



Osteoporosis: Diagnosis, Treatment and Fracture Prevention

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Scope

Osteoporosis (OP) is a significant risk factor for fragility fracture. This guideline summarizes current recommendations for risk estimation, diagnosis, prevention, and treatment of osteoporosis and related fractures in a general adult population (age 19+ years).

► Diagnostic Code: 733.0: Osteoporosis

The following steps are outlined in this guideline (See Algorithm 1):

1. Assessment of Risk
2. Risk Stratification
3. Lifestyle Advice (regardless of risk level)
4. Therapy
5. Monitoring

Step 1: Assessment of Risks of Osteoporosis or Fracture

There are two aspects of risk that can be explored by identifying known risk factors:

- Risk of developing OP (Section 1.1); and
- Risk of fracture within 10 years (Section 1.2).

► 1.1 Risk of Developing Osteoporosis

Family History	<ul style="list-style-type: none"> • Parental history of hip fracture
Medical History	<ul style="list-style-type: none"> • Advanced age • Frailty* • Hyperthyroidism (including iatrogenic) or hyperparathyroidism • Celiac and other malabsorption syndromes • BMI < 20 kg/m² or weight loss • Medication history, particularly chronic glucocorticoid use** (see Appendix A) • Rheumatoid arthritis • Chronic liver or kidney disease
For Men	<ul style="list-style-type: none"> • Androgen deficiency (primary or secondary)

* See www.BCGuidelines.ca – Frailty in Older Adults – Early Identification and Management for definition

** i.e., ≥ 3 months (consecutive) therapy at a dose of prednisone ≥ 7.5 mg per day or equivalent

Risk of Developing Osteoporosis *continued*

For Women	<ul style="list-style-type: none"> • Estrogen deficiency (primary or secondary) • Early menopause (< 45 years), including surgical • Cessation of menstruation for 6-12 consecutive months (excluding pregnancy, menopause or hysterectomy)
Lifestyle	<ul style="list-style-type: none"> • Smoking (current or former) • Daily alcohol consumption > 3 units (1 unit = 5 oz wine, 1.5 oz spirits, 12 oz beer) • Caffeine intake > 4 cups/day • Inadequate calcium and vitamin D intake • Lack of sunlight exposure (may cause vitamin D deficiency) • Prolonged immobility and lack of weight-bearing exercise

► 1.2 Calculate the 10-year Fragility Fracture Risk

The fracture risk of a patient can be estimated as Low (< 10% in next 10 years), Moderate (10 - 20% in next 10 years), or High (> 20% in next 10 years) using known risk factors and a clinical assessment tool. There are two tools available to calculate 10-year fracture risk. One is the FRAX® (see Appendix C), developed by the World Health Organization (WHO), and the other is produced by the Canadian Association of Radiologists and Osteoporosis Canada (CAROC).¹⁻³

FRAX®* employs a web-based (www.shef.ac.uk/FRAX) calculator that includes a number of risk factors; including bone mineral density (BMD) which is optional. The CAROC paper-based risk table takes into account age, sex, fracture history and glucocorticoid use to determine a ten-year absolute risk of all osteoporotic fractures but BMD is required to calculate risk.

► 1.3 Falls and the Risk of Fracture (also see “Falls prevention strategies” in Section 4.1)

Over and above the risk of OP, other clinical factors predict those at increased risk of fracture, including:⁴

• Previous fragility fracture:

- Fractures sustained in falls from standing height or less, in which bone damage is disproportional to the degree of trauma. Includes vertebral compression fractures not attributable to previous major trauma, which may be suggested by height loss.
- Where other disease has been ruled out, patients with low trauma fragility fractures may have OP and are at **high** risk of other fragility fractures within 10 years.
- Fractures of the hip, vertebra, humerus, and wrist are most closely associated with OP and increased future fracture risk whereas those of the skull, fingers, toes, and patella fractures are not.

