

Medication-related osteonecrosis of the jaw: introducing the MRONJ prevention algorithm

What is MRONJ and what causes it?

Medication-related osteonecrosis of the jaw (MRONJ) is an infrequent complication of treatment with bisphosphonates or denosumab,¹ which are used to treat many bone-related conditions, including: osteoporosis in postmenopausal women and men at increased risk of fractures; bone loss associated with adjuvant therapy for cancer; bone loss associated with long-term systemic glucocorticoid therapy; and unresectable giant cell tumour of bone in adults and skeletally mature adolescents.²⁻⁵ These agents are also used to prevent painful skeletal-related events in adults with advanced malignancies involving bone.^{2,4}

The implementation of a prevention strategy has been shown to significantly reduce the risk of developing MRONJ.^{6,7} To be effective, MRONJ prevention strategies need to be tailored to individual patients.⁸⁻¹¹ Prevention and management of MRONJ should be coordinated by a multidisciplinary healthcare team that includes an oral healthcare team.^{9,11}

The algorithm overleaf will assist the practitioner in selecting the appropriate intervention, taking into account the phase of treatment, the dosing regimen and the length of time during which the patient has been treated.

What is the incidence of MRONJ?

Bisphosphonates or denosumab may be administered at low or high doses depending on the condition being treated; **the risk of MRONJ is associated with the dose and duration of treatment.**¹² In patients receiving high-dose denosumab for metastatic bone disease, the reported incidence of confirmed MRONJ adjusted for years of patient follow-up was 1.1% in year 1 of treatment, 3.7% in year 2 and 4.6% per year, every year thereafter.¹³ The risk of MRONJ in patients

receiving low-dose denosumab for osteoporosis appears to be very low: 0.04% at 3 years, 0.06% at 5 years and 0.44% at 10 years.³

How can MRONJ be prevented?

As a first step, it is important to determine whether a patient is about to receive or is currently receiving low-dose or high-dose therapy. For low-dose treatment, no further action is required if no risk factors for MRONJ are present and the patient has complied with the preventive dental check-ups applicable to the general population.⁸ Patients prescribed high-dose treatment should always receive a screening dental assessment before starting therapy.^{8,9}

Once treatment with a bisphosphonate or denosumab has started, no special precautions are required for patients receiving a low-dose regimen for no more than 3 years.¹² In patients receiving high-dose treatment or prolonged (> 3 years) low-dose therapy, expert advice is required before performing any invasive dental procedures (e.g. dental extractions) to determine whether alternative treatments that do not involve trauma to the underlying bone should be considered.¹⁴

Early diagnosis of MRONJ is associated with improved outcomes; therefore, all patients with suspected MRONJ should be immediately referred to an oral and maxillofacial surgeon or a dentist experienced in managing MRONJ and given an oral antiseptic rinse (e.g. chlorhexidine). Patients with signs of infection should also receive antibiotics.¹⁵ These measures may help to bridge the time until the patient can be assessed by a specialist experienced in managing MRONJ.¹⁶ If emergency invasive dental procedures are required, the prophylactic use of antibiotics is recommended for patients receiving high-dose therapy.¹⁷

References

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CANDIDATE FOR BISPHOSPHONATE OR DENOSUMAB THERAPY

Low-dose therapy (= Low risk)

- For example, patients with osteoporosis
- Commonly used schedules include:
 - denosumab 60 mg every 6 months SC
 - zoledronic acid 5 mg once a year IV
 - oral bisphosphonates weekly or monthly

High-dose therapy (= Increased risk)

- For example, patients with bone metastases
- Commonly used schedules include:
 - denosumab 120 mg every 4 weeks SC
 - zoledronic acid 4 mg every 3–4 weeks IV
 - zoledronic acid 4 mg every 3–6 months IV⁹
 - oral bisphosphonates daily

PREVENTION – BEFORE START OF THERAPY

Risk factors present?

- Prior use of bisphosphonates or denosumab
- Use of corticosteroids, chemotherapy or anti-angiogenics
- Radiotherapy in the head and neck region
- Poor dental hygiene, periodontitis or ill-fitting dentures
- Smoking
- Other conditions: cancer, haematological disease, immunological disorders, diabetes, anaemia

Yes

Screening dental visit required

- Detect and treat pockets of occult infection
- Extract teeth with poor prognosis
- Check dentures
- Encourage smoking cessation
- Educate patient to recognise signs and symptoms of MRONJ
- Educate patients to maintain good oral hygiene

No

Screening dental visit not required

- Recommendations for preventive dental check-ups for the general population apply
- In case of non-compliance, a dental check-up should be advised

PREVENTION – DURING THERAPY

Maintain optimal dental status by providing:

- prophylactic dental cleaning
- dental fillings, non-traumatic treatments or prosthetics without bone anchoring
- patient education on maintaining good oral hygiene

Therapy \geq 3 years?

No = Low risk

No special precautions apply

- Very low MRONJ risk
- All dental procedures may be performed as indicated
- Regular preventive dental check-ups should be performed in line with recommendations for the general population

Yes =
Increased
risk

Invasive dental procedures require expert advice

- Including dental extractions, periodontal surgery, root planing and implants

Low threshold to refer patients to OMFS or dentist experienced in managing MRONJ

- In case of unexplained symptoms (e.g. dental pain, swelling, purulent discharge)

Prophylactic antibiotics in case of unavoidable or emergency procedures

IF MRONJ IS SUSPECTED?

Refer to OMFS

- Provide an oral antiseptic rinse (e.g. chlorhexidine 0.12% three times daily) and an empirical broad-spectrum antibiotic treatment (e.g. amoxicillin/clavulanic acid 500/125 mg three times daily), if there are signs of infection¹⁸