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HEALTHY BONES AUSTRALIA | Protect Build Support

Healthy Bones Australia Consensus Statement: **Medication-related Osteonecrosis of the Jaw (MRONJ) and Osteoporosis**

Interdisciplinary working party on MRONJ, Healthy Bones Australia

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Target audience and the need for national guidance on MRONJ

The purpose of this consensus statement is to provide succinct guidance to healthcare professionals, including dental care providers on:

- Medication-related osteonecrosis of the jaw (MRONJ) and osteoporosis therapies
- Risk stratification and incidence of MRONJ
- Prevention and management strategies

This statement has been written by a committee of Australian Endocrinologists, Dentists, Oral Medicine Specialists, and Oral Maxillofacial Surgeons and has been endorsed by the following groups: Healthy Bones Australia (HBA), Australian Dental Association (ADA), Australia and New Zealand Bone and Mineral Society (ANZBMS), Endocrine Society of Australia (ESA), Australian Rheumatology Association (ARA).

ANZBMS | ADA AUSTRALIAN DENTAL ASSOCIATION | esa endocrine society of australia | Australian Rheumatology Association

Practice tips have been summarised in table below.

For a more comprehensive summary, including detailed references, we refer readers to recent national and international guidelines

- American Association of Oral and Maxillofacial Surgeon's Position Paper 2022
- Royal Australian College of General Practitioners/Healthy Bones Australia Osteoporosis Management Guidelines 2024

Practice tips for counselling patients on MRONJ and risk precautions

- MRONJ is a known but uncommon complication of bone-modifying osteoporosis therapies (i.e. bisphosphonates, denosumab)
- When a patient on osteoporosis therapy requires a dental procedure, risk stratification, patient counselling and providing properly informed consent to the patient are essential:
  - We advise a 3-step risk stratification process to determine whether a patient is at high, intermediate or low risk of MRONJ.
  - This is based on a determination of both patient and procedure-related risk factors. See Figure for our traffic-light risk matrix.
- Patients at low risk of MRONJ may undergo simple dental procedures safely without the need for specialist care.
- Patients at high risk or with established MRONJ require early referral to specialist care.
- Good oral hygiene and regular dental care reduces the risk of MRONJ.
- Proactive dental treatment planning is recommended prior to initiation of osteoporosis therapies or during early phases of treatment.
- Osteoporosis therapies should not be discontinued without a discussion with the prescribing healthcare provider.
- Sudden discontinuation of denosumab is unsafe. Rebound increase in bone turnover may occur with painful vertebral fractures.[1,2]
- A multidisciplinary team approach is recommended to ensure coordinated, patient-centred care and optimal outcomes.

Risk, perception of risk and clinical conversations on MRONJ

Since the original description of MRONJ and its association with osteoporosis therapies in the early 2000's,[3] this condition has generated widespread concern amongst patients, dentists and doctors prescribing these therapies.

At its worst, MRONJ is a serious condition with significant adverse impacts on a patient's quality of life[4] and may require specialist management and care. Fortunately, MRONJ is uncommon in patients using bone protective therapies at recommended doses for osteoporosis and most patients will not be at high risk of MRONJ. Other potentially modifiable risk factors play a contributory role, including poor oral hygiene, infrequent or irregular dental care, the presence of active dental infections and poorly controlled diabetes mellitus.

Osteoporosis therapies, including bisphosphonates (BP's) and denosumab, reduce the risk of fracture by up to 70% and have been associated with increased survival in older individuals.[5,6] Despite this, the uptake of osteoporosis therapies is suboptimal, with inappropriately low treatment rates for primary and secondary fracture prevention in Australia.[7] The fear of MRONJ and misperception of risks of osteoporosis therapies, as perpetuated by lay media and online sources, may be a significant factor contributing to reluctance in initiating or continuing treatment.[8]

To address this, an individualised approach to risk stratification in patients with osteoporosis needing invasive, oral surgical treatment is essential. Greater collaboration between dental health care providers and doctors on the issue of MRONJ will provide greater reassurance to consumers and allow individualised treatment plans which balance risks and benefits in a safe and consistent manner.[9]

Understanding osteoporosis therapies

Osteoporosis is the most common disease of ageing, impacting 10% of people over 50 years and 30% over 80 years.[7] One in 5 men and one in 3 women in Australia will experience an osteoporotic fracture in their lifetime. Fractures cause >52,000 admissions to Australian hospitals every year at a substantial cost to patients, their communities and the economy.