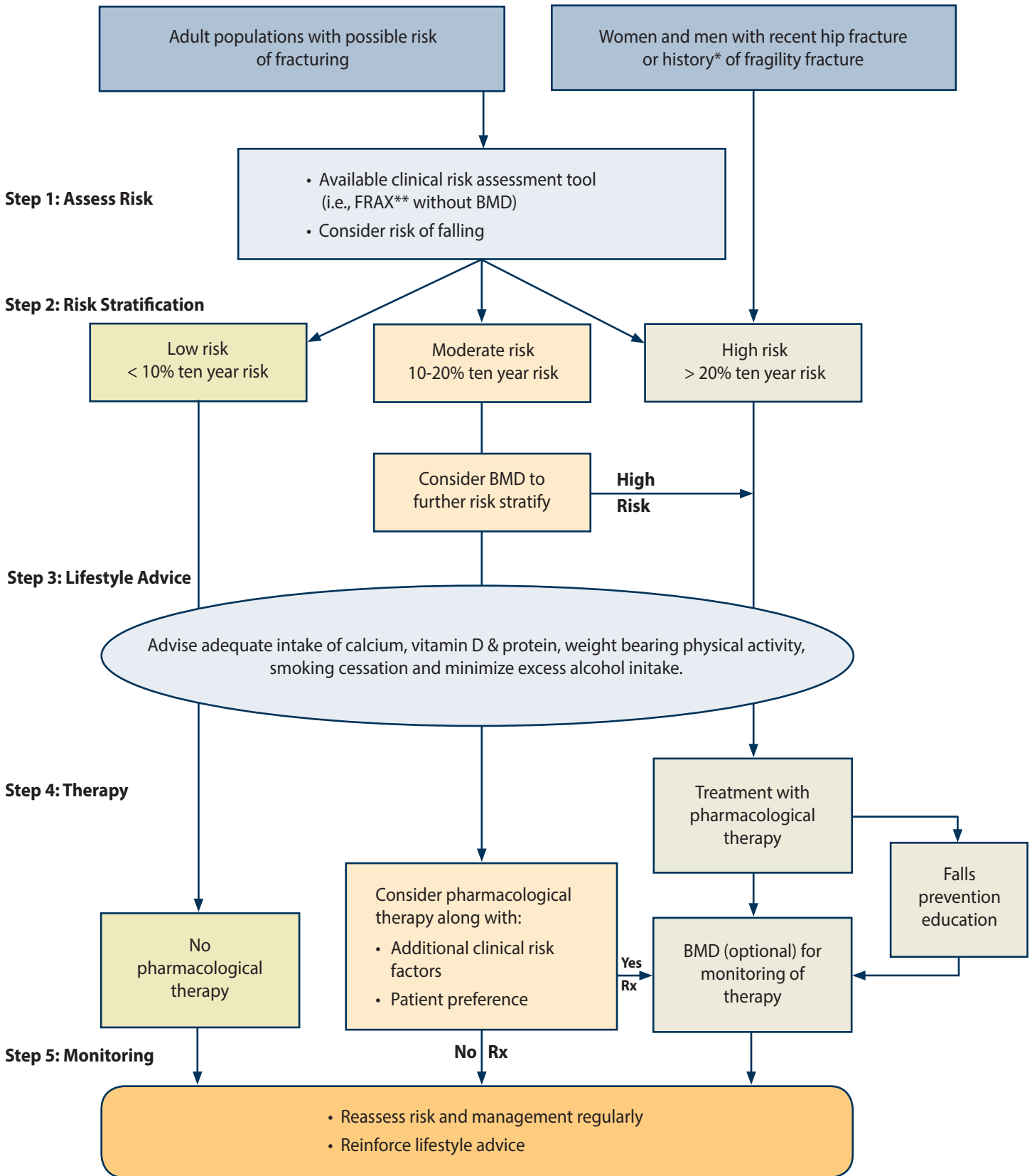
• A fall in the last year

• High risk of falling as determined by:

- Physical frailty or significant weight loss (loss of muscle mass). Refer to BCGuidelines.ca - Frailty in Older Adults – Early Identification and Management.
- A global assessment of functional mobility like the timed ‘Up and Go’ test⁵
- Poor strength
- Balance problems
- Gait problems
- Dizziness
- Poor vision
- Psychotropic medications
- Cardiac insufficiency
- Urinary frequency and toileting issues
- Other validated tests⁶

* Although the FRAX® tool has been developed for prognosis and is not prescriptive, this guideline suggests the use of a tool to identify all risk groups for whom treatment will depend on individual clinical parameters and specific therapeutic indications listed in Steps 3 and 4 (e.g., age, previous vertebral fracture, T score, where appropriate).

Algorithm 1: Recommendations for evaluation and management of osteoporotic and fragility fracture risk



* Review available lateral thoracolumbar x-ray for evidence of fragility fracture

** FRAX not applicable at < 40 years

Step 2: Risk Stratification

► 2.1 Levels of Risk

Fracture risk estimation, using known risk factors and a clinical assessment tool, can be used to categorize patients as Low (< 10% in next 10 years), Moderate (10 – 20 % in next 10 years) or High (> 20% in 10 years) fracture risk.

► 2.2 Risk stratification using Dual-Energy X-Ray Absorptiometry (DXA) BMD

BMD is not indicated unless patients (men and women) are age > 65 years, at moderate risk of fracture (10 - 20% 10-year risk), and results are likely to alter patient care.^{7,8,9} There has been a shift away from BMD and towards emphasizing multivariate fracture risk using a risk calculation model (FRAX® or CAROC). BMD is not recommended to be used alone as it explains only a portion of fracture risk. If a clinical risk assessment tool suggests moderate fracture risk category, consider BMD testing to further stratify risk and guide treatment; if high risk, consider treatment.

BMD is NOT indicated for:

- Investigation of chronic back pain
- Investigation of exaggerated dorsal kyphosis (fractures are best excluded by radiography)
- Screening women aged < 65 years, unless significant clinical risk factors have been identified
- Part of a routine evaluation around the time of menopause
- Confirmation of OP when a fragility fracture occurs

T-score classification (number of standard deviations above or below the mean peak BMD):⁶

- Normal: T is -1 and above
- Osteopenia: T is -1.1 to -2.4
- OP: T -2.5 and below
- Established or severe OP: T is -2.5 or below and one or more prevalent low-trauma fractures

DXA is a quantitative test and it requires careful quality assurance. Structural abnormalities, positioning, artifacts (e.g., body weight), and analysis can significantly affect results.⁹

► 2.3 Laboratory testing (bone turnover markers and vitamin D)

Indications: Blood tests are not indicated to make an OP diagnosis or determine risk. Blood tests are only useful to establish or to rule out secondary causes of OP. Refer to *Appendix B - Testing for Suspected Secondary Causes of OP in Selected Patients*.

Bone turnover markers: At present no single or combined assay is recommended except in specific circumstances.¹⁰ Assays have a proven use in research studies involving large samples but they are complex and variation is too great to be useful at the individual level.

Vitamin D: Routine testing is not required to diagnose OP or before/after starting vitamin D supplementation. Refer to *BCGuidelines.ca - Vitamin D Testing Protocol*.

Step 3: Lifestyle Advice (Regardless of Risk Level)

Nutrition: Help reduce fracture risk via adequate daily calcium and vitamin D. Note: doses recommended below for calcium and vitamin D represent total intake from diet and supplements.

