ONJ can usually be managed by:
 - 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
- 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
- There is a lack of data supporting discontinuation of bone-protective therapy (a 'drug holiday'). If ONJ develops, the patient's oncologist may consider temporarily discontinuing the therapy until soft tissue closure is achieved
- A multidisciplinary management plan should be set up in close collaboration with the patient's clinician

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

Preventing ONJ

- 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
- Patients should be advised to maintain good oral hygiene
- Patients receiving high-dose bone-protective therapy should be referred to a specialist if they require invasive dental treatment or develop tooth or gum disease that does not respond to treatment within a few weeks

Oral healthcare providers should ask their patients to:



report any problems with their mouth or teeth as soon as possible (see the list of oral signs and symptoms for details)



notify them about any planned dental treatments as soon as possible



report any problems with the fit of dentures, if worn



seek smoking cessation advice



have 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)

References

Barasch A *et al*. *J Dent Res* 2011;90:439-44 | Drudge-Coates L *et al*. *Support Care Cancer* 2020;28:4019-29 | European Medicines Agency. Bisphosphonates. Available from: <https://www.ema.europa.eu/en/medicines/human/referrals/bisphosphonates> (Accessed 28 September 2020) | European Medicines Agency. Adclasta[®] (zoledronic acid) summary of product characteristics. Available from: https://www.ema.europa.eu/en/documents/product-information/adclasta-epar-product-information_en.pdf (Accessed 28 September 2020) | European Medicines Agency. Prolia[®] (denosumab) summary of product characteristics. Available from: https://www.ema.europa.eu/en/documents/product-information/prolia-epar-product-information_en.pdf (Accessed 28 September 2020) | European Medicines Agency. XGEVA[®] (denosumab) summary of product characteristics. Available from: https://www.ema.europa.eu/en/documents/product-information/xgeva-epar-product-information_en.pdf (Accessed 28 September 2020) | European Medicines Agency. Zometa[®] (zoledronic acid) summary of product characteristics. Available from: https://www.ema.europa.eu/en/documents/product-information/zometa-epar-product-information_en.pdf (Accessed 28 September 2020) | European Oral Care in Cancer Group. Oral Care Guidance and Support. Available from: <http://www.eocc.co.uk/wp-content/uploads/2018/01/EOCC-Guidance-English.pdf> (Accessed 28 September 2020) | Khan AA *et al*. *J Bone Miner Res* 2015;30:3-23 | Myeloma UK. Osteonecrosis of the jaw (ONJ). Available from: <https://www.myeloma.org.uk/wp-content/uploads/2018/03/Myeloma-UK-Osteonecrosis-of-the-jaw-Infoshheet.pdf> (Accessed 28 September 2020) | Nicolatou-Galitis O *et al*. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2019;127:117-35 | Nicolatou-Galitis O *et al*. *Oral Dis* 2020;26:955-66 | Royal Osteoporosis Society. Osteonecrosis of the jaw (ONJ). Available from: <https://theros.org.uk/information-and-support/medication-and-treatment/health-risks/osteonecrosis-of-the-jaw> (Accessed 28 September 2020) | Yarom N *et al*. *J Clin Oncol* 2019;37:2270-90.



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^aONJ related to bone-protective therapy is sometimes referred to as 'medication-related ONJ' or 'MRONJ'; ^bAlso known as 'bone-modifying agents', 'bone-targeted agents' or 'anti-resorptive agents'; ^cBisphosphonates include zoledronic acid, risedronate, alendronate, ibandronate, pamidronate disodium, clodronate, tiludronate and etidronate; ^dOther indications include giant cell tumour of the bone and Paget's disease of bone. For full details, please refer to the summary of product characteristics for each therapy on the European Medicines Agency website; ^eMay not always be clinically visible.