Osteoporosis therapies increase bone density and reduce risk of fracture by up to 70%.[6] Osteoporosis drugs are cost-effective and generally safe. They are broadly divided by their mechanism of action into anti-resorptive therapies that reduce bone turnover (bisphosphonates and denosumab), and osteoanabolic therapies that primarily increase bone mass (teriparatide and romosozumab). Denosumab is the most commonly prescribed treatment for osteoporosis in Australia.

Osteoporosis therapies are recommended in patients with a history of osteoporotic fracture or at high risk of fracture (i.e. FRAX >20% absolute risk of major osteoporotic fracture or > 3% absolute risk of hip fracture over 10 years).[10] In these groups, the benefits of treatment greatly outweigh risks, with significantly greater number of fractures prevented for every uncommon adverse event. See FRAX fracture risk calculator

Patients with cancer may receive higher and more frequent doses of anti-resorptive therapy to directly target skeletal metastases. Typically, denosumab is given at 120 mg monthly in patients with metastatic breast and prostate cancer. This confers a substantially higher risk of MRONJ than in patients receiving osteoporosis doses of 60 mg every 6 months.

For further information on the indication, therapeutic responses and side effect profile of osteoporosis drugs, please refer to the Royal Australian College of General Practitioners/HBA 2024 guidelines. HBA RACGP Osteoporosis Guidelines 2024

Understanding MRONJ

Medication-related osteonecrosis of the jaw (MRONJ) refers to an area of exposed bone, bone that can be readily probed, or bone that is connected by a sinus tract in the jaw persisting for more than 8 weeks in a patient treated with particular drugs, who has not received radiation therapy to the head or face or metastatic disease of the jaw.[11] Drugs consistently associated with MRONJ include anti-resorptive therapies, namely bisphosphonates and/or denosumab, anti-angiogenic therapies used in cancer and tyrosine kinase inhibitors (e.g. bevacizumab, cabozantinib, sunitinib).[12] Glucocorticoids and immunomodulator therapies for patients with inflammatory conditions are additional risk factors.[11]

The staging of MRONJ is determined by the presence of exposed or probe-able bone and infection. In advanced stages, intraoral or extraoral fistulae that communicate with necrotic bone may occur. MRONJ may occur following invasive dental procedures, including extraction or dental implant insertion, and less commonly, in patients with ill-fitting dentures or "spontaneously", that is without known preceding oral surgical procedures or other dental trauma.[12] Late implant failure is a manifestation of peri-implant MRONJ.[13]

The mechanisms leading to necrosis of the mandible and/or maxilla in MRONJ are not fully elucidated, but the following have been proposed:

- Chronic inflammation and bacterial infection in the periapical region (that is the bone within the region of the tooth root apex)
- Impairment in gum and bone healing due to aberrations in vascular supply and ischaemia (compounded by smoking, diabetes, anti-angiogenic therapy)
- Nutritional aspects contributing to poor tissue healing
- Disordered osteoclast activity and reduced local remodelling
- Genetic factors relating to collagen formation, bone turnover and angiogenesis[14, 15]

Risk factors are categorised in patient-related and procedure-related domains (see Figure on page 4). Note that this figure does not specifically relate to patients receiving anti-resorptive therapy for a cancer indication, which poses a very high risk of MRONJ, but is focussed primarily on osteoporosis doses.

Incidence of MRONJ

Although patients commencing anti-resorptive therapies may have one or more risk factors, most will not develop MRONJ. MRONJ remains an uncommon complication of anti-resorptive therapies, although the risk does increase with higher dosage, duration and frequency of administration, and invasive dental procedures. For patients receiving bisphosphonates for osteoporosis, the risk for MRONJ appreciably increases with 4 years of bisphosphonate therapy. For denosumab, the risk for MRONJ also increases with long-term therapy.[16] Be aware that some patients may have started bisphosphonate therapy for their osteoporosis and switch to denosumab or vice versa and so the cumulative time on both therapies needs to be considered.