- Calcium: Recommend 1000-1200 mg elemental calcium per day including supplements, if necessary.¹¹⁻¹³ See *OP Patient Guide*. Advise patients not to exceed recommended amounts, as evidence does not support higher doses of calcium supplementation.¹⁴ In addition, a 2010 meta-analysis reported an increase in myocardial infarction in men and women given calcium supplementation (i.e., ≥ 500 mg elemental calcium per day) versus placebo. Note: this meta-analysis studied calcium supplementation alone and not in combination with vitamin D and the increased risk was associated with dietary intakes of greater than 800 mg (approximately) elemental calcium per day.¹⁵
- Vitamin D: Recommend 800-1000 IU per day of vitamin D₃, including supplements if necessary, to adults over the age of 50.¹⁷ Higher doses (i.e., 2000 IU per day) may be needed in some cases and is considered safe.¹⁶ See *Patient Guide and BCGuidelines.ca - Vitamin D Testing Protocol*.
- Protein: Recommend an adequate intake of dietary protein (1g/kg/day).²¹

Exercise: Regular weight-bearing and muscle-strengthening reduce the risk of falls and fractures by improving agility, strength, posture, and balance, as well as general health benefit.

Smoking: Tobacco products are detrimental to the skeleton as well as to overall health.

Alcohol: Intake of 3 or more units per day is detrimental to bone health and increases the risk of falling.

Step 4: Therapy

► 4.1 Falls Prevention Strategies

Falls prevention is the first line of treatment (versus OP medications) for those at high risk for falling.

Items to identify falls risk and reduce falls (review with patient at least annually):

- Ask about falls in the past year
- Assess the time taken to stand from sitting
- Assess muscle strength, balance, and gait by watching the patient walk and move
- Check and correct postural hypotension and cardiac arrhythmias
- Evaluate any neurological problems
- Review prescription meds that may affect balance
- Provide a checklist for improving safety at home, i.e., The Safe Living Guide-A Guide to Home Safety for Seniors, www.phac-aspc.gc.ca

Consider referral to geriatric medicine, a falls prevention program, homecare, occupational therapy or physical therapy.

► 4.2 Pharmacological Therapy

(See also Appendix D - Prescription Medication Table for Osteoporosis)

Medications may be recommended, depending on fracture risk assessment. Manage based on degree of risk:
Section 4.1: Items to identify falls risk and reduce falls (review with patient at least annually)

Low risk: Generally require lifestyle advice and daily intake of calcium and vitamin D.²²

Moderate risk: Medication is usually not necessary but can be considered in addition to lifestyle advice and adequate daily intake of calcium and vitamin D. When considering medications, take into account patient preference and additional clinical risk factors (Table 3).²²

Additional Clinical Risk Factors:

- Vertebral fractures (> 25% height loss with end-plate disruption)
- Men receiving androgen deprivation therapy for prostate cancer
- Women receiving aromatase inhibitor therapy for breast cancer
- Long-term or repeated systemic corticosteroid use (oral or parenteral) that does not meet the conventional criteria for recent prolonged systemic corticosteroid use (i.e., ≥ 3 months (consecutive) therapy at a dose of prednisone ≥ 7.5 mg per day or equivalent)
- Recurrent falls

Consider referral to geriatric medicine, a falls prevention program, homecare, occupational therapy or physical therapy.

High risk: Consider medication in addition to lifestyle advice and adequate daily intake of calcium and vitamin D.²³ Patients with hip and other fragility fractures are considered to be high risk. Individuals can be considered as candidates for medication after implementing fall prevention strategies and providing lifestyle advice (see Step 3).

OP medications available in Canada include (alphabetically): alendronate, calcitonin, denosumab, estrogens (with or without progesterone), etidronate, raloxifene, risedronate, teriparatide, and zoledronic acid.²³ Data are insufficient to determine if one drug class is superior to another for fracture prevention.²² Medication adherence (compliance and persistence) is required for fracture reduction, yet rates of adherence to OP treatments are low.²⁴

- Consider barriers to adherence including mode of administration, dosing regimens, side effects, and cost (see Appendix D - Prescription Medication Table for Osteoporosis).
- Combine adequate calcium and vitamin D with all pharmacological treatments. (See Step 3)

For information regarding PharmaCare coverage of these medications please refer to Appendix D.

► 4.2.1 Bisphosphonates

These drugs preserve bone by decreasing rate of bone turnover and enhancing bone mineralization.^{22,23,25,26,30}

To date, this class of drugs (specifically alendronate, risedronate, and zoledronic acid) has the largest body of randomized controlled trial evidence for osteoporosis. Superiority of one bisphosphonate over another has not been conclusively shown. Most studies have been in post-menopausal women and the optimal duration of therapy is unknown (to date most studies, with fractures as an endpoint, have had an average five years duration).

Bisphosphonates	Points to Consider
Alendronate (oral) & Risedronate (oral)	<ul style="list-style-type: none"> • Post-menopausal women: prevents vertebral, non-vertebral, and hip fractures^{31,32} • Men: Some evidence of decreased risk of vertebral fractures;^{27,28} some evidence of increased hip bone density, but no significant hip fracture reduction • Glucocorticoid induced osteoporosis (GIO): Some evidence of decreased vertebral fracture risk
Etidronate (oral)	<ul style="list-style-type: none"> • Post-menopausal women: prevents vertebral fractures³³ • GIO: maintains BMD in GIO although data is limited; Health Canada approved indication is for GIO prevention only (not treatment)²⁹
Zoledronic acid (intravenous)	<ul style="list-style-type: none"> • Post-menopausal women: prevents vertebral, non-vertebral, and hip fractures³⁴ • Men: Data is limited; Some evidence of decreased risk of vertebral and non-vertebral fractures (study included those with prior hip fracture and only 24% men),³¹ • GIO: maintains BMD • Cost effectiveness may limit use • Consider for high-risk patients who are unable to tolerate oral therapy or have poor adherence

► 4.2.2 Selective Estrogen Receptor Modulators [SERMs]: Raloxifene

SERMs can act as estrogen agonists or antagonists. Raloxifene acts as an estrogen agonist on bone tissue.

