SOGC

Osteoporosis Products Available in Canada for the Treatment and Prevention of

Postmenopausal Osteoporosis

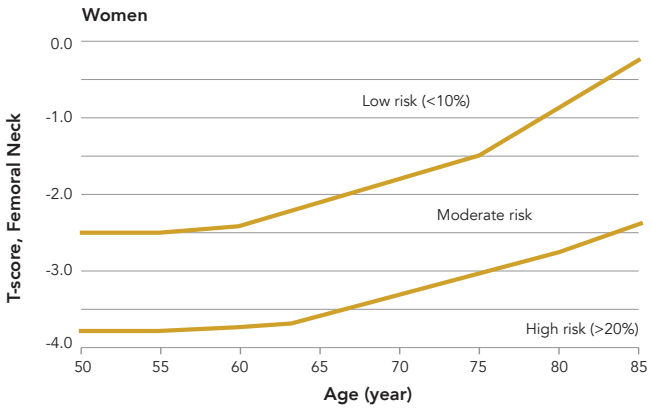
Physician Desk Reference - 2nd Edition

A clinical resource provided to you by:
The Society of Obstetricians and Gynaecologists of Canada

ASSESSING RISK

The goals of osteoporosis management includes assessment of fracture risk and prevention of fracture, both vertebral (manifested as height loss) and nonvertebral. A Bone Mineral Density (BMD) test is only one component of assessing a woman's risk for fracture. The fracture risk assessment requires integration of the key multiple risk factors for fracture.

ASSESSMENT OF BASAL 10-YEAR FRACTURE RISK – WOMEN



Key risk factors to assess fracture risk in women age ≥ 50 years

- Sex
- Age
- BMD
- Fragility fracture after age 40
- Prolonged systemic glucocorticoid use (≥3 mos in the prior year of a prednisone equivalent ≥7.5 mg daily) in the prior year

CAROC

Osteoporosis Canada recommends that 10 year absolute fracture risk be determined by integrating key risk factors for fracture by using the 2010 Canadian Association of Radiologists/ Osteoporosis Canada (CAROC) tool or the FRAX tool (www.osteoporosis.ca).

FRAX

A World Health Organization collaborating centre has developed the FRAX tool to calculate fracture risk at the hip or for a major fragility fracture (spine, hip, radius or humerus) over the following 10 years (www.shef.ac.uk/FRAX). It is based on the BMD at the femoral neck as well as the following important risk factors for fracture: Age, weight, height, prior fragility fracture, parental history of hip fracture, smoking status, use of prednisone, presence of rheumatoid arthritis, presence of a secondary cause for osteoporosis such as hyperthyroidism, alcohol intake of 3 or more drinks per day. Treatment is recommended if the 10 year fracture risk at the hip is ≥ 3% or for a major osteoporotic fracture is ≥ 20%.

Risk factors are additive, meaning that the more risk factors, the greater the risk of developing osteoporosis. Assessing risk factors can help identify those that are modifiable, which include lifestyle factors. Making lifestyle changes such as smoking cessation can lower fracture risk and can improve bone health. (Osteoporosis Canada, 2011)

PHYSICAL ACTIVITY, NUTRITION AND SUPPLEMENTS FOR OSTEOPOROSIS MANAGEMENT

SOGC Recommendations on Lifestyle Strategies to Manage Osteoporosis

Early assessment of skeletal health, initiation of vitamin D supplements as well as a diet enriched in calcium, and a strenuous daily exercise program are essential in the prevention and treatment of osteoporosis.[1]

Osteoporosis Canada Recommendations on Lifestyle Interventions

For all patients, regular weight-bearing, balance and strengthening exercises, smoking cessation, and optimization of total (dietary and supplements) calcium and vitamin D intake are recommended. For patients at risk of falls, fall-prevention strategies should also be implemented.[2]

Regular exercise	■ Resistance training appropriate for the individual's age and functional capacity and/or weight-bearing aerobic exercises ■ Exercises to enhance core stability ■ Exercises that focus on balance or on balance and gait training
Calcium and vitamin D	**Total daily intake of elemental calcium through diet and supplements (if needed):** ■ Adults 19 to 50: 1,000 mg ■ Adults 50+: 1,200 mg **Vitamin D daily supplementation:** ■ Adults 19 to 50: 400–1,000 IU ■ Adults 50+ (or those younger adults at high risk (with osteoporosis, multiple fractures, or conditions affecting vitamin D absorption): 800–2,000 IU, or as required for the patient based on the results of serum 25 hydroxyvitamin D (ideal range is 75–125 nmol/l)
Diet/nutrition	■ Limit coffee intake (<4 cups/day) ■ Limit alcohol intake (<2 drinks/day)
Smoking cessation should be strongly advised	