MRONJ Risk Stratification in Patients with Osteoporosis

Patient Factors

Low Risk

- Anti-resorptive therapy for osteoporosis
- Duration of BP and/or Dmab for <4 years
- No adverse systemic conditions
- No other adverse drugs
- Good baseline dentition

High Risk

- Duration of BP and/or Dmab ≥4 years
- Systemic conditions:
  - Diabetes with poor control
  - Anaemia, poor nutrition
  - Inflammatory rheumatic disorders
  - Smoking
- Adverse Drugs:
  - Anti-angiogenic or tyrosine kinase inhibitor (TKI) for cancer
  - Glucocorticoids
- Active dental infection, poor oral health, periodontal disease, protracted dental infection

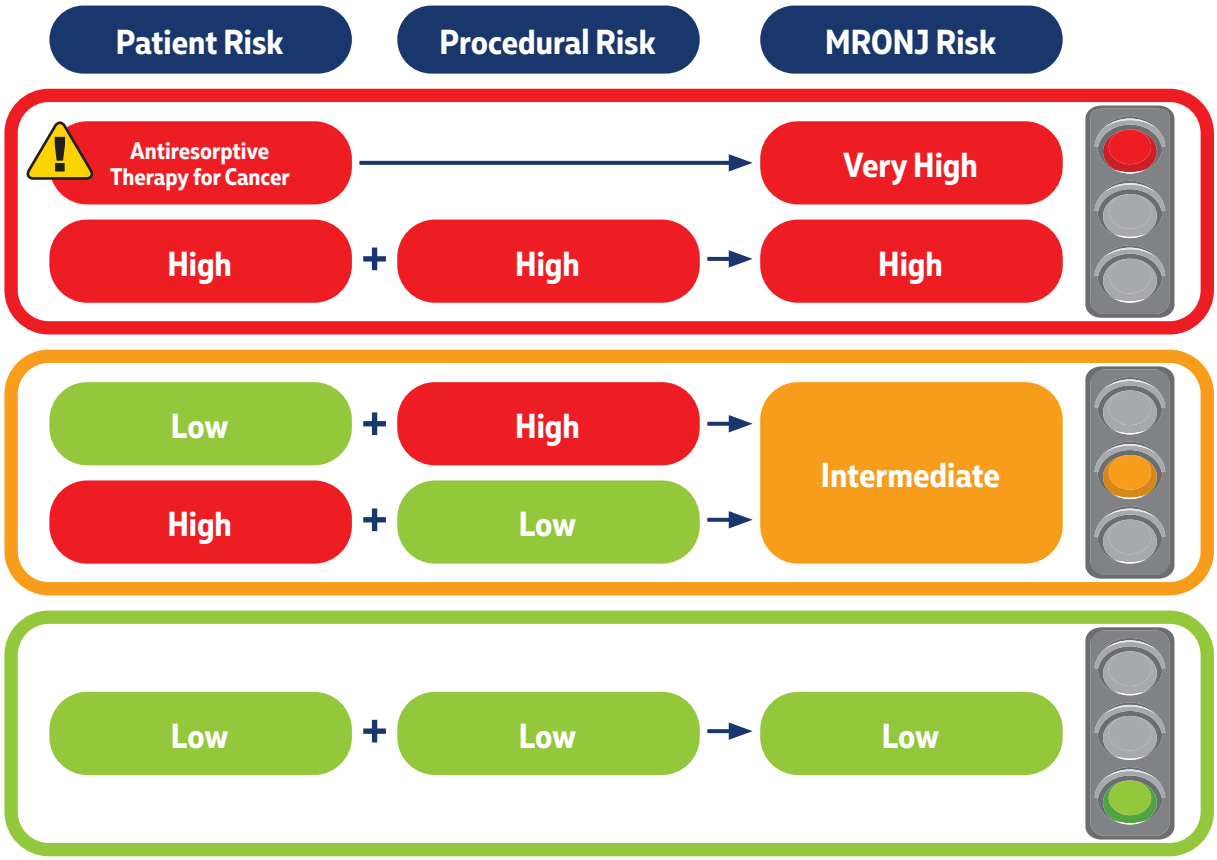
Procedural Factors

Low Risk

- Simple extraction and/or minor, non-invasive procedure
- Uncomplicated implant placement
- Not involving posterior mandible

