PHARMACY BULLETIN
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Osteoporosis

KEY POINTS[1,2]

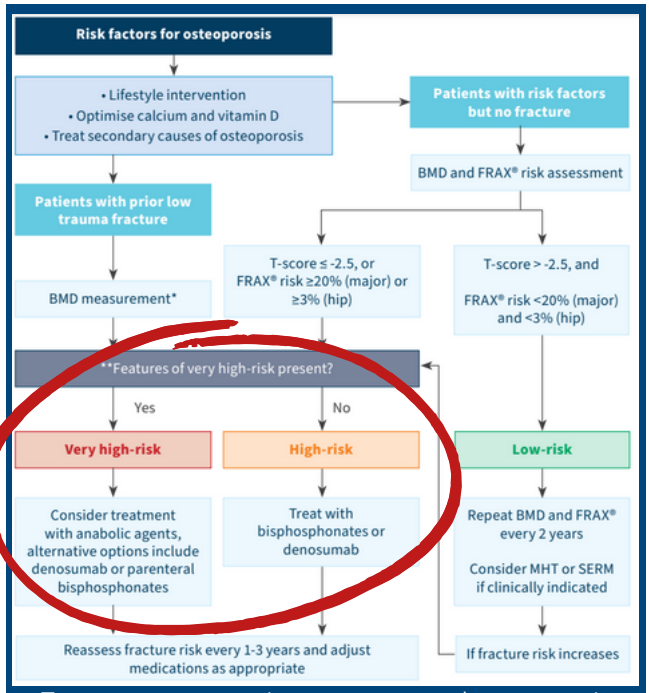
1. In 2000, 1.4 million osteoporosis cases were reported in Malaysia, and are expected to increase to 3.3 million in 2050. The Chinese had the highest incidence of hip fractures, compared to Malay and Indian (44.8% are Chinese women).
2. All individuals with osteoporosis should have an adequate intake of calcium (at least 1200mg/day elemental calcium) in combination with Vitamin D (at least 800IU/day).
3. High-risk individuals should be treated with anti-resorptives as first line therapy.
4. Very high-risk individuals should be initiated with anabolic agents as first line therapy followed by anti-resorptives to maintain anti-fracture efficacy.

PPIs and risk of fractures[3,4,5,6]

Proton Pump Inhibitors (PPIs) are antacids that binds to H+/K+ ATPase enzyme system and inhibit the gastric acid secretion. Concerns about long term safety have been raised due to the possible increased risk of overall fractures in chronic use of PPIs. It is said that greatest risk is associated with patients taking the PPIs one year or greater.

Meta analysis concluded that PPI use was associated with increased risk of osteoporosis and moderately increased risk of hip, spine and any-site fracture. The mechanism behind it remain unclear, it has been suggested in theory that PPI could reduce intestinal calcium absorption by blocking the gastric acid secretion and lead to decrease in bone mineral density (BMD).
However, pooled result of studies assessing BMD did not suggest significant correlation between PPI use and BMD. They also concluded that no significant difference in term of dose and duration of use between the risk of hip fracture and PPI use. Short term use (<1 year) and longer use (>1 year) were similarly associated with increased risk of fracture. Same goes to high dose and low dose group.

Many systematic reviews revealed an association between PPI use and increased fracture incidence. Thus, taking PPIs for inappropriate indications or receiving PPI therapy without prescription should be discouraged.



Treatment sequence in postmenopausal osteoporosis. (CPG Management of Osteoporosis, 3rd Ed. 2022)

- Anti-resorptive drugs primarily inhibit osteoclastic bone resorption with later secondary effects on bone formation.
- Anabolic agents primarily stimulate osteoblastic bone formation with variable effects on bone resorption.

Fall Prevention Program: Fall Risk Score[7,8]

STOP when possible, SWITCH to safer alternatives or REDUCE to the lowest effective dose.
If the patient is taking more than one medication in a particular risk category, the score should be calculated by (risk level score) x (number of medications in that risk level category)

Point value (Risk level)	Drug Class (example)	Potential Side Effects
3 (High)	Opiates (morphine), antipsychotics (clozapine), anticovulsants (phenytoin), sedative-hypnotics including benzodiazepines (diazepam)	Sedation, dizziness, postural disturbances, altered gait and balance, impaired cognition
2 (Medium)	Antihypertensive (prazosin), cardiac drugs (digoxin), antiarrhythmics (amiodarone), antidepressants (amitriptyline)	Induced orthostasis, impaired cerebral perfusion, poor health status
1 (Low)	Diuretics (furosemide)	Increased ambulation, induced orthostasis

Score ≥ 6 : Higher risk for fall; evaluate patient.

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7. Beasley, B., & Patatanian, E. (2009). Development and Implementation of a Pharmacy Fall Prevention Program. Hospital Pharmacy, 44(12), 1095–1102. doi:10.1310/hpj4412-1095
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Osteoporotic Agents in HCTM

ANTIRESORPTIVES

First line for high risk individuals

BIPHOSPHONATES

	Alendronate 70mg + Cholecalciferol 5,600IU (Fosamax® Plus)	Ibandronic Acid 150mg (Bonviva®)	Denosumab 60mg (Prolia®)
Dose	**Oral: 1 tab once weekly**	**Oral: 1 tab once a month**	**SC: 60mg every 6 month**
Evidence level: ↑ **BMD** / **Vertebral** ↓ fracture rate / **Hip** fracture ↓ rate	A A A	A A -	A A A
Contraindications	Hypocalcemia, inability to sit upright, patient with esophagus abnormalities.		Hypocalcemia, pregnancy, those aged <18yo.
Renal impairment	eGFR <35mL/min not recommended	eGFR <30mL/min not recommended	Limited data, no adjustment in renal impairment. Monitor for hypocalcemia
Common Side Effects	Upper GI symptoms commonly nausea, bowel disturbances, headache & muscle pain		Cellulitis, eczema, hypocalcemia, flatulence.
Drug Holiday	After 3-5 years of therapy, may consider 2 years drug holiday. Review BMD no longer than 2 years after starting drug holiday. There's increased risk of hip & vertebral fractures after 2 years drug holiday.		Not recommended. Associated with rebound increase in bone turnover and increased risk of multiple vertebral fracture, over an average of 3-6 months since last injection was due. Consider alternative antiresorptives 6 months following denosumab cessation.
Price in NF Pharmacy*	RM 21/tab (RM 84/month) RM 504 for 6 months	RM 99/month RM 594 for 6 months	RM 770/injection

*prices are subject to change

ANABOLIC AGENTS

First line for very high risk individuals

	Teriparatide 20ug Inj. (Forteo®)	Romosozumab 105mg inj. (Evenity®)
Dose	**SC: 20ug once daily**	**SC: 210mg (two injections) once monthly**
Evidence level: ↑ **BMD** / **Vertebral** ↓ fracture rate / **Hip** fracture ↓ rate	A A -	A A -
Contraindications	Metabolic bone disease other than osteoporosis, pre-existing hypercalcemia, eGFR <30mL/min	Hypocalcemia, history of myocardial infarction or stroke
Renal impairment	No adjustment, use with caution	No adjustment, monitor calcium
Duration of treatment	24 months	12 months
	Sequential therapy with antiresorptives is required to maintain the bone density gains. (ie Alendronate or Denosumab) as benefit wean off within 1 year of discontinuation	
Price in NF Pharmacy*	RM 1,682/inj	RM 1,083/ box of 2 inj.

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