MIONJ
-monitored by MHRA (Medicine and healthcare products regulatory agency)
-if pt suspected MIONJ, GDP have to notify MHRA via Yellow card scheme.

Antiresorptive agents (inhibit osteoclast function and differentiation, causing less bone resorption)
(a) Bisphosphonates
-used to tx cancer (breast, prostate cancer), multiple myeloma → given as high IV dose
-used to tx osteoporosis and others (Pagets, osteogenesis imperfecta, fibrous dysplasia) → given orally (once a week) OR IV infusion quarterly or yearly
-binds to hydroxyapatite irreversibly, can stay up to 10 years

(b) Denosumab (Prolia, Xgeva)
- RANKL inhibitor, a fully human monoclonal Ab
-used for osteoporosis and cancer
-X bind to bone unlike bisphospho and the effects go away within 9 months of tx completion

Antiangiogenic agents (Aflibercept, Sunitinib, Bevacizumab)
-inhibits angiogenesis, restricting tumor vascularisation

Bisphosphonates

Alendronic acid	Binosto, Fosamax, Fosavance	Osteoporosis
Risedronate sodium	Actonel	Osteoporosis, Pagets
Zoledronic acid	Aclasta, Zometa	Osteoporosis, Pagets, cancer
Ibandronic acid	Bondronat, Bonviva, Iasiban, Quidixor	Osteoporosis, cancer
Pamidronate disodium	Aredia	Osteoporosis, cancer
Sodium clodronate	Bonefos , Clasteon, Loron	Osteoporosis, cancer

Conditions that may be treated with bisphosphonates
Non Malignant : osteoporosis, paget, osteogenesis imperfecta, FD, 1º hyperparathyroidsm, cystic fibrosis
Malignant : multiple myeloma, breast, prostate cancer, bony metastatic lesions

Definition of MIONJ
-exposed bone, or bone that can be probed through an intraoral or extraoral fistula, persisted for >8 weeks - history of tx with anti-resorptive or anti-angiogenic drugs
-no history of radiation therapy to the jaw or no obvious metastatic disease to the jaws.

SnS
-Delayed healing after xla / oral surgery, exposed bone
-Pain, Numbness , Paresthesia, ST infection , Swelling

Risk factors
(1)Underlying medical problem (Cancer has ↑↑ risk than those osteoporosis)
(2) Previous episode of MIONJ ↑↑ risk
(3) Trauma (Dentoalveolar surgery (xla) / any procedure that affects bone, mucosal trauma from ill fitting denture
CAN also occur spontaneously
(4) Duration and dosage of bisphosphonate (Cumulative dose of drug ↑↑)
(5) Concurrent medication (Glucocorticoid, combination of bisphospho + anti-angiogenic)
Patients taking calcium / Vitamin D supplements are not at risk of MIONJ

Implant placement in these pt

If before drug therapy : tell pt there is small risk of MIONJ. Provide info to minimise risk (OHI at implant site)

If during / after drug therapy : tell pt risk of MIONJ, compromised bone healing and small risk of long term implant failure. Provide info to minimise risk (OHI at implant site)

Drug holiday

-Not much evidence cause the drug can stay in bone for few years . **Not recommended**

-One of the acceptable mx : For pt with osteoporosis and tx with 6 monthly S/C injection of denosumab, delay any non-urgent invasive dental treatment in asymptomatic tooth until the month prior to pt's next scheduled drug administration. Only resume denosumab when ST/ xla socket healed.Need to liaise with GMP

Bisphosphonates remain for very long time.

Denosumab will go away within 9 months of tx completion

Anti-angiogenic drugs not thought to remain in body for long time

Bisphosphonate therapy should be re-evaluated every 5 years to assess if benefit outweigh risk. Note that any low risk patient who continues to take bisphosphonate drugs after their five-year medication review should be reclassified as higher risk.

