Medication-related osteonecrosis of the jaws (MRONJ) review: what Irish dentists need to know, from international guidelines to current controversies

Introduction: Medication-related osteonecrosis of the jaws (MRONJ) is a potentially severe adverse drug reaction, resulting in progressive bone destruction of the jaws. MRONJ is associated with two classes of therapeutic drugs: antiresorptive and anti-angiogenic agents. There are several hypotheses that attempt to explain the aetiology of the process and its unique localisation to the jaws. Dental screening and appropriate treatment are fundamental to reduce the risk of osteonecrosis before patients begin taking these medications. The treatment of MRONJ often presents great difficulty and an optimal therapy strategy is yet to be established. For this reason, prevention occupies a pivotal role in the management of these patients.

Objective: To review the scientific literature that supports measures used primarily in the prevention of MRONJ in both nationally and internationally published guidelines.

Methodology: A bibliographic search using the PubMed/MEDLINE database was performed by the authors, with no time limitation and restricting the search to the English language. The authors selected key papers and engaged in collaborative data extraction and synthesis of the selected reference material. Practice guideline documents were assessed using the Appraisal of Guidelines for Research & Evaluation (AGREE II) Instrument.

Conclusion: Knowledge of the risk factors and aetiology of MRONJ is rapidly expanding, and guidelines for prevention and treatment of this condition are developing as more publications are released. On the basis of the findings of this literature review, the authors highlight important practice points in a concise instruction list, reflective of current high-quality clinical practice guidelines.

Key words: Medication-related osteonecrosis of the jaws (MRONJ); osteochemonecrosis; anti-resorptive osteonecrosis of the jaws (ARONJ); bisphosphonate-related osteonecrosis of the jaws (BRONJ); bisphosphonate-related osteonecrosis (BRON); bisphosphonate osteonecrosis (BON); bisphosphonate-associated osteonecrosis of the jaw (BAONJ); dental interventions; tooth extraction.


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Medication-related osteonecrosis of the jaws (MRONJ) represents an adverse drug reaction, consisting of progressive bone destruction in the mandible or maxilla (Figure 1). A patient may be considered to have developed MRONJ if there is exposed bone or bone that can be probed through an intra-oral or extra-oral fistula(e) in the maxillofacial region, which has persisted for a period of more than eight weeks after prior therapy with bisphosphonates (BPs) or other drugs that affect bone metabolism. There must be no history of radiation therapy or obvious metastatic disease to the jaws. Despite the above definition being the most current and widely accepted, caution must be taken when coming to a final diagnosis. Fedele et al. described 28.9% of a 332-patient group having clinical manifestations of ONJ without frank bone exposure or radiological change, thereby being called Stage 0 MRONJ.1 Progression of the condition can lead to tooth loss and necrosis of entire sections of the jawbone, including pathological fracture of the mandible.5

As MRONJ is an evolving clinical condition, with knowledge regarding pathophysiology and management constantly expanding, the implications of these medications in the dental clinical setting are still being determined. A recent audit in this area highlighted a need to re-evaluate nationally published guidance in relation to the prevention of MRONJ.5

The primary aim of this paper is to review the scientific literature that supports measures proposed in international guidelines on the prevention of MRONJ. The predominant focus of this review will be in the area of prevention and of management of those patients at risk of MRONJ. No discussion would be complete, however, without touching upon treatment strategies as the prevention and management of MRONJ reflect a continuum. A secondary aim is to assess the quality of clinical practice guidelines and provide a clear set of instructions to Irish dentists that is reflective of current international practice.

Aetiology and pathophysiology

Antiresorptive therapy is a collective term for a group of drugs that are potent inhibitors of osteoclast function and osteoclast-mediated bone resorption.6-10 Osteonecrosis of the jaw (ONJ) may be caused by three pharmacological agents: antiresorptive agents, including BPs; receptor activator of nuclear factor kappa-B ligand (RANK-L) inhibitors; and, anti-angiogenic agents.11-13

Although Marx first recognised and reported cases of ONJ 15 years ago, the pathophysiology of this disease process has yet to be fully elucidated.17 There is ongoing debate in the literature attempting to explain its unique localisation to the jaws (Table 1).