The estrogenic effects of raloxifene on bone in postmenopausal women decrease bone turnover.^{22,25,26,35}

Drug	Points to Consider
Raloxifene (oral)	<ul style="list-style-type: none"> • Post-menopausal women: reduces the incidence of vertebral fractures • May be considered in post-menopausal women who are unable to tolerate bisphosphonates and have no history of thromboembolic disease • Caution: Significantly increases the risk of venous thromboembolic disease and stroke

► 4.2.3 RANK Ligand Inhibitor: Denosumab

Denosumab is an injectable monoclonal antibody to the receptor activator of nuclear factor- κ B ligand (RANKL).

It inhibits bone resorption by osteoclasts by blocking the interaction between RANKL and its receptor RANK on the surface of osteoblasts.^{35,39,40}

Drug	Points to Consider
Denosumab (subcutaneous)	<ul style="list-style-type: none"> • Postmenopausal women: prevents vertebral, non-vertebral, and hip fractures • Cost and lack of long term safety data may limit use

► 4.2.4 Synthetic Parathyroid Hormone: Teriparatide

Teriparatide is an anabolic agent that improves bone quality, quantity, and increases bone strength.^{22-24,30,36}

Drug	Points to Consider
Teriparatide (subcutaneous)	<ul style="list-style-type: none"> • Post-menopausal women: prevents vertebral and non-vertebral fractures in postmenopausal women with severe OP • Men: increases BMD; currently no fracture data available • GIO: Some evidence of benefit in the treatment of GIO • Cost and need for daily subcutaneous injection may limit use • Consider for patients at increased risk of fracture or lack of response to other therapies • Maximum lifetime exposure is 24 months • Bisphosphonates must be discontinued prior to treatment • Gains in BMD decline once treatment with teriparatide is discontinued; consider anti-resorptive therapy after completing treatment course

► 4.2.5 Calcitonin Peptides: Calcitonin Salmon

Calcitonin Salmon is an inhibitor of bone resorption; available in parenteral and nasal spray formulations. Although calcitonin does not build bone, in women > 5 years beyond menopause, it appears to slow bone loss and increase spinal bone density.^{26,37,38}

Drug	Points to Consider
Calcitonin (nasal)	<ul style="list-style-type: none"> • Post-menopausal women: Reduces incidence of vertebral fractures however evidence for benefit is limited • Consider as an alternative when other more effective drugs cannot be used • Effective in decreasing acute pain associated with vertebral osteoporotic fractures • Calcitonin injection is currently not approved for the treatment of OP; it is sometimes prescribed for patients who have pain due to acute vertebral fractures (See Appendix D - Prescription Medication Table for Osteoporosis) • The intranasal spray formulation is used for OP. However, Health Canada is currently assessing the possibility of an increased risk of cancer with long-term use of calcitonin

► 4.2.6 Hormone Replacement Therapy [HRT] (estrogen with or without progesterone)

HRT is primarily indicated for the management of moderate to severe menopausal symptoms in women.^{22,24-26,35}

A beneficial effect has been seen on BMD and fracture risk due to the significant anti-resorptive activity of estrogen.

Drug	Points to Consider
HRT (oral or transdermal)	<ul style="list-style-type: none"> • Post-menopausal women: Shown to prevent vertebral, hip and non-vertebral fractures • Is not recommended for the sole indication of OP prevention and for long term use for this indication; consider benefits versus risks (See Appendix D) • May be appropriate for OP prevention when it is already being used for the management of menopausal symptoms

Step 5: Monitoring

► 5.1 Clinical Re-assessment

Re-assess patients as clinically indicated to monitor side effects, compliance, height loss, incident fractures, and risk of falls, which may alter patient management.

► 5.2 Follow-up BMD Measurements

There is insufficient evidence to recommend a testing frequency for patients not taking OP medications. Based on a patient's risk profile, BMD retesting may be indicated in 3-10 years.

For patients on OP medication, repeat BMD examinations are not justified based on current evidence. If a BMD is to be done, any changes would be difficult to detect prior to 3 years.⁴¹ Consider more frequent testing in specific high risk situations (e.g., multiple risk factors, or receiving ≥ 7.5 mg prednisone daily or its equivalent for 3 months consecutively who require a baseline examination and repeat scans at 6-month intervals while on treatment).

Women > 65 years will usually lose bone. A stable BMD value on treatment may reflect successful treatment and appreciable decreases in fracture risk may accompany minor increases in BMD. Minor increases in BMD may also be due to testing variance. Ideally, any follow-up BMD testing is recommended to be done on the same DXA machine and at the same time of year.

► Patient Education

A patient guide to OP is included with this guideline. Further information for patients about OP is available at Health Link BC (www.healthlinkbc.ca).