Recommendations for patients on how to take calcium supplements:

- Encourage patients to meet their calcium requirements from dietary sources, such as 3–4 servings of dairy daily (each glass of milk contains approximately 300 mg elemental calcium). Visit HerNutrition.ca for additional sources of calcium.
- If calcium requirements are not met from dietary sources, then supplements should be taken.
- Calcium carbonate is 40% elemental calcium, and is best absorbed in an acidic gastric pH.
- Individuals taking proton pump inhibitors are advised to take their calcium supplement with food to ensure best absorption.
- Calcium citrate is approximately 21% elemental calcium and can be taken at any time as it does not require an acidic pH for absorption. It is suitable for those with achlorhydria or those using PPIs.
- Other calcium supplements, such as calcium gluconate or calcium lactate, are not recommended as they contain a very small amount of elemental calcium.
- TUMS® contain calcium carbonate and are useful calcium supplements.
- It is best to have patients take smaller doses of calcium more frequently, or a slow release formulation rather than a large dose once a day.

PRESCRIBING THERAPIES FOR POSTMENOPAUSAL OSTEOPOROSIS

For individuals with postmenopausal osteoporosis, there are a variety of drug treatments available. This guide aims to assist physicians with optimizing treatment decisions by summarizing some of the key information about all of the drug treatments currently available in Canada.

For complete information about the individual treatments in this guide, please consult the respective product monographs on Health Canada's drug product database.[3]

Providers should check the full prescribing information for appropriate dosages for the indication and any updates or information that is not provided here, such as warnings and contraindications.

First-line medications for postmenopausal osteoporosis treatment and/or prevention

SOGC Recommendations on Treatment of Osteoporosis

> *Pharmacologic therapy is considered in postmenopausal women after exclusion of secondary causes of low bone density. If the 10-year absolute fracture risk is greater than 20% (high), then drug therapy is advised. In those with a moderate risk (10% to 20%), management decisions are individualized.*[1]

Selective Estrogen-Receptor Modulator (SERM)

ACTIVE INGREDIENT(S)	PRODUCT / MANUFACTURER	DOSAGE FORM / STRENGTH	SCHEDULE	CLINICAL INDICATION(S) HEALTH CANADA
Raloxifene hydrochloride	**EVISTA** Eli Lilly Canada Inc.	**Tablet** 60 mg	Daily	■ Treatment and prevention of osteoporosis in postmenopausal women

Estrogen and Selective Estrogen-Receptor Modulator (SERM)

ACTIVE INGREDIENT(S)	PRODUCT / MANUFACTURER	DOSAGE FORM / STRENGTH	SCHEDULE	CLINICAL INDICATION(S) FDA
Conjugated estrogens +bazedoxifene	**DUAVIVE** Pfizer Canada Inc.	**Tablet** 0.45 mg conjugated estrogens + 20 mg bazedoxifene	Daily	■ Prevention of osteoporosis

Parathyroid hormone

ACTIVE INGREDIENT(S)	PRODUCT / MANUFACTURER	DOSAGE FORM / STRENGTH	SCHEDULE	CLINICAL INDICATION(S) HEALTH CANADA
Teriparatide (recombinant human parathyroid hormone)	**FORTEO** Eli Lilly Canada Inc.	**Subcutaneous injection** 20 mcg (The maximum lifetime exposure for an individual patient is 24 months)	Daily	■ Treatment of postmenopausal women with severe osteoporosis who are at high risk of fracture or who have failed or are intolerant to previous osteoporosis therapy