High Risk

- Extensive surgical site (e.g. ≥3 contiguous teeth)
- Presence of mandibular tori
- Implants or extractions in posterior mandible (molar/premolar)



There are several challenges in accurately calculating the incidence of MRONJ in patients on osteoporosis therapies and these are as follows:

- Clinical trials are not sufficiently powered to detect and report the incidence of MRONJ in treatment versus placebo groups.
- MRONJ diagnosis requires individual dental evaluation and therefore, cases may be difficult to adjudicate in larger real-world cohort studies.
- The attribution of additional risk factors, independent of osteoporosis therapies, is difficult to ascertain in the development of MRONJ.
- MRONJ may occur in patients without exposure to osteoporosis therapies although the incidence is very low.
- Early stages of MRONJ may resolve spontaneously or with supportive care and may be not have been identified as MRONJ.

A wide range of incidence estimates can be found in current literature:

- In patients on bisphosphonates for the treatment of osteoporosis, MRONJ may occur in 0.02-0.04% (up to 4 per 10,000).[17]
- The risk may be higher in denosumab users receiving treatment for osteoporosis at 0.04 to 0.3% (up to 3 per 1000) but this may also relate to bisphosphonate pre-treatment in these groups.[18, 19]
- The risk is significantly higher in patients receiving bisphosphonates or denosumab for cancer versus osteoporosis – a relative 100-fold greater incidence.[11, 12]
- While cases of MRONJ have been reported in patients receiving romosozumab, this may relate to prior or subsequent treatment with anti-resorptive therapy. The incidence of MRONJ in treatment-naïve patients receiving romosozoumab is unknown but likely to be negligeable in the absence of risk factors.

The risk of MRONJ in patients exposed to an invasive dental procedure who receive osteoporosis therapies may range from 1 to 2.5%[16, 20, 21] underscoring the role of invasive procedures as a significant risk factor for this condition. An Australian retrospective study of high-risk patients on osteoporosis therapies reported an MRONJ incidence of 5.5% following dental extractions and the majority of patients were receiving denosumab.[21] However, this is variable with a lack of prospective data to provide guidance.

Precautions to reduce the risk of MRONJ

There is robust evidence in the literature supporting the role of oral hygiene and regular dental review in reducing the risk of MRONJ.[11, 22] Even in patients with high risk of MRONJ (e.g. cancer patients), regular attention to dental hygiene has been associated with a reduction in MRONJ incidence.[23]

General advice on good oral hygiene includes the following:

- Brushing teeth and gums for at least 2 minutes twice daily with fluoridated toothpaste (1000ppm)
- Cleaning in between the teeth once a day with floss or interdental brushes
- Regular professional oral examinations and radiographs, where necessary
- Seeking early management of dental symptoms
- Ensuring dentures fit optimally, as required
- Cessation of smoking and vaping
- Optimal diet and nutrition
- Excellent advice and consumer resources on dental care can be found here teeth.org.au

In patients with osteoporosis, assessment by a dentist, where possible to identify and treat any serious dental disease prior to initiation of anti-resorptive therapy is recommended as per general population guidelines. However, in patients with a fragility fracture, timing is critical with a heightened risk of subsequent fracture in the ensuing months (known as the 'fracture cascade'). Patients at very high, imminent fracture risk warrant urgent osteoporosis therapy.[24] Awaiting review by a dentist should not unduly delay treatment and similarly, use of anti-resorptive drugs should not unduly delay necessary dental interventions. Clinicians are advised to balance the need for a pre-dental assessment with a patient's imminent fracture risk and prior dental history.