Since the introduction of BPs, the archetypal drug of this category, antiresorptive agents have been effectively utilised to reduce skeletal related events and improve the overall quality of life for patients with osteoporosis, Paget's disease, osteogenesis imperfecta, and fibrous dysplasia.9,6 These drugs are also used to reduce the symptoms and complications of metastatic bone diseases (particularly those associated with multiple myeloma, and breast and prostate cancer).14,15

The RANK-L inhibitor denosumab is a newer antiresorptive medication that inhibits osteoclast function, decreases bone resorption, and increases bone density.16-19 It is used in patients affected by osteoporosis or metastatic bone diseases.18,20,21 Denosumab is not incorporated into the skeleton and thus exhibits a much shorter half-life than BPs, which have a half-life in the order of five to 15 years.22-24 The effects of denosumab on bone turnover diminish within nine months of treatment completion.22

Anti-angiogenic medications hinder the development of new blood vessels, blocking the angiogenesis-signalling cascade.25 They are used in cancer treatment to restrict tumour vascularity. The vascular endothelial growth factor (VEGF) inhibitors bevacizumab and aflibercept and the receptor tyrosine kinase (RTK) inhibitor sunitinib have been associated with MRONJ.26-30

At present, it is estimated that osteoporosis affects 300,000 Irish people, with an increase expected in the future due to a rise in our ageing population.31 Knowledge within the dental profession of these agents and their effects is therefore paramount to ensure that care is provided to this subset of patients without delay, to the highest standard, and in an appropriate setting.32

Incidence

The literature shows wide variation in the reported incidence and prevalence of MRONJ due to the rare nature of the condition. In oncology patients treated with intravenous antiresorptive agents, MRONJ risk varies from 0-27%.33-44 The estimates towards the higher end of this range are derived from studies with small sample sizes, which have a tendency to overestimate the risk of low-frequency events.45 In studies that include larger sample sizes (over 500 patients), the risk approximates 1%.44 This contrasts greatly with the extremely low (0-0.1%) incidence of MRONJ when therapy is administered orally for the management of osteoporosis and other bony diseases.46-51
Table 2: Potential risk factors for the development of MRONJ.

1. **Systemic risk factors**
   - Advanced age
   - Longer duration of treatment
   - Concomitant therapy with corticosteroids
   - Compromised immune status or immunodeficiency

2. **Local risk factors**
   - Dento-alveolar surgery
   - Intra-oral trauma (e.g., ill-fitting dentures)
   - Poor oral hygiene
   - Oral infection

3. **Medication-related risk factors**
   - Concomitant therapy with corticosteroids
   - Increased potency
   - Greater frequency of administration
   - Increased cumulative dose

**Risk factors**

Among publications, potential risk factors for the development of MRONJ are classified as local (i.e., oral disease, invasive dental procedures) and systemic. Current literature suggests that the most significant risk factor for MRONJ development is the underlying medical condition for which the patient is being treated, with patients receiving therapy for a malignancy at greater risk than those being treated for osteoporosis. Risk stratification is a cornerstone of management in recently published international guidelines. Some international guidelines advocate that those at high risk of developing MRONJ should be referred to an oral and maxillofacial surgeon for invasive dental procedures, including dental extractions. In early publications, emphasis was placed on the route of administration and the potency of BPs when deciding upon a patient’s risk of developing MRONJ. It has now become apparent that the underlying condition for which the patient is being treated with either antiresorptive or anti-angiogenic agents is paramount among risk factors. Those suffering from underlying malignant disease appear to be most at risk. Increased duration of malignant disease and increased duration of bony metastases, as well as the specific type of cancer, may be associated with increased risk of MRONJ development. MRONJ predominantly occurs in patients being treated for breast cancer, multiple myeloma and prostate cancer.