Bisphosphonates*

ACTIVE INGREDIENT(S)	PRODUCT / MANUFACTURER	DOSAGE FORM / STRENGTH	SCHEDULE	CLINICAL INDICATION(S) HEALTH CANADA
Zoledronic acid	**ACLASTA** Novartis Pharmaceuticals Canada Inc.	**IV** 5 mg/100 mL infused for at least 15 minutes	Once yearly	■ Treatment of osteoporosis in postmenopausal women
Risedronate sodium	**ACTONEL** Warner Chilcott Canada Co. (Allergan)	**Tablet** 5 mg 35 mg 150 mg	Daily (5 mg) Once weekly (35 mg) Once monthly (150 mg)	■ Treatment and prevention of osteoporosis in postmenopausal women
Risedronate sodium (delayed release)	**ACTONEL DR** Warner Chilcott Canada Co. (Allergan)	**Tablet** 35 mg	Once weekly	■ Treatment of osteoporosis in postmenopausal women
Alendronate sodium	**FOSAMAX** Merck Canada Inc.	**Tablet** 10 mg 70 mg	Daily (10 mg) Once weekly (70 mg)	■ Treatment and prevention of osteoporosis in postmenopausal women
Alendronate sodium + cholecalciferol (vitamin D_3)	**FOSAVANCE** Merck Canada Inc.	**Tablet** 70 mg alendronate + 70 mcg cholecalciferol (2,800 IU vitamin D_3) 70 mg alendronate + 140 mcg cholecalciferol (5,600 IU vitamin D_3)	Once weekly	■ Treatment of osteoporosis in postmenopausal women

Prescribing tip: Because calcium interferes with the absorption of bisphosphonates, calcium supplements must be taken at other times of the day.

RANK ligand inhibitor**

ACTIVE INGREDIENT(S)	PRODUCT / MANUFACTURER	DOSAGE FORM / STRENGTH	SCHEDULE	CLINICAL INDICATION(S) HEALTH CANADA
Denosumab	**PROLIA** Amgen Canada Inc.	**Subcutaneous injection** 60 mg/mL in a single use prefilled syringe	Once every 6 months	■ Treatment of postmenopausal women with osteoporosis at high risk for fracture

First-line hormone therapy products for postmenopausal osteoporosis treatment and/or prevention

Hormonal therapy – Oral

ACTIVE INGREDIENT(S)	PRODUCT / MANUFACTURER	DOSAGE FORM / STRENGTH	SCHEDULE	CLINICAL INDICATION(S) HEALTH CANADA
17ß-estradiol (micronized)	**ESTRACE** Acerus Pharmaceuticals Corporation	**Tablet** 0.5 mg 1 mg 2 mg	Daily	■ Prevention of osteoporosis
Conjugated estrogens	**PREMARIN** Pfizer Canada Inc.	**Tablet** 0.3 mg 0.625 mg 1.25 mg	Daily	■ Prevention of osteoporosis

Hormonal therapy – Transdermal

ACTIVE INGREDIENT(S)	PRODUCT / MANUFACTURER	DOSAGE FORM / STRENGTH	SCHEDULE	CLINICAL INDICATION(S) HEALTH CANADA
17ß-estradiol	**CLIMARA** Bayer Inc.	**Patch** 0.05 mg 0.075 mg 0.1 mg	Once weekly	■ Prevention of osteoporosis
17ß-estradiol	**ESTRADOT** Novartis Pharmaceuticals Canada Inc.	**Patch** 0.025 mg 0.0375 mg 0.05 mg 0.075 mg 0.1 mg	Twice weekly	■ Prevention of osteoporosis

*Bisphosphonate Drug Holidays:

Bisphosphonates have long term skeletal retention. Long term use beyond 5 years has uncommonly been associated with potential harmful effects including atypical femoral fractures. The bisphosphonate can be interrupted after 3–5 years of use if the fracture risk is moderate and there is no history of a prior fragility fracture and the femoral neck T-score is >-2.5. If the fracture risk is high, ongoing drug therapy is necessary, and consideration can be given to switching to another proven agent, such as teriparatide or denosumab.[4]

If the fracture risk is low, drug therapy is not required beyond adequate calcium and vitamin D supplementation.[1]

**Atypical Femoral Fractures (AFF):

These fractures occur in the femoral shaft and can develop with minimal or no trauma. They can be seen with long term bisphosphonate or denosumab use, or may rarely occur without the use of an antiresorptive agent.[5] AFF are usually preceded by thigh or groin pain. If such symptoms are present, full bilateral femur x-rays are advised to exclude the presence of an incomplete AFF. If features of an early AFF are present, the antiresorptive therapy should be discontinued and consideration should be given to using teriparatide.[5]

**Osteonecrosis of the Jaw (ONJ):

This is a rare complication of antiresorptive therapy with an incidence of 0.01%–0.001%. Risk factors for ONJ include chemotherapy, major oral surgery or dental trauma, periodontal disease, diabetes, glucocorticoid therapy, long term bisphosphonate or denosumab therapy, as well as antiangiogenic therapy.[6] Patients with ONJ require close monitoring and treatment by a dentist and oral surgeon.[6] The antiresorptive therapy should be discontinued if ONJ develops until the surgical site has fully healed.[6]

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3. Health Canada Product Monographs.
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