SUPPLEMENTARY GUIDE

Published: **7 Nov 2018**
www.ace-hta.gov.sg

Summary of osteoporosis treatment options available in Singapore

	Evidence of effectiveness in[1]	Contraindications	Clinical considerations/precautions
Alendronate^, risedronate, or ibandronate (bisphosphonates, oral)* for information on monitoring bisphosphonates treatment see specific section on the back page	✓ Vertebral fracture ✓ Non-vertebral fracture *(alendronate and risedronate)* ✓ Hip fracture *(alendronate and risedronate)*	• CrCl <30 mL/minute • Hypocalcaemia • Oesophageal or gastric abnormalities such as gastric ulcers, achalasia, uncontrolled GORD • Inability to stand or sit upright for at least 30 minutes • Aspiration risk and difficulty swallowing liquids	<u>When taking alendronate or risedronate</u>, advise patients to: • Swallow tablet whole with plain water at least 30 minutes before taking food, beverages, or other medications (especially antacids, calcium, iron, or mineral supplements) • Remain upright until after eating <u>When taking ibandronate, advise patients to:</u> • Swallow tablet whole with plain water at least 60 minutes before taking food, beverages, or other medications (especially antacids, calcium, iron, or mineral supplements) • Remain upright until after eating
Zoledronic acid* (bisphosphonate, intravenous) for information on monitoring bisphosphonates treatment see specific section on the back page	✓ Vertebral fracture ✓ Non-vertebral fracture ✓ Hip fracture	• CrCl <35 mL/minute • Hypocalcaemia	• Give IV infusion for at least 15 minutes • Ensure patient is adequately hydrated before use • Use with caution in patients with significant vitamin D deficiency • Check serum calcium and phosphate at 9 to 14 days after infusion if patient shows symptoms of hypocalcaemia or hypophosphataemia
Denosumab* (RANKL inhibitor, subcutaneous)	✓ Vertebral fracture ✓ Non-vertebral fracture ✓ Hip fracture	• Hypocalcaemia	• Ensure adequate calcium and vitamin D intake • Caution to be exercised in patients with pre-existing eczema, patients with renal impairment, and patients with recurrent infections
Teriparatide (recombinant parathyroid hormone, subcutaneous)	✓ Vertebral fracture ✓ Non-vertebral fracture ✗ Hip fracture	• CrCl <30 mL/minute • Hyperparathyroidism or hypercalcaemia • Paget's disease of bone or unexplained increased alkaline phosphatase levels • History of bone radiation	• Daily SC injection • Should not use for longer than two years and should be followed by an anti-resorptive agent Consider referring to a specialist before commencing treatment
Raloxifene (SERM, oral)	✓ Vertebral fracture ✗ Non-vertebral fracture ✗ Hip fracture	• CrCl <30 mL/minute • History of or current VTE (including DVT, PE, and retinal vein thrombosis)	• Ensure adequate intake of calcium and vitamin D • Use in younger post-menopausal women with no hot flushes

Information on contraindications and clinical considerations/precautions sourced from Package Inserts and UptoDate (www.uptodate.com). Please refer to Package Inserts for full details.

* Available on government subsidy list. List updated as of 7 November 2018

^ Alendronate is currently available in generic form. CrCl = creatinine clearance; GORD = gastro-oesophageal reflux disease; IV = intravenous; BP = bisphosphonates; SC = subcutaneous; VTE = venous thromboembolism; DVT = deep vein thrombosis; PE = pulmonary embolism; RANKL = receptor activator of nuclear factor kappa-beta ligand; SERM = selective estrogen receptor modulator

Menopausal hormone therapy (including tibolone) can be considered for prevention of osteoporosis or fragility fractures in post-menopausal women before 60 years of age or within 10 years after menopause.[2] Menopausal hormone therapy can also be considered for prevention of osteoporosis or fragility fractures in women who experience early menopause (45 years and younger) until the normal age of menopause, unless contraindicated. The decision to start menopausal hormone therapy should be based on an individual woman's history and risk factors (especially risk of venous thromboembolism, coronary artery disease, stroke), including the need to treat vasomotor symptoms.