**Methodology**

A bibliographic search using the PubMed/MEDLINE database was performed by the authors, with no time limitation and restricting the search to the English language. The authors selected key papers and engaged in collaborative data extraction and synthesis of the selected reference material. Clinical practice guideline documents pertaining to the dental management of patients at risk of MRONJ were assessed using the Appraisal of Guidelines for Research & Evaluation (AGREE II) instrument. The AGREE II tool consists of a 23-item checklist categorised into six domains (scope and purpose, stakeholder involvement, rigour of development, clarity of presentation, applicability, and, editorial independence). Each domain aims to measure a different aspect of guideline development quality and identify potential biases. Each of the AGREE II checklist items are rated on a seven-point Likert scale ranging from ‘strongly disagree’ to ‘strongly agree’. A quality score is then calculated for each of the six AGREE II domains. Domain scores are calculated by summing up all the scores of the individual items in a domain and by scaling the total as a percentage of the maximum possible score for that domain. The six domain scores are independent and are not aggregated into a single quality score. Finally, the overall quality of each guideline is rated on a seven-point Likert scale ranging from ‘lowest possible quality’ to ‘highest possible quality’.

**Results and discussion**

**Preventive strategies**

Appropriate dental care and preventive measures are crucial for all patients receiving a course of therapy that places them at risk of MRONJ, irrespective of the type of drug prescribed or the route of administration. Optimising the dental health of those at risk of MRONJ development should be the focus of preventive therapy because the majority of patients who develop MRONJ experience this complication following simple dento-alveolar surgery. Similar to head and neck cancer patients who are about to receive radiation therapy to the mouth and jaw, these patients should receive a comprehensive dental evaluation.

Several studies have reported a reduction in the incidence of MRONJ in high-risk patients who have undergone dental assessment, oral hygiene instruction, and appropriate dental treatment prior to commencing antiresorptive therapy. If possible, antiresorptive/anti-angiogenic therapy should be delayed until dental health is optimised or all unsalvageable teeth are extracted.

For patients who have already commenced intravenous BP treatment, every effort should be made to avoid dento-alveolar surgery and maintain heightened vigilance with regard to dental health. Avoidance of more invasive procedures should always be advocated in the first instance for the treatment of dental/endodontic pathology, such as: orthograde endodontic therapy; and, coronectomy/coronal amputation and endodontic treatment of retained roots. Forced eruption with the aid of elastic orthodontic ligatures has also been proposed as an alternative to extraction for this patient cohort. However, in light of the fact that this process can take up to six weeks to complete exfoliation, and because patients will most often present in an acute setting, the clinical efficacy of this treatment must be questioned.

MRONJ is often considered quite debilitating and can be notoriously difficult to treat, especially in severe cases. Therefore, the pinnacle of management rests on prevention. MRONJ is most commonly associated with procedures that stimulate the alveolar bone turnover, namely routine and surgical dental extractions, as well as dento-alveolar procedures such as enucleation, apicectomy and periodontal flap surgery. A prospective study by Bramati et al. examined the effectiveness of preventive dental measures on the occurrence of MRONJ. Some 212 patients who were scheduled to receive intravenous zoledronic acid for the treatment of metastatic cancer with bony involvement were recruited. Prior to commencing BP therapy the patients underwent clinical oral examination, professional oral hygiene therapy and surgical treatment of any active oral pathology, eliminating all potential sources of infection. The patients were followed up for 60 months and an incidence rate of 0% MRONJ was reported. The authors...
Table 3: Preventive measures.

