Updated October 2020
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MEDICATIONS USED IN TREATMENT OF OSTEOPOROSIS AND EFFICACY OF USE

Medication (Cost generic if available)	**Indication**	**Dosing for TREATMENT of osteoporosis**	**Cautions/ADR**	**Efficacy** (NNT to prevent 1 fracture over 3 yrs)
Oral Bisphosphonates Alendronate (Fosamax) ($40 for 3 months) Risedronate (Actonel) ($40 for 3 months)	First line therapy for prevention and management of osteoporosis or corticosteroid induced osteoporosis ** consider stopping after 5 years of use** • May continue up to 10 years if patient at high risk of fracture	**Alendronate (Fosamax):** 10 mg daily 70 mg weekly* **Risedronate (Actonel):** 5 mg daily 35 mg weekly* 150 mg monthly *Alendronate 70 mg and Risedronate 35 mg are regular benefits through Alberta Blue Cross	• MSK pain • GI effects • Jaw necrosis in 0.04% of patients treated with oral bisphosphonates (1 per 10 000 patient year) Do not use in patients with <u>CrCl < 30 ml/min</u>	<u>Vertebral Fractures</u>: Alendronate: NNT 15 Risedronate: NNT 20 <u>Hip Fractures:</u> Alendronate: NNT 91 Risedronate: NNT 91 Best evidence for initial therapy with Risedronate and alendronate. Best tolerability and compliance with once weekly dosing
IV Bisphosphonate **Zoledronic Acid** (Aclasta) ($360 per year)	Consider if patient : • unable to take oral bisphosphonates due to GI issues or unwilling to adhere to therapy • corticosteroid induced OP who is not appropriate for oral bisphosphonates • treatment failure with oral bisphosphonates	5 mg IV Once per year Consider stopping after 3 years for most patients, in high risk patients, may continue for up to 6 yrs Special authorization required for Alberta Blue Cross Will need to fill out infusion enrollment form: • **Infuze** for generic Zoledronic acid and • **For my Bones** for Aclasta	• Risk of jaw osteonecrosis and atypical thigh fractures. • Osteonecrosis may occur in up to 12% of patients treated with IV bisphosphonates • Avoid in patients with hypocalcemia Other ADR: MSK pain, flu-like reaction, acute renal failure • Do not use in patients with <u>CrCl <35 ml/min</u>	<u>Vertebral Fractures</u>: NNT: 14 <u>Hip Fractures:</u> NNT 91

Teriparatide (Forteo) (Parathyroid hormone analog) ($3125 for 3 months or $12,500 per year)	Consider for postmenopausal women with: • high risk of fracture (corticosteroid induced osteoporosis, previous osteoporotic fracture, multiple risk factors, very low BMD • Failure to respond to bisphosphonates May consider in males with primary or hypogonadal osteoporosis	20 mcg sc daily *limited to lifetime exposure of 2 years due to dose-dependent risk of osteosarcoma in rats NOT a benefit for Alberta Blue Cross.	• • Joint pain, diarrhea • Hypercalcemia and hypercalciuria (Transient and 4 to 6 hrs after dose) • Orthostatic hypotension (within 4 hours of injection) • Increased Risk of osteosarcoma (animal models) • Do not use in severe renal impairment(73% increase with <u>CrCl <30 ml/min</u>) • Avoid use in Paget's disease, metabolic bone disease, previous skeletal irradiation, elevated ALP	<u>Vertebral Fractures:</u> NNT 11 <u>Non-vertebral Fractures:</u> NNT 33 ** so far has not been shown to reduce hip fractures specifically**

May 2018 Trudy Arbo, PharmD

Denosumab (Prolia) RANKL inhibitor ($800 per year - $400 per sc injection)	• For patients with high fracture risk (previous fracture, multiple risk factors) • Treatment failure or unable to take other OP treatment options such as bisphosphonates • Patients with breast cancer receiving an aromatase inhibitor • Patients with prostate cancer receiving androgen deprivation therapy for prostate cancer • Patients with corticosteroidinduced osteoporosis unable to take oral or IV bisphosphonates or parathyroid analogs	60 mg sc q 6 months *Consider stopping after 5 yrs Requires special authorization with Alberta Blue Cross	• Avoid in patients with stage 5 CKD or patients on dialysis due to hypocalcemia • In patients with renal impairment – increased risk of hypocalcemia (eGFR <30 ml/min) – monitor Calcium levels • Atypical femur fractures (glucocorticoids may increase risk) • Hypocalcemia • Osteonecrosis of jaw (ONJ) • Bone, joint pain post injection (can be days to months after) Note: BMD may rapidly decline after stopping therapy (although in some trials benefit was maintained up to 2 years post d/c) – some experts suggest to initiate therapy with another osteoporosis med if possible (i.e. bisphosphonate)	<u>Vertebral Fractures</u>: NNT 21 <u>Hip Fractures</u>: NNT 200
Raloxifene (Evista) ($50-60)	For use in patient unable to tolerate other osteoporosis therapies. May be used in patients with high risk of breast cancer	60 mg po daily	• Thromboembolic events, including pulmonary embolism • Can cause hot flashes • Do not use in patients with history of VTE or in patients where hip fracture is primary concern No adjustments required for renal function	<u>Vertebral Fracture</u>: NNT 29 No evidence for benefit in hip or non-vertebral fractures <u>Breast cancer prevention</u> NNT 125