Resources

► References

- 1 Kanis JA, Johnell O, Oden A, et al. FRAX and the assessment of fracture probability in men and women from the UK. *Osteoporos Int.* 2008;19(4):385-97.
- 2 Kanis JA, Compston J, Cooper A, et al. Guidelines for the diagnosis and management of osteoporosis in postmenopausal women and men from the age of 50 years in the UK. *Maturitas.* 2009 Feb 20;62(2):105-8.
- 3 Siminoski K, Leslie WD, Frame H, et al. Recommendations for bone mineral density reporting in Canada. *Can Assoc Radiol J.* 2005 June;56(3):178-88.
- 4 Papaioannou A, Joseph L, Ioannidis G, et al. Risk factors associated with incident clinical vertebral and nonvertebral fractures in postmenopausal women: the Canadian Multicentre Osteoporosis Study (CaMos). *Osteoporos Int.* 2005;16(5):568-78.
- 5 Podsiadlo, D, Richardson, S. The timed 'Up and Go' Test: a test of basic functional mobility for frail elderly persons. *J Am Geriatr Soc.* 2000 Jan;48(1):104-5.
- 6 Lord SR, Menz HB, Tiedemann A. A physiological profile approach to falls risk assessment and prevention. *Phys Ther.* 2003;83(3):237-52.
- 7 National Osteoporosis Foundation, Clinician's guide to the prevention and treatment of osteoporosis, c2008 [updated 2010 Jan.; cited April 1, 2010]. Available from: http://www.nof.org/professionals/pdfs/NOF_ClinicianGuide2009_v7.pdf
- 8 Osteoporosis: review of the evidence for prevention, diagnosis and treatment and cost-effectiveness analysis. *Osteoporos Int.* 1998;8 Suppl 4:S7-80.
- 9 Khan AA, Brown JP, Kendler DL, et al. The 2002 Canadian bone densitometry recommendations: take-home messages. *CMAJ.* 2002 Nov;12;167(10):1141-5.
- 10 Garnero P, Mulleman D, Munoz F, et al. Long-term variability of markers of bone turnover in postmenopausal women and implications for their clinical use: the OFELY study. *J Bone Miner Res.* 2003 Oct;18(10):1789-94.
- 11 Health Canada. Dietary reference intakes: reference values for elements. C2005 [cited March 1, 2011]. Available from: http://www.hc-sc.gc.ca/fn-an/nutrition/reference/table/ref_elements_tbl-eng.php
- 12 Society of Obstetricians and Gynecologists Canada. Bone Health. *JOGC.* 2009;31:S34-41.
- 13 National Institute of Health, Office of Dietary Supplements. C2010 [cited June 11, 2010]. Available from: <http://ods.od.nih.gov/factsheets/calcium.asp>.
- 14 Tang B, Eslick G, Nowson C, et al. Use of calcium or calcium in combination with vitamin D supplementation to prevent fracture and bone loss in people aged 50 years and older: a meta-analysis. *Lancet* 2007;370:657-66.

- 15 Bolland MJ, Avenell A, Baron JA, et al. Effect of calcium supplements on risk of myocardial infarction and cardiovascular events: meta-analysis. *BMJ* 2010;341:c3691
- 16 Vieth R. Vitamin D toxicity, policy and science. *J Bone Miner Res.* 2007;22:S2;V64-V68.
- 17 Hanley DA, Cranney A, Jones G, et al. Vitamin D in adult health and disease: a review and guideline statement from Osteoporosis Canada. *CMAJ.* 2010 Jul 19. [Epub ahead of print]
- 18 Institute of Medicine. Vitamin D. In: *Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride.* Washington, DC: National Academy Press, 1997; p.250-87.
- 19 Briot K, Audran M, Cortet B, et al. Vitamin D: skeletal and extra skeletal effects; recommendations for good practice. *Presse Med.* 2009;38:43-54.
- 20 Cranney A, Horsley T, O'Donnell S, et al. Effectiveness and safety of vitamin D in relation to bone health. *Evid Rep Technol Assess (Full Rep).* 2007 Aug;(158):1-235. Review.
- 21 Hannan MT, Tucker KL, Dawson-Hughes B, et al. Effect of dietary protein on bone loss in elderly men and women: The Framingham Osteoporosis Study. *J Bone Miner Res.* 2000;15(12):2504-12.
- 22 MacLean C, Newberry S, Maglione M, et al. Systematic review: comparative effectiveness of treatments to prevent fractures in men and women with low bone density or osteoporosis. *Ann Intern Med.* 2008;148:197-213.
- 23 Compendium of Pharmaceuticals and Specialties: The Canadian Drug Reference for Health Professionals. Toronto, Ontario;2010.
- 24 Stroup J, Kane M, Abu-Baker A. Therapy Update: Teriparatide in the treatment of osteoporosis. *Am J Health-Sys Pharm.* 2008;65(6):532-9.
- 25 Marcus R, Wong M, Heath H III, et al. Antiresorptive treatment of postmenopausal osteoporosis: comparison of study designs and outcomes in large clinical trials with fracture as an endpoint. *Endocr Rev.* 2002;23:16-37.
- 26 Reid R, Blake J, Abramson B, et al. Menopause and osteoporosis update 2009. *JOGC.* 2009;31(Supp 1):S1-49. Available from: http://www.sogc.org/guidelines/documents/Menopause_JOGC-Jan_09.pdf
- 27 Orwoll E, Ettinger M, Weiss S, et al. Alendronate for the treatment of osteoporosis in men. *N Engl J Med.* 2000;343:604-610.
- 28 Ringe JD, Faber H, Dorst A. Alendronate treatment of established primary osteoporosis in men: Results of a 2-year prospective study. *J of Clin Endocrinol Metab.* 2001;86:5252-5255.
- 29 Adachi JD, Bensen WG, Brown J, et al. Intermittent etidronate therapy to prevent corticosteroid-induced osteoporosis. *N Engl J Med.* 1997;337:382-387.
- 30 Boucher M, Murphy G, Coyle D, et al. Bisphosphonates and teriparatide for the prevention of osteoporotic fractures in postmenopausal women [Technology overview no 22]. 2006. Ottawa, Canadian Agency for Drugs and Technologies in Health.
- 31 Alendronate for the primary and secondary prevention of osteoporotic fractures in postmenopausal women. Wells, George A. Cranney, Ann. Peterson, Joan. Boucher, Michel. Shea, Beverley. Welch, Vivian. Coyle, Doug. Tugwell, Peter. Cochrane Musculoskeletal Group Cochrane Database of Systematic Reviews. 2, 2011..
- 32 Risedronate for the primary and secondary prevention of osteoporotic fractures in postmenopausal women. Wells, George A. Cranney, Ann. Peterson, Joan. Boucher, Michel. Shea, Beverley. Welch, Vivian. Coyle, Doug. Tugwell, Peter. Cochrane Musculoskeletal Group Cochrane Database of Systematic Reviews. 4, 2010.
- 33 Etidronate for the primary and secondary prevention of osteoporotic fractures in postmenopausal women. Wells, George A. Cranney, Ann. Peterson, Joan. Boucher, Michel. Shea, Beverley. Welch, Vivian. Coyle, Doug. Tugwell, Peter. Cochrane Musculoskeletal Group Cochrane Database of Systematic Reviews. 4, 2010.
- 34 Intravenous zoledronate for postmenopausal osteoporosis. Albergaria, Ben-Hur. Gomes Silva, Brenda Nazare. Atallah, Alvaro N. Fernandes Moca Trevisani, Virginia. Cochrane Musculoskeletal Group Cochrane Database of Systematic Reviews. 1, 2009.
- 35 The North American Menopause Society: NAMS Continuing medical education activity; Management of Osteoporosis in Postmenopausal Women: 2010 Position Statement 2010;17(1):23-56. Available from: <http://www.medscape.com/viewarticle/714984>
- 36 Orwoll E, Scheele WH, Paul S, et al. The effect of teriparatide [human parathyroid hormone (1-34)] therapy on bone density in men with osteoporosis. *J Bone Miner Res.* 2003;18(1):9-17.
- 37 Ishida Y, Kawai S. Comparative efficacy of hormone replacement therapy, etidronate, calcitonin, alfacalcidol, and vitamin K in postmenopausal women with osteoporosis: The Yamaguchi Osteoporosis Prevention Study. *Am J Med.* 2004;117:549-55.
- 38 Tóth E, Csopor E, Mészáros S, et al. The effect of intranasal salmon calcitonin therapy on bone mineral density in idiopathic male osteoporosis without vertebral fractures – an open label study. *Bone.* 2005;36:47-51.
- 39 Reid IR, Miller PD, Brown JP, et al. Effects of denosumab on bone histomorphometry: the FREEDOM and STAND studies. *J Bone Miner Res.* 2010;10:2256-65.
- 40 Cummings SR, San Martin J, McClung MR, et al. Denosumab for prevention of fractures in postmenopausal women with osteoporosis. *N Engl J Med.* 2009;361(8):756-65.
- 41 Compston J. Monitoring osteoporosis treatment. *Best Pract Res Clin Rheumatol.* 2009 Dec;23:781-8.