Bisphosphonates (BP) treatment only

Key facts about osteonecrosis of the jaw (ONJ) risk with BP

- Very rare side effect with oral BP[3, 4]
- Higher likelihood with use of IV BP and in cancer patients
- Optimising oral hygiene prior to initiating BP (especially IV BP) may reduce the incidence of ONJ
- Obtaining dental clearance not necessary before initiating BP treatment for osteoporosis (complete any dental procedures before starting treatment)
- Modifiable factors that increase risk of ONJ should be properly managed (advise to stop smoking)

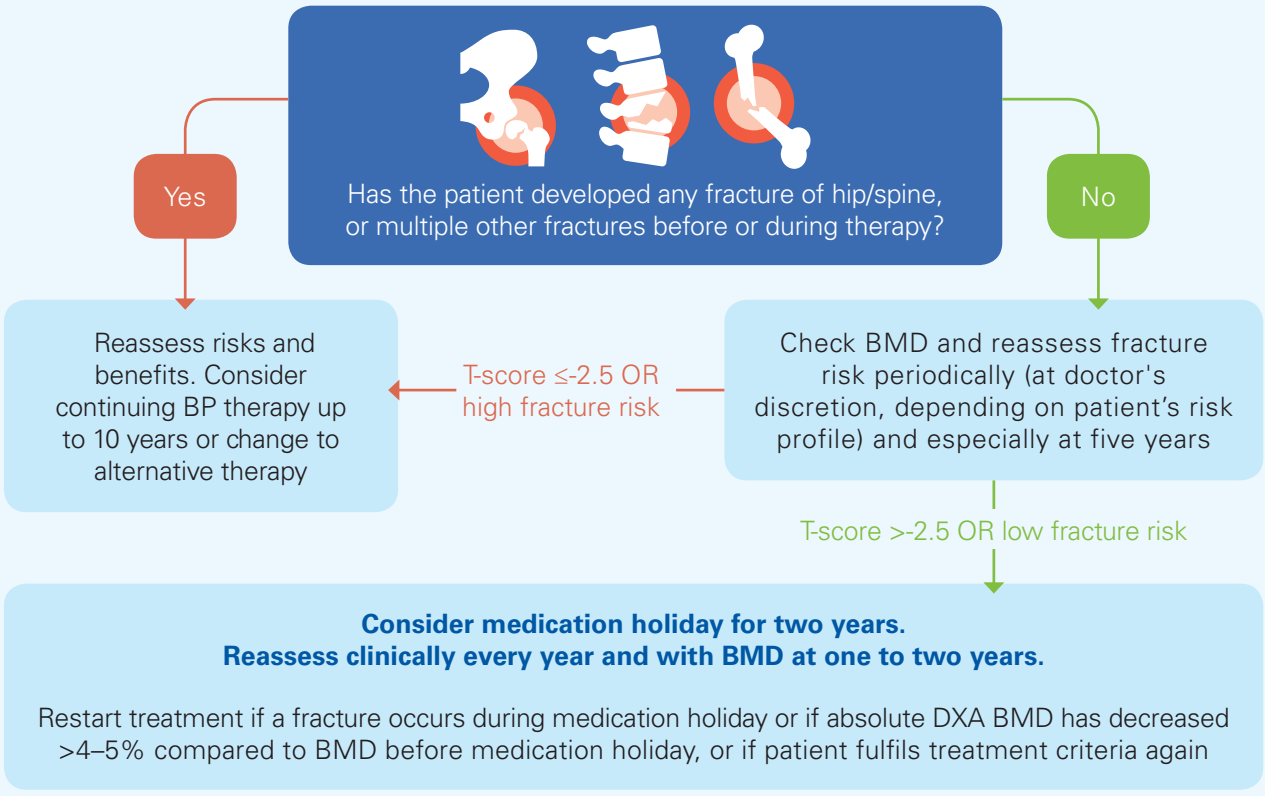
Key facts about atypical femoral fracture (AFF) risk with BP

- Uncommon side effect[3, 4]
- Assess occurrence of AFF especially if patient develops thigh/hip/groin pain while on BP (or denosumab)
- Overall, benefits of treatment outweigh risks when treatment is appropriate

Patients should be adequately informed of the very small risk associated with these adverse events, in light of the patient's likelihood to benefit from treatment.

Re-evaluate patients five years after initiating oral BP or three years after IV zoledronic acid therapy for potential medication holiday.[3, 4]

The guide below is based on limited evidence. It should always be accompanied by clinical judgement. A careful risk-benefit assessment and follow-up are strongly recommended.



References

1. Qaseem A, et al. (2017) Treatment of Low Bone Density or Osteoporosis to Prevent Fractures in Men and Women: A Clinical Practice Guideline Update From the American College of Physicians. Ann Intern;166:818-839
2. De Villiers TJ, et al. (2016) Revised Global Consensus Statement on Menopausal Hormone Therapy, Climacteric, DOI: 10.1080/13697137.2016.1196047
3. Adler RA, et al. (2015) Managing Osteoporosis in Patients on Long-Term Bisphosphonate Treatment: Report of a Task Force of the American Society for Bone and Mineral Research. Journal of Bone and Mineral Research, Vol. 31, No. 1, 16–35
4. Adler RA, et al. (2016) CORRIGENDUM Managing Osteoporosis in Patients on Long- Term Bisphosphonate Treatment: Report of a Task Force of the American Society for Bone and Mineral Research. Journal of Bone and Mineral Research, Vol. 31, No. 10, 19-10