HRT	For patients who are not able to tolerate other treatments of OP medication. Caution as risk of breast cancer may outweigh benefits of preventing fractures • Can be used as first line in patients with menopausal symptoms	Minimum DAILY dose of estrogen: • 0.625 mg conjugated estrogen • 2 mg po estradiol • 15 mcg of oral ethinylestradiol • 50 mcg transdermal estradiol ** addition of progesterone does not impair beneficial effects of estrogen on BMD	• Avoid in patients with CVD or history or risk of breast cancer, stroke or DVT • Evaluate risks and benefits of long-term HRT use in the management of osteoporosis, taking into account the increased risk of breast cancer and cardiovascular disease, availability of other pharmacologic modalities (e.g., alendronate, calcitonin, calcium, raloxifene, risedronate, vitamin D), and life-style factors that can be modified.	
Calcitonin (Calcimar)	For patients who cannot tolerate bisphosphonates In patients with bone pain from vertebral compression fractures	100 units SC/IM daily 200 units (1 spray) in one nostril daily *Nasal spray not available in Canada	Avoid in patients where hip fracture is primary concern Not for patients less than 5 years postmenopausal (not proven effective)	Vertebral Fracture: NNT 12 (in patients with previous vertebral fractures)
Rosmosozumab (Evenity)				

- High risk of fractures defined as femoral neck T-score less than -2.5 or previous vertebral fracture and femoral neck T-score less than or equal to -2
- No direct comparisons have been made between agents NNT are based on placebo comparisons

Clinical Pearls

1. Ensure adequate dietary intake of Calcium and Vitamin D: Recommend: Vitamin D 800 to 1000 units daily and Calcium 1000 to 1200 mg/day
    a. Limit oral supplementation to 500 mg daily wherever possible (especially for CKD patients).
2. Chronic renal disease – if eGFR < 30 ml/min do not start bisphosphonates. May consider raloxifene (postmenopausal women) or denosumab provided absence of mineral and bone disorder
3. Limited evidence to support rechecking DXA while patient is currently receiving therapy
    a. Canadian guidelines recommend rechecking q 3 to 5 years once medications have stopped
        i. If T score decreases to -2.5 or new risk factor develops, consider restarting therapy

Risk factors for osteoporosis

1. Fragility fracture after age 40
2. Vertebral compression fracture
3. Osteopenia (T scores between -1 and -2.5)
4. Parental hip fracture (family Hx)
5. Use of other high risk medications (long term glucocorticoid therapy, leuprolide, aromatase inhibitors) 6. High alcohol intake (>3 units per day)
7. Current cigarette smoker
8. Major weight loss (10% below their body weight at 25 yrs) 9.

   Disease states associated with osteoporosis:
    a. Rheumatoid arthritis, malabsorption syndrome, hypoparathyroidism, hypogonadism, premature menopause, chronic liver disease, inflammatory bowel disease

When to screen:

1. Patients 50 to 64 years old with ***no*** fragility fractures or other known risk factors for osteoporosis – use Osteoporosis Self-Assessment Tool (OST) which is: **Wt in kg – Age = OST**
    a. If $\geq$ 10 low risk and recheck in 5 years
    b. If < 10 recommend screening with DXA
2. Patients 50 to 64 yrs with one or more risk factors or previously low BMD
3. All women $\geq$ 65 years old
4. Men $\geq$65 years and older with 1 risk factor

When to treat:

1. If 10 year fracture risk is > 10% (patient considered moderate to high risk)
2. Postmenopausal women and men > 50 with a T-score of -2.5 or lower (i.e. osteoporosis)
3. Postmenopausal women and men > 50 yrs old with previous hip or spine fracture
4. Patients with T-Score between -1 and -2.5 (i.e. osteopenia) with the following risks per the FRAX tool a. 10 year hip fracture > 3% or higher
    b. 10 year risk of major osteoporotic fracture of 20% or higher (high risk) or 10% or higher (Moderate risk)
5. Consider treatment for patients with low trauma or fragility fractures

When to stop medications

1. Oral bisphosphonates: Reassess treatment at 5 years and consider discontinuing. If high risk of fracture may consider up to 10 years
2. Zoledronic acid (IV): may be continued for 3 years in most patients, may continue to 6 years in high risk patients
3. Denosumab: Consider discontinuing after 5 years of therapy
4. Teraparatide: Lifetime maximum of 2 years of therapy