► Resources

- BC Guidelines: www.bcguidelines.ca
 - Frailty in Older Adults – Early Identification and Management
 - Vitamin D Testing Protocol
- BC Health and Seniors Information Line 1-800-465-4911, Victoria 250-952-1742 and website www.seniorsbc.ca/healthcare/
- Injury Prevention and Mobility Laboratory, Simon Fraser University www.sfu.ca/ipml
- Centre for Hip Health and Mobility, University of British Columbia www.hiphealth.ca
- Public Health Agency of Canada, Falls Prevention www.phac-aspc.gc.ca/seniors-aines/publications/public/injury-blessure/pathways-voie/index-eng.php
- BC Ministry of Health, Seniors' Falls Prevention www.health.gov.bc.ca/prevention/fallprevention.html

► List of Abbreviations

BMD	bone mineral density	GIO	glucocorticoid induced osteoporosis
BMI	body mass index	HRT	hormone replacement therapy
DXA	dual-energy x-ray absorptiometry	IU	international units
FDA	Food & Drug Administration (U.S.A)	OP	osteoporosis

► Appendices

Appendix A: Examples of Medications that May Contribute to Bone Loss

Appendix B: Testing for Suspected Secondary Causes of OP in Selected Patients

Appendix C: Using the FRAX® Calculator to Assess Absolute Fracture Risk

Appendix D: Prescription Medication Table for Osteoporosis

This guideline is based on scientific evidence current as of the Effective Date.

This guideline was developed by the Guidelines and Protocols Advisory Committee, approved by the British Columbia Medical Association, and adopted by the Medical Services Commission.

THE GUIDELINES AND PROTOCOLS ADVISORY COMMITTEE

The principles of the Guidelines and Protocols Advisory Committee are to:

- encourage appropriate responses to common medical situations
- recommend actions that are sufficient and efficient, neither excessive nor deficient
- permit exceptions when justified by clinical circumstances

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Disclaimer

The Clinical Practice Guidelines (the "Guidelines") have been developed by the Guidelines and Protocols Advisory Committee on behalf of the Medical Services Commission. The Guidelines are intended to give an understanding of a clinical problem, and outline one or more preferred approaches to the investigation and management of the problem. The Guidelines are not intended as a substitute for the advice or professional judgment of a health care professional, nor are they intended to be the only approach to the management of clinical problem.



Osteoporosis

Appendix A – Examples of Medications That May Contribute to Bone Loss*

ANTICOAGULANTS - heparin, warfarin

ANTICONVULSANTS - carbamazepine, phenytoin

AROMATASE INHIBITORS - anastrozole, letrozole, exemestane

BARBITUATES - phenobarbital

CHEMOTHERAPEUTIC/CYTOTOXIC AGENTS - various

CYCLOSPORINE

DEPO-MEDROXYPROGESTERONE

GLUCOCORTICOIDS ** - various

GONADOTROPIN RELEASING HORMONE AGONISTS - buserelin, goserelin, leuprolide acetate

LITHIUM

PROTON PUMP INHIBITORS

SELECTIVE SEROTONIN REUPTAKE INHIBITORS - various

TACROLIMUS

THIAZOLIDINEDIONES - pioglitazone, rosiglitazone

THYROID HORMONES IN EXCESS

*This is not a complete list of medications.