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<tr>
<th>Pre-operative</th>
<th>Intra-operative</th>
<th>Postoperative</th>
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<tbody>
<tr>
<td>Drug holiday 85</td>
<td>Prior rinsing with chlorhexidine digluconate 86</td>
<td>Soft diet/cold semi-liquid diet 86</td>
</tr>
<tr>
<td>C-telopeptide test 87,88</td>
<td>Use of local anaesthetic without vasoconstrictor 88</td>
<td>Postoperative antibiotics 89-91</td>
</tr>
<tr>
<td>Oral hygiene instruction and chlorhexidine digluconate rinsing 80</td>
<td>Atraumatic surgical technique and the use of ultrasonic surgical equipment 83</td>
<td>Rinsing postoperatively with chlorhexidine digluconate/hydrogen peroxide for one week 86</td>
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<tr>
<td>Tooth debridement and polishing 74</td>
<td>Osteoplasty of the alveolar ridge to avoid sharp surfaces that might delay postoperative healing 89,91</td>
<td>Vacuum-formed splint 86</td>
</tr>
<tr>
<td>Antibiotic prophylaxis 99-101</td>
<td>Extraction sockets packed with scaffold-like autologous platelet concentrates and sealed with autologous fibrin 52</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Primary wound closure 92,93,94</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Low-level laser therapy 85,95</td>
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</table>

Preventive strategies recommended in the scientific literature can be divided into pre-operative, intra-operative and postoperative measures (Table 3). These measures related specifically to patients undergoing dental extraction/dento-alveolar surgical procedures in the pre-, intra-, and postoperative period.

Various novel treatment protocols have been proposed for patients at risk of MRONJ undergoing surgical procedures. The use of low-level laser therapy and autologous platelet concentrates and fibrin has been purported to aid in wound healing postoperatively.92,96-98 There is a growing body of evidence to support low-level laser therapy, more recently called photobiomodulation, having an important role in the management of radiation and/or chemotherapy-related mucositis in cancer patients.99-105 Accordingly, it has also been utilised in the prevention and treatment of MRONJ by harnessing the anti-inflammatory properties of the lasers to aid and encourage mucosal repair. There is little data to support this claim, however, with only two uncontrolled case series examining the use of low-level laser therapy in preventing MRONJ.95,96

Recently, platelet-rich plasma (PRP), platelet-rich growth factors (PRGF), and platelet-rich fibrin (PRF) have been reported to be effective in the acceleration of tissue healing and bone regeneration following oral surgery procedures.106,107 The underlying concept is based on the collection of highly concentrated platelets whose granules are rich in substances fundamental for the promotion of the healing process. A systematic review carried out on the use of autologous platelet concentrates after tooth extraction in patients at risk of MRONJ found that of the 697 extractions performed, only 0.99% of cases developed osteonecrosis, suggesting that platelet concentrations stimulate tissue healing and/or regeneration.98 These findings were based on the results of three controlled trials in the use of platelet concentrates in the prevention of MRONJ post dental extraction.97,98

Current guidelines

Clinical practice guidelines are systematically developed statements that assist practitioners in healthcare decision-making processes. These guidelines must aim to be methodologically sound to provide recommendations with the least bias possible. The AGREE II instrument was developed to assess the methodological rigour of developed guidelines by focusing on the transparency of their development.77

The search strategy employed in this review yielded 12 clinical practice guidelines related to the management of dental patients at risk of MRONJ. The development methodology of the retrieved guidelines was assessed using the AGREE II instrument in six different domains and each guideline was assigned an overall quality score (Table 4). The majority of these guidelines were found to be of suboptimal quality in relation to the AGREE II instrument.