In patients receiving osteoporosis therapy who require dental procedures, please see the Figure for traffic-light risk matrix as determined by combination of patient and procedure-related domains. The patient's risk will determine subsequent precautions, as appropriate. See Figure on page 6.

In general, patients should **not** be advised to cease osteoporosis therapy in preparation for an invasive dental procedure as the risk of fragility fracture may be high and treatment interruptions may have adverse consequences on bone health.

There is no evidence that treatment breaks from osteoporosis drugs reduce the risk of MRONJ and international guidelines provide inconsistent advice on this issue.

The following practice points may be helpful:

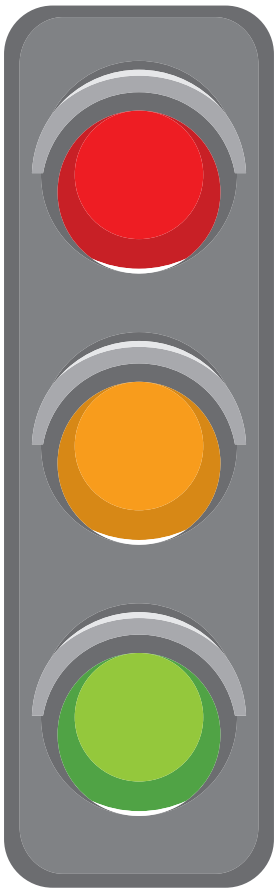
- Stopping bisphosphonates for a short period of time may be safe in patients at low risk of fracture due to the prolonged mechanism of action. There is however little evidence that this would reduce the risk of MRONJ.
- Stopping denosumab or delaying the dose beyond 4 weeks is **not safe** due to the risk of rapid decline in bone density and fractures due to its short mechanism of action.[1, 2]
- Please see a safety update from the Therapeutics Goods Administration on the risks of delaying denosumab.

- In patients on denosumab, guidelines have suggested timing the dental procedure at the 2-4 week point before the next dose of denosumab is due, to allow time for wound healing prior to denosumab administration. Whilst there is no robust evidence to support this emerging practice, the underlying principle is that the next dose of denosumab should not be unduly delayed. Physician discretion and a thorough discussion with the patient on the risks of delaying denosumab are warranted.
- Discussion between dentists and physicians on the patient's condition is essential to plan timing of procedure and osteoporosis treatments in an individualised fashion.
- Measurement of serum C-terminal telopeptide (CTX) in patients requiring invasive dental procedures is not recommended as it has no utility in MRONJ risk assessment.
- Clinicians electing to care for patients at risk of MRONJ should have a sufficient level of surgical skill and experience to undertake extractions and the placement of implants. Referral to specialist services is recommended in complicated cases of implant insertion and/or in high-risk patients.

Early identification of MRONJ and referral to specialist services (oral medicine, oral maxillofacial surgeons and oral surgeons) is essential.

Data regarding non-operative adjunctive therapies remain scarce. Teriparatide, an osteoanabolic agent used for the treatment of osteoporosis, has shown promise as an adjunctive treatment when used for a 2-month period, with faster MRONJ resolution.[25] Whilst its use is off-label for this indication, it may be a useful option for ongoing osteoporosis therapy in patients with active MRONJ lesions.

Finally, MRONJ is an uncommon complication of osteoporosis therapies. This statement provides tips on individual risk stratification based on patient and procedure-related factors and appropriate interventions. Multidisciplinary care and shared decision-making between dental and medical healthcare providers improves patient confidence and leads to safer outcomes.

MRONJ Risk	Management Precautions
	• Refer to Specialist Centre or practitioner with MRONJ expertise • Discussion with osteoporosis specialist regarding ongoing use of antiresorptives and treatment goals
	• Minimise active dental infection • Antibacterial mouthwash ≥ 1 week prior and following extraction • Consider periprocedural antibiotics* • Atraumatic surgical approach • Consider primary closure with tension-free sutures (if appropriate)** • Close wound safely, monitor oral hygiene, frequent follow-up • Consider referral to Specialist Centre or practitioner with MRONJ experience
	• General precautions • Advise low MRONJ risk • Proceed with routine extractions and implants • Consider primary closure (if appropriate)** • Close wound safely, monitor oral hygiene, frequent follow-up

*The benefit of postoperative antibiotic use to prevent MRONJ is unclear. Individual patient risk assessment is warranted.
**Primary closure is not routinely recommended. This is appropriate in select cases.