Low risk	Higher risk
If any of the following is present : •Patients being treated for osteoporosis or other non malignant disease of bone (Paget's disease) with oral bisphosphonates for **less than 5 years who are X** being concurrently treated with systemic glucocorticoids •Patients being treated for osteoporosis or other non malignant disease of bone (Paget's disease) with quarterly or yearly infusion of IV bisphosphonates for **less than 5 years who are X** being concurrently treated with systemic glucocorticoids •Patients being treated for osteoporosis or non malignant disease of bone with denosumab who are **X** being treated with systemic glucocorticoids.	If any of the following is present : •Patients being treated for osteoporosis or other non malignant disease of bone (Paget's disease) with oral bisphosphonates / quarterly or yearly infusion of IV bisphosphonates for **more than 5 years.** •Patients being treated for osteoporosis or other non malignant disease of bone with bisphosphonates or denosumab for **any length of time** who are being concurrently treated with **systemic glucocorticoids**. •Patients being treated with anti-resorptive or anti-angiogenic drugs (or both) as part of cancer mx •Patients with previous dx of MIONJ
• If a patient has taken bisphosphonates in the past, allocate to a risk group as if they are still taking the drugs. • If a patient has taken denosumab in the past 9 months, allocate to a risk group as if they are still taking the drug. • Patients who have previously taken anti-angiogenic drugs in combination with anti- resorptive drugs should be allocated to a risk group based on their history of anti-resorptive drug use.	

For patients who are about to commence anti resorptive or anti angiogenic drugs, or those who have recently started drug therapy,

• Assess pt's risk of MIONJ and assign risk category

•Advise them that there is small risk of them developing MIONJ. Its important that pt is not discouraged from taking these drugs or undergoing dental tx.

•Give preventive advice

- Healthy diet, reduce sugary snacks and drinks
- Maintain excellent OH
- Use fluoride toothpaste and fluoride mouthwash
- Stop smoking, limit alcohol intake
- Regular dental checkup

•Prioritise care that will reduce mucosal trauma or will avoid future xla / surgery that will impact the bone

- Obtain Xrays to identify possible infection areas
- Xla of teeth of poor prognosis without delay
- Minimise periodontal infection
- Adjust / replace poorly fitting dentures
- Tell patients not to hold the bisphosphonate tablet in the mouth due to risk of damage to oral mucosa

•Aim to get pt as dentally fit as feasible, with xla when required, and then treat routinely for SnP, simple fillings, recall and radiographic review.

•For medically complex patients, consult oral surgery / specialist about clinical assessment and tx planning.

For low risk patients, having made the pt as dentally fit as feasible :

•Carry out all routine dental tx like normal and provide preventative advice

•If an xla / other procedure that impacts bone is required

- Discuss risk and benefits of tx with pt to ensure valid consent
- Treat pt as normal for xla
- X prescribe Ab or antiseptic prophylaxis unless for other clinical reason
- Advice pt to contact practice if they have (pain, tingling, numbness, swelling in xla area)
- Review healing. If xla socket X healed at **8 weeks** and you suspect pt has MIONJ, refer to oral surgery / special care dentistry specialist

•Consider reporting any suspected case of MIONJ to MHRA via Yellow card scheme.

For higher risk patients, having made the pt as dentally fit as feasible :

•Carry out all routine dental tx like normal and provide preventative advice

•For medically complex pt, including higher risk pts, consult oral surgery / specialist about clinical assessment and tx planning

•If an xla is indicated, explore other alternatives where teeth can be retained (retain roots in absence of infection)

•If xla remains the most appropriate tx,

- Discuss risk and benefits of tx with pt to ensure valid consent
- X prescribe Ab or antiseptic prophylaxis unless for other clinical reason
- Advice pt to contact practice if they have (pain, tingling, numbness, swelling in xla area)
- Review healing. If xla socket X healed at **8 weeks** and you suspect pt has MIONJ, refer to oral surgery / special care dentistry specialist

•Consider reporting any suspected case of MIONJ to MHRA via Yellow card scheme.

Refer any patient with evidence of spontaneous MIONJ

that, in general, for cases where only a small amount of bone is exposed treatment may include monitoring, oral hygiene instruction, antibiotics or antibacterial mouth rinses. In cases where a large amount of bone is exposed, surgery may be indicated. However, the treatment they will receive will depend on their individual symptoms and clinical presentation.