International guidance

While a number of international professional associations have established expert panels to review the evidence and construct guidelines, much of the available published material represents the views of single groups, and is based only on their individual experience.108,109

The latest revisions to international guidance are from the National Health Service (UK) in January 2015, the American Association of Oral and Maxillofacial Surgery in October 2014, and the Scottish Dental Clinical Effectiveness Programme (SDCEP) in March 2017.2,67,68 Some of the more comprehensive guidance documents recently published make reference to high-quality evidence in certain aspects of management, but continued research in these specific areas is indicated in order to draw any meaningful conclusions on management strategies.2,68

Current Irish practice

Current Irish practice is determined by a combination of guidance published in...
There has been no evidence published to support the assertion that this circulating Irish literature and information used by national health organisations. Another source of guidance nationally, although lacking the same clarity, is what undergraduate dental students are currently taught in our national dental hospitals. The publication ‘Guidelines for treating patients taking bisphosphonates prior to dental extractions’ in the Journal of the Irish Dental Association (2010) is the most current Irish guidance, upon which other national guidance documents have been based.66

Current controversies
There are areas of controversy among recommendations from all eligible publications, which warrant further discussion.

C-telopeptide test
The role of testing the serum bone turnover marker C-telopeptide (CTX) level as an indicator of risk for MRONJ in this patient population remains controversial. Some publications recommend serum CTX levels before invasive dental procedures to predict an individual’s risk of developing MRONJ, with dental treatment modifications based on those results.87,88 However, other publications, including the latest American Dental Association (ADA) guidelines, have indicated that serum CTX levels display neither reliability nor accuracy in predicting the risk for MRONJ and do not recommend routine testing.1,2,6,117-119

Drug holidays
The concept of a drug holiday in individuals receiving BP therapy who require tooth extractions has been a subject of ongoing controversy, with little data to support current recommendations. There is currently no strong evidence to show that interrupting BP therapy alters the risk of MRONJ development in patients following tooth extraction due to the lengthy half-life of the drugs.6,61 Until more conclusive evidence in the form of clinical trials becomes available, reference to the benefit of a drug holiday should be removed from guidelines to prevent confusion among practitioners.
In contrast, although not strictly a drug holiday, it has been proposed that any non-urgent dento-alveolar surgery in patients taking denosumab for the treatment of osteoporosis is delayed until a month prior to the patient’s next scheduled drug administration.7 Resumption of denosumab treatment following invasive dental treatment should be delayed until the socket has healed.2,68 This requires close communication with the prescribing physician.

Prophylactic antibiotic therapy
There are conflicting and varying recommendations regarding prophylactic antibiotic therapy before and after dental treatment for prevention of MRONJ.89,90,120 Australian, German and Spanish guidelines recommend the use of antibiotic prophylaxis, whereas more recent ADA and SDCEP guidelines state that there is no evidence to support the use of antibiotics and/or antiseptic rinses. This literature review found only observational studies, most of which were underpowered and lacking a control group, reporting a benefit in the use of antibiotics.96-98 Generally, antibiotic regimes were included as part of a combination of preventive measures, making it difficult to interpret the individual role of these measures in reducing the risk of MRONJ. The role, if any, of oral commensal bacteria in the development of MRONJ remains ambiguous and the value of antibiotics is thus unclear.121-123 Due to the increasing incidence of bacterial resistance and adverse effects associated with antibiotic use, there must be clear evidence that their use confers a benefit to the patient.

Further investigation of current controversies
Continued research is required to order to fully elucidate the underlying pathophysiology of MRONJ at both cellular and molecular levels. The value of proposed preventive measures needs to be established, such as dental screening prior to commencing treatment, antibiotic therapy, drug holidays and CTX testing. Future research into the mechanisms underlying MRONJ would strategically enhance development of evidence-based clinical practice guidelines.
There are proposals to avoid the use of vasoconstrictors in local anaesthetics.68 There has been no evidence published to support the assertion that this