Traffic-light system of risk stratification for patients on osteoporosis therapies in whom a dental procedure is planned. This risk matrix requires a 3-step process of considering patient factors, procedure factors and then a combined risk assessment with a green/ amber/ red risk profile. This risk matrix gives general guidance to aid clinical discussions around an individual's risk of MRONJ and appropriate precautions. This figure is specifically for patients receiving anti-resorptive therapy for osteoporosis indication. Patients receiving anti-resorptive therapy for cancer indication are generally a very high-risk group for MRONJ, regardless of the risk stratification presented here.

References

[1] Kim KM, Jang SA, Hong NK, Kim CS, Rhee Y, Park SW, et al. Association of Delayed Denosumab Dosing with Increased Risk of Fractures: A Population-Based Retrospective Study. Endocrinol Metab (Seoul). 2024;39(6):946-55.

[2] Kumar S, Wang M, Kim AS, Center JR, McDonald MM, Girgis CM. Denosumab discontinuation in the clinic: implications of rebound bone turnover and emerging strategies to prevent bone loss and fractures. J Bone Miner Res. 2025;40(9):1017-34.

[3] Migliorati CA. Bisphosphanates and oral cavity avascular bone necrosis. J Clin Oncol. 2003;21(22):4253-4.

[4] Murphy J, Mannion CJ. Medication-related osteonecrosis of the jaws and quality of life: review and structured analysis. Br J Oral Maxillofac Surg. 2020;58(6):619-24.

[5] Ayers C, Kansagara D, Lazur B, Fu R, Kwon A, Harrod C. Effectiveness and Safety of Treatments to Prevent Fractures in People With Low Bone Mass or Primary Osteoporosis: A Living Systematic Review and Network Meta-analysis for the American College of Physicians. Ann Intern Med. 2023;176(2):182-95.

[6] Handel MN, Cardoso I, von Bulow C, Rohde JF, Ussing A, Nielsen SM, et al. Fracture risk reduction and safety by osteoporosis treatment compared with placebo or active comparator in postmenopausal women: systematic review, network meta-analysis, and meta-regression analysis of randomised clinical trials. BMJ. 2023;381:e068033.

[7] Bohingamu Mudiyanselage S, Watts J, Gebremariam K, Abimanyi-Ochom J. Osteoporosis and fractures in Australia. A burden of disease analysis, 2023 to 2033. 2024. Available from: https://healthybonesaustralia.org.au/wp-content/uploads/2024/09/bod-2024-digital-isbn-final.pdf

[8] Sambrook PN, Chen JS, Simpson JM, March LM. Impact of adverse news media on prescriptions for osteoporosis: effect on fractures and mortality. Medical Journal of Australia. 2010;193(3):154-6. Ruggiero SL, Dodson TB, Aghaloo T, Carlson ER, Ward BB, Kademani D. American Association of Oral and Maxillofacial Surgeons' Position Paper on Medication-Related Osteonecrosis of the Jaws-2022 Update. J Oral Maxillofac Surg. 2022;80(5):920-43.

[9] Sturrock A, Preshaw PM, Hayes C, Wilkes S. General dental practitioners' perceptions of, and attitudes towards, improving patient safety through a multidisciplinary approach to the prevention of medication-related osteonecrosis of the jaw (MRONJ): a qualitative study in the North East of England. BMJ Open. 2019;9(6):e029951.

[10] Wong P, Chen W, Ewald D, Girgis C, Rawlin M, Tsingos J, et al. 2024 Royal Australian College of General Practitioners and Healthy Bones Australia guideline for osteoporosis management and fracture prevention in postmenopausal women and men over 50 years of age. Med J Aust. 2025;222(9):472-80.