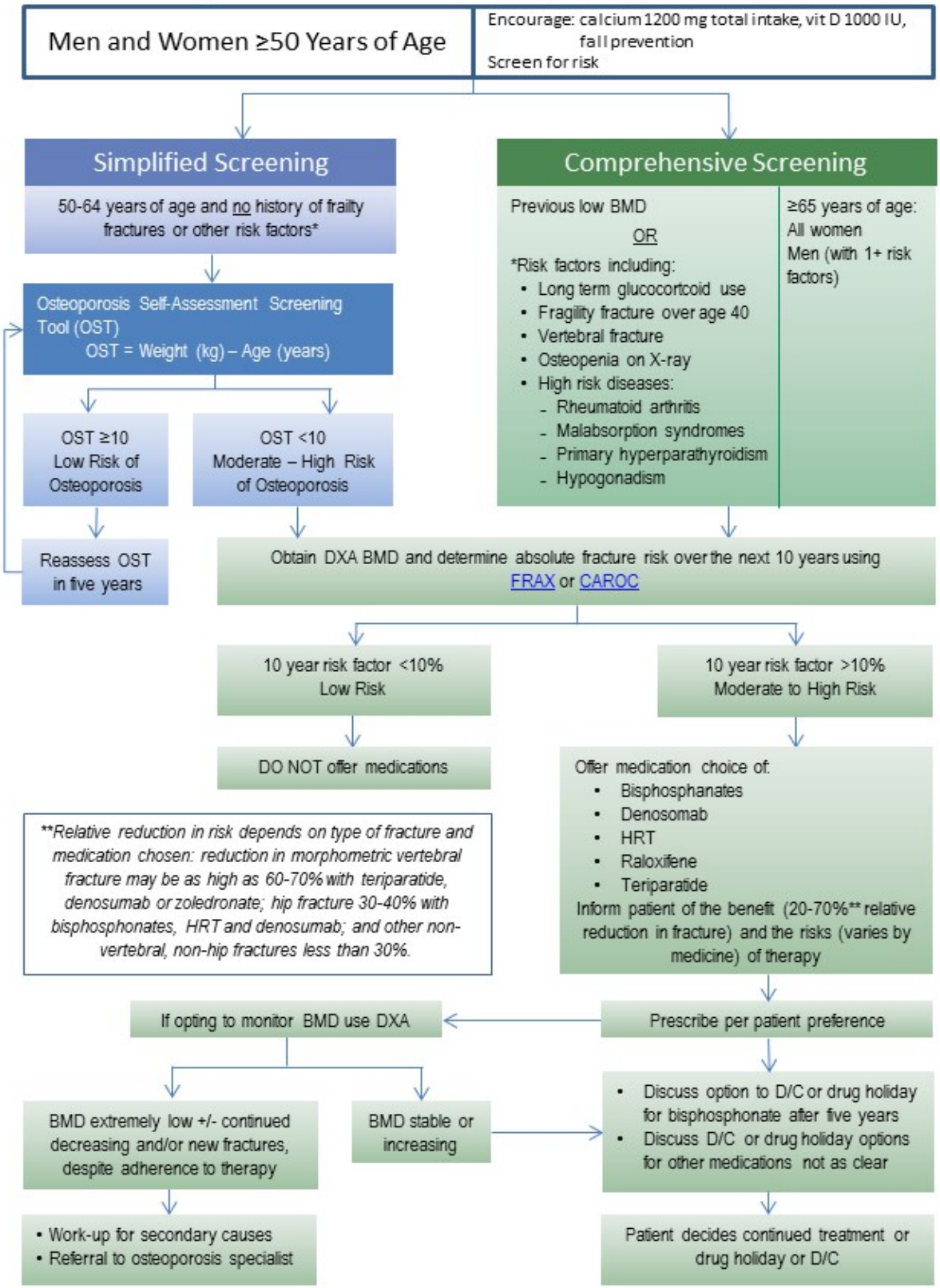
New and novel therapies:

Duavive (conjugated Estrogens/bazedoxifene) currently marketed in Canada for treatment of moderate to severe vasomotor symptoms associated with menopause in women with a uterus. Currently not approved by Health Canada for use in treatment of osteoporosis and no primary outcome on fractures available to date. Marketed and approved in the USA for prevention of osteoporosis in women less than 75 years old, especially women who also require therapy for vasomotor menopausal symptoms. Cost is approximately $1200 per year in Canada.

Useful tools for patients:

1. Osteoporosis website: https://osteoporosis.ca/
    a. Contains information on calculating your dietary intake of calcium
    b. Information on nutrition
    c. Patient stories
    d. Also information for healthcare professionals regarding tools for practice and treatment guidelines

Screening and Treatment for Osteoporosis and Fracture Risk



Towards Optimized Practice: https://www.topalbertadoctors.org/download/1907/Osteoporosis%20CPG.pdf

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