<table>
<thead>
<tr>
<th>Expert panel representation</th>
<th>Year of publication</th>
<th>Scope and purpose</th>
<th>Stakeholder involvement</th>
<th>Rigour of development</th>
<th>Clarity of presentation</th>
<th>Applicability</th>
<th>Editorial independence</th>
<th>Overall guideline assessment</th>
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</thead>
<tbody>
<tr>
<td>Scottish Dental Clinical Effectiveness Programme</td>
<td>2017</td>
<td>95%</td>
<td>86%</td>
<td>88%</td>
<td>91%</td>
<td>79%</td>
<td>86%</td>
<td>6/7</td>
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<tr>
<td>American Society for Bone and Mineral Research</td>
<td>2015</td>
<td>100%</td>
<td>48%</td>
<td>32%</td>
<td>57%</td>
<td>14%</td>
<td>93%</td>
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<tr>
<td>American Academy of Oral and Maxillofacial Surgeons</td>
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<td>57%</td>
<td>33%</td>
<td>23%</td>
<td>24%</td>
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<td>American Academy of Oral Medicine</td>
<td>2005</td>
<td>90%</td>
<td>30%</td>
<td>25%</td>
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<tr>
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<td>20%</td>
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<tr>
<td>American Association of Endodontists</td>
<td>2012</td>
<td>67%</td>
<td>19%</td>
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<tr>
<td>American Dental Association</td>
<td>2011</td>
<td>91%</td>
<td>57%</td>
<td>41%</td>
<td>67%</td>
<td>18%</td>
<td>14%</td>
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<tr>
<td>Allied Task Force Committee of Japanese Society for Bone and Mineral Research</td>
<td>2010</td>
<td>65%</td>
<td>33%</td>
<td>23%</td>
<td>40%</td>
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<tr>
<td>French Expert Panel</td>
<td>2009</td>
<td>82%</td>
<td>19%</td>
<td>23%</td>
<td>40%</td>
<td>14%</td>
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<tr>
<td>German Society of Senology</td>
<td>2009</td>
<td>55%</td>
<td>35%</td>
<td>14%</td>
<td>35%</td>
<td>18%</td>
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<tr>
<td>Spanish Expert Panel</td>
<td>2007</td>
<td>70%</td>
<td>14%</td>
<td>18%</td>
<td>30%</td>
<td>14%</td>
<td>40%</td>
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<tr>
<td>Australian Dental Association</td>
<td>2006</td>
<td>70%</td>
<td>14%</td>
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measure decreases MRONJ risk. Notwithstanding the lack of such evidence, this has been advocated in international publications as a simple, prudent measure to aid maintenance of vascularity.134-136 Questions also remain about the relationship between the risk of developing MRONJ and the extent of invasiveness in dental procedures.

Conclusion
Currently, there is a lack of evidence to support guidelines given the rare occurrence of this condition and inherent difficulties in carrying out high-quality research on this patient cohort. The authors propose a clear instruction list to Irish dentists to more closely align practice to internationally agreed standards when treating patients at risk of MRONJ (Appendix 1). The authors acknowledge that there is very little evidence to support the efficacy of some measures proposed here. However, given their relatively conservative nature, these measures have been advocated based on good surgical principles and practice. In the current climate of uncertainty, and with a lack of robust evidence, individual judgment brought to each clinical situation by the patient’s general/specialist dental practitioner is an important consideration.

References


Appendix 1

Instruction list for dental patients at risk of medication-related osteonecrosis of the jaws.

The following instruction list has been formulated as an aid to clinicians in general and hospital-based practice when managing patients at risk of medication-related osteonecrosis of the jaws (MRONJ). The clinical guidance is based upon best practice international guidelines from the National Health Service (United Kingdom), the American Association of Oral and Maxillofacial Surgery, and the Scottish Dental Clinical Effectiveness Programme (SDCEP).

1. Risk assessment

Carry out a comprehensive medical history for all patients at risk of MRONJ. This would include precise records regarding the nature of antiresorptive and anti-angiogenic therapeutic regimes:

- underlying medical condition;
- drug type, formulation, dosage, route of administration and frequency, and;
- date of commencing (and ceasing, if relevant) treatment.