[11] Ruggiero SL, Dodson TB, Aghaloo T, Carlson ER, Ward BB, Kademani D. American Association of Oral and Maxillofacial Surgeons' Position Paper on Medication-Related Osteonecrosis of the Jaws-2022 Update. J Oral Maxillofac Surg. 2022;80(5):920-43.

[12] Anastasilakis AD, Pepe J, Napoli N, Palermo A, Magopoulos C, Khan AA, et al. Osteonecrosis of the Jaw and Antiresorptive Agents in Benign and Malignant Diseases: A Critical Review Organized by the ECTS. J Clin Endocrinol Metab. 2022;107(5):1441-60.

[13] Kim DY, Choi S, Han JJ. Analysis of prosthetic risk factors for peri-implant medication-related osteonecrosis of the jaw: an observational study. Sci Rep. 2025;15(1):16060.

[14] Lee KH, Kim SH, Kim CH, Min BJ, Kim GJ, Lim Y, et al. Identifying genetic variants underlying medication-induced osteonecrosis of the jaw in cancer and osteoporosis: a case control study. J Transl Med. 2019;17(1):381.

[15] Tetradis S, Allen MR, Ruggiero SL. Pathophysiology of Medication-Related Osteonecrosis of the Jaw-A Minireview. JBMR Plus. 2023;7(8):e10785.

[16] Watts NB, Grbic JT, Binkley N, Papapoulos S, Butler PW, Yin X, et al. Invasive Oral Procedures and Events in Postmenopausal Women With Osteoporosis Treated With Denosumab for Up to 10 Years. J Clin Endocrinol Metab. 2019;104(6):2443-52.

[17] Grbic JT, Black DM, Lyles KW, Reid DM, Orwoll E, McClung M, et al. The incidence of osteonecrosis of the jaw in patients receiving 5 milligrams of zoledronic acid: data from the health outcomes and reduced incidence with zoledronic acid once yearly clinical trials program. J Am Dent Assoc. 2010;141(11):1365-70.

[18] Higuchi T, Soga Y, Muro M, Kajizono M, Kitamura Y, Sendo T, et al. Replacing zoledronic acid with denosumab is a risk factor for developing osteonecrosis of the jaw. Oral surgery, oral medicine, oral pathology and oral radiology. 2018;125(6):547-51.

[19] Voss P, Steybe D, Poxleitner P, Schmelzeisen R, Munzenmayer C, Fuellgraf H, et al. Osteonecrosis of the jaw in patients transitioning from bisphosphonates to denosumab treatment for osteoporosis. Odontology. 2018;106(4):469-80.

[20] Colella A, Yu E, Sambrook P, Hughes T, Goss A. What is the Risk of Developing Osteonecrosis Following Dental Extractions for Patients on Denosumab for Osteoporosis? J Oral Maxillofac Surg. 2023;81(2):232-7.

[21] Chang YS, Nanayakkara S, Yaacoub A, Cox SC. Prevention of medication-related osteonecrosis of the jaw: institutional insights from a retrospective study. Aust Dent J. 2025;70(1):70-7.

[22] Yarom N, Shapiro CL, Peterson DE, Van Poznak CH, Bohlke K, Ruggiero SL, et al. Medication-Related Osteonecrosis of the Jaw: MASCC/ISOO/ASCO Clinical Practice Guideline. J Clin Oncol. 2019;37(25):2270-90.

[23] Vandone AM, Donadio M, Mozzati M, Ardine M, Polimeni MA, Beatrice S, et al. Impact of dental care in the prevention of bisphosphonate-associated osteonecrosis of the jaw: a single-center clinical experience. Ann Oncol. 2012;23(1):193-200.

[24] Wong RMY, Wong PY, Liu C, Wong HW, Chung YL, Chow SKH, et al. The imminent risk of a fracture-existing worldwide data: a systematic review and meta-analysis. Osteoporos Int. 2022;33(12):2453-66.

[25] Sim IW, Borromeo GL, Tsao C, Hardiman R, Hofman MS, Papatziamos Hjelle C, et al. Teriparatide Promotes Bone Healing in Medication-Related Osteonecrosis of the Jaw: A Placebo-Controlled, Randomized Trial. J Clin Oncol. 2020;38(26):2971-80.