**Particularly chronic glucocorticoid use i.e., ≥ 3 months of consecutive therapy at a dose of prednisone ≥ 7.5 mg per day or equivalent

References

Briot K, Roux C. Drug-induced osteoporosis: Beyond glucocorticoids. *Current Rheumatology Reports*. 2008;10:102-9.

Kaunitz AM, Arias R, McClung M. Bone density recovery after depot medroxyprogesterone acetate injectable contraception use. *Contraception*. 2008;77:67-76.

National Osteoporosis Foundation. Clinician's guide to prevention and treatment of osteoporosis. c2008 [updated 2010 Jan; cited 2010 June 15]. Available from http://www.nof.org/professionals/pdfs/NOF_ClinicianGuide2009_v7.pdf

Qaseem A, Snow V, Shekelle P, et al. Pharmacologic treatment of low bone density or osteoporosis to prevent fractures: A clinical practice guideline from the American College of Physicians. *Annals of Internal Medicine* 2008; 149:404-15.

Sweet MG, Sweet JM, Jeremiah MP, Galazka SS. Diagnosis and treatment of osteoporosis. *Am Fam Physician*. 2009;79(3):193-200,201-202.

Targownik LE, Lix LM, Metge CJ, et al. Use of proton pump inhibitors and risk of osteoporosis-related fractures. *CMAJ*. 2008;179(4):319-26.



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Appendix B – Testing for Suspected Secondary Causes of OP in Selected Patients*

If Clinically Suspected	Tests May Include
Bone marrow malignancy	CBC
Malabsorption	CBC, calcium (low), 25-hydroxyvitamin D
Hyperthyroidism	Thyroid-stimulating hormone, calcium (high)
Hypogonadism	FSH & total testosterone (men)
Hyperparathyroidism	Albumin-corrected serum calcium**
Multiple myeloma	Serum protein electrophoresis
Celiac	Celiac serology

* This is not a complete list of etiology or tests.

** Corrected Ca = Ca.measured + (40-alb) X 0.02, [Ca in mmol/L; albumin in g/L]



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Appendix C – Using the FRAX Calculator to Assess Absolute Fracture Risk

Access online at: <http://www.shef.ac.uk/FRAX/>

The screenshot shows the FRAX WHO Fracture Risk Assessment Tool interface. At the top, it says 'FRAX® WHO Fracture Risk Assessment Tool'. Below that, there are navigation links: Home, Calculation Tool, Paper Charts, FAQ, and References. The language is set to English. The main heading is 'Calculation Tool'. Below this, it says 'Please answer the questions below to calculate the ten year probability of fracture with BMD.' The interface is for 'Canada'. There are input fields for 'Name/ID' and a link 'About the risk factors'. The questionnaire consists of 12 questions:

- Age (between 40-90 years) or Date of birth: Age (Y, M, D) and Date of birth (Y, M, D) fields.
- Sex: Male (selected) or Female.
- Weight (kg): Input field.
- Height (cm): Input field.
- Previous fracture: No (selected) or Yes.
- Parent fractured hip: No (selected) or Yes.
- Current smoking: No (selected) or Yes.
- Glucocorticoids: No (selected) or Yes.
- Rheumatoid arthritis: No (selected) or Yes.
- Secondary osteoporosis: No (selected) or Yes.
- Alcohol 3 or more units per day: No (selected) or Yes.
- Femoral neck BMD (g/cm²): Select DXA (dropdown) and input field. Includes 'Clear' and 'Calculate' buttons.

On the right side, there are two conversion tools: 'Weight Conversion' (Pounds to Kgs) and 'Height Conversion' (Inches to Cms), both with input fields and 'Convert' buttons.

- From "Calculation Tool" menu, choose "Canada " model
- Enter patient's age or date of birth
- Enter patient's sex
- Enter patient's weight
- Enter patient's height
- Choose "no" or "yes" for risk factors 5-11
- If BMD score available (#12), select type of DXA scanner and enter femoral neck or total hip BMD as g/cm²
(Note: A BMD test is not required to estimate fracture risk)
- Click on "Calculate"
- The 10-year hip fracture probability estimate to can be used to determine type of treatment based on level of risk



Appendix D: Pharmacological Therapy for Osteoporosis ^{21-23, 28}

Generic Name	Strength (Brand name)	Route	Adult dose	Approximate annual cost of therapy ^A	PharmaCare coverage	Therapeutic considerations ^B
Bisphosphonates						
Alendronate	Tablets: 10 mg and 70 mg (Fosamax [®] , G)	Oral	10 mg once daily	\$393 (G) \$778	Limited Coverage	<p>Administration: swallow whole with full glass of water 30 min before first food of day; patients must not lie down for at least 30 min after dose</p> <p>To enhance absorption and decrease gastrointestinal side effects emphasize proper administration</p> <p>Contraindications: renal impairment [i.e., CrCl < 30 mL/min], hypocalcemia</p> <p>Precautions: upper gastrointestinal problems</p> <p>Adverse effects: abdominal pain, dyspepsia, nausea, esophagitis, esophageal ulcers, joint/muscle pain [may need to discontinue if persists], ocular inflammation, osteonecrosis of the jaw (ONJ) [more commonly reported with higher doses of bisphosphonates given intravenously i.e., as used in oncology], atypical femoral fractures [although rare, seems to be more common with long term bisphosphonate use and can present as thigh or groin pain], esophageal cancer [causality unknown], atrial fibrillation [data is conflicting, causality unknown]</p>
			70 mg once weekly	\$249 (G) \$560		
Alendronate plus cholecalciferol (Vitamin D ₃)	Tablets: 70 mg/5600 IU and 70 mg/2800 IU (Fosavance [®])	Oral	70 mg/ 5600 IU once weekly 70 mg/ 2800 IU once weekly	\$249	Limited Coverage	<p>Note: combination product containing vitamin D – adjust supplementation as needed</p> <p>See alendronate therapeutic considerations</p>
Etidronate plus calcium carbonate	Tablets: 400 mg etidronate; 1250 mg calcium carbonate, (Didrocal [®] , G)	Oral	One tablet once daily	\$92 (G) \$182	Regular Coverage	<p>Note: calcium carbonate 1250 mg = 500 mg elemental calcium</p> <p>Administration [etidronate]: swallow whole with full glass of water at bedtime 2 hours before or after eating; 90 day cycle: 400 mg etidronate once daily for 14 days followed by 1250 mg calcium carbonate daily for 76 days; then repeat</p> <p>See alendronate therapeutic considerations</p>
Risedronate	Tablets: 5 mg, 35 mg, and 150 mg (Actonel [®] , G)	Oral	5 mg once daily	\$302 (G) \$711	Limited Coverage ^C	See alendronate therapeutic considerations
			35 mg once weekly	\$229 (G) \$541		
			150 mg once monthly	\$635		
Zoledronic Acid	Solution for injection: 5 mg/ 100 mL (Aclasta [®])	Intravenous (IV)	5 mg once yearly	\$671	Limited Coverage	<p>Administration: IV infusion given over at least 15 minutes</p> <p>Precautions: ensure patient is well hydrated [at least 500 mL fluid prior to and following administration]</p> <p>Adverse effects: transient flu like syndrome, atrial fibrillation [uncommon, data conflicting], gastrointestinal effects [less than what is seen with oral bisphosphonates], renal dysfunction</p> <p>Also see alendronate therapeutic considerations for more information on contraindications, precautions and adverse effects</p>
Synthetic Parathyroid Hormone						
Teriparatide	Solution for injection: 2.4 mL pre-filled pen; delivers 20 mcg per dose; 28 doses per pen (Forteo [®])	Sub-cutaneous	20 mcg once daily	\$9628	No coverage	<p>Maximum lifetime exposure for an individual patient is 24 months.</p> <p>Administration: subcutaneous injection into the thigh or abdominal wall; administer initially under circumstances in which the patient can sit or lie down [may cause orthostatic hypotension]</p> <p>Contraindications: severe renal impairment, hypercalcemia, pregnancy</p> <p>Adverse effects: nausea, dizziness, leg cramps, transient hypercalcemia, syncope, osteosarcoma has been noted in rats receiving teriparatide (dose and duration dependent): the significance of this in humans is still unknown</p>

Generic Name	Strength (Brand name)	Route	Adult dose	Approximate annual cost of therapy ^A	PharmaCare coverage	Therapeutic considerations ^B
Selective Estrogen Receptor Modulators (SERMS)						
Raloxifene	Tablet: 60mg (Evista [®] , G)	Oral	60 mg once daily	\$542(G) \$715	Limited Coverage	Note: bone loss often resumes once treatment is stopped Contraindications: pregnancy, history of venous thromboembolic events (VTE) Precautions: consider baseline cardiovascular risk (increased risk of stroke and VTE) Adverse effects: vasomotor symptoms, flushing, leg cramps, flu syndrome, thromboembolic events [see above]
Calcitonin Peptides						
Calcitonin salmon	Nasal Spray: 200 IU per metered dose; 14 doses per bottle (Miacalcin NS, G)	Intra-nasal	200 IU intra-nasally once daily, alternate nostrils daily	\$614 (G) \$813	No Coverage	Note: salmon calcitonin is also available in an injectable form^P Adverse effects: common adverse effects appear to be localized, transient nasal reactions Health Canada is currently assessing the possibility of an increased risk of cancer with long-term use of calcitonin
RANK Ligand Inhibitor						
Denosumab	Solution for injection: 60 mg/ mL pre-filled syringe or vial (Prolia [™])	Sub-cutaneous	60 mg sub- cutaneously once every 6 months	\$660	Limited Coverage	Administration: subcutaneous injection into the upper arm, upper thigh, or abdomen Contraindications: hypocalcemia Adverse effects: cellulitis, dermatitis, eczema, rashes, pancreatitis, osteonecrosis of the jaw (rare)
Hormone Replacement Therapy (HRT)^{E, F}						
Conjugated estrogen	Tablets: 0.625 mg (Premarin (equine) [®] / C.E.S. [®])	Oral	0.625 mg once daily	\$38 (CES [®]) \$109.50 (Premarin)	Regular Coverage	Prescribe with progestin for women with an intact uterus Note: risk versus benefit needs to be taken into account when prescribing; consider using only in light of other available treatments Administration: use continuous or cyclical regimes and adjust dose as needed; topical – apply to skin, rotate sites Contraindications: history of thromboembolic events, breast cancer Adverse effects^G: nausea, vomiting, abdominal discomfort, breast tenderness thromboembolic events, breast cancer; topical - skin irritation
Micronized estradiol-17 β	Tablets: 0.5 mg (Estrace [®])	Oral	0.5 mg once daily	\$49	Regular Coverage	See conjugated estrogens therapeutic considerations.
Estradiol-17 β	Dermal patches: 50 mcg, 75 mcg, 100 mcg released per 24 hour (Sandoz Estradiol Derm) Dermal patches: 25mcg, 37.5 mcg, 50 mcg, 75 mcg, 100 mcg released per 24 hours (Estradot) Dermal patches: 25, 100 mcg released per 24 hours (Estraderm [®]) Dermal patches: 50, 75, 100 mcg released per 24 hours (Climara [®])	Trans-dermal	50 mcg patch applied twice weekly 50 mcg patch applied twice weekly 100 mcg patch applied twice weekly 50 mcg patch applied once weekly	\$192 \$307 \$451 \$295	Limited Coverage Limited Coverage ^H	Alternative to oral therapy Adjust dose as