Assign patients to low- or high-risk categories according to the criteria proposed by the SDCEP’s ‘Management of Patients at Risk of Medication-related Osteonecrosis of the Jaw – Dental Clinical Guidance’ (Table 1).

<table>
<thead>
<tr>
<th>Table 1: Risk stratification for patients at risk of medication-related osteonecrosis of the jaws (MRONJ).</th>
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<tr>
<td><strong>High risk</strong></td>
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<tr>
<td>Patients being treated for osteoporosis or other non-malignant diseases of bone (Paget’s disease of bone, osteogenesis imperfecta, etc.) with oral bisphosphonates, or quarterly or yearly infusions of intravenous bisphosphonates, for &gt;5 years</td>
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<tr>
<td>Concurrent use of systemic corticosteroids or other immunosuppressants</td>
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<tr>
<td>Patients being treated with antiresorptive or anti-angiogenic drugs (or both) as part of the management of cancer</td>
</tr>
<tr>
<td>Patients with a previous diagnosis of MRONJ</td>
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</tbody>
</table>
2. Initial dental management of patients prior to commencing antiresorptive/anti-angiogenic therapy

Aim to optimise the oral health of the patient, rendering them as dentally fit as possible.

- Establish optimal preventive regimes:
  - smoking cessation;
  - report any symptoms such as exposed bone, loose teeth, non-healing cores or lesions, pus or discharge, tingling, numbness or altered sensation, pain or swelling as soon as possible;
  - optimal oral hygiene instruction – use of fluoride toothpaste and mouth rinse;
  - caries risk assessment and tailored caries management plan;
  - reduction of sugar intake and frequency;
  - prescription of high fluoride toothpaste in patients with increased caries risk; and,
  - six-monthly dental examinations (patients at higher risk of MRONJ may benefit from shorter recall intervals, e.g., three monthly, especially if other oral health risk factors are present).

- Treat any source of active caries, or periodontal or peri-apical infection, appropriately.
- Extraction of teeth with poor prognosis.
- Adjustment or replacement of ill-fitting dentures.

3. Dental treatment of patients undergoing antiresorptive or anti-angiogenic treatment

Low-risk patients

- Perform simple extractions and other dento-alveolar procedures in primary care:
  - advise the patient that there is a very small risk of MRONJ occurring to ensure valid consent;
  - consider the use of pre- and postoperative chlorhexidine rinsing;
  - consider the use of plain local anaesthetic without vasoconstrictor;
  - atraumatic surgery must be performed to reduce crushing of bone and further delay in healing;
  - sutures may be placed to approximate wound edges, but not tightly as this may cause ischaemia; and,
  - a soft diet postoperatively.

- Do not prescribe antibiotic prophylaxis specifically to reduce the risk of MRONJ.

- Review the patient appropriately to ensure mucosal healing. If the socket has not healed after eight weeks, or you suspect MRONJ, refer to an oral/oral and maxillofacial surgeon for assessment and management.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Pre-operative dose</th>
<th>Postoperative dose</th>
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<tbody>
<tr>
<td>Amoxicillin</td>
<td>3g stat</td>
<td>500mg three times daily for seven days</td>
</tr>
<tr>
<td>Clindamycin (if allergic to amoxicillin)</td>
<td>600mg stat</td>
<td>150-300mg four times daily for seven days</td>
</tr>
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</table>

As described in the SDCEP’s ‘Management of Patients at Risk of Medication-related Osteonecrosis of the Jaw – Dental Clinical Guidance’, there is no benefit in referring the patient to a specialist or to secondary care based solely on their exposure to antiresorptive or anti-angiogenic drugs. Patients will feel more comfortable in the familiar surroundings of the general dental practitioner’s surgery. For medically complex patients, or those requiring specialist procedures, and about whom you would normally seek advice, consider consulting/referral to an oral/oral and maxillofacial surgeon for clinical assessment and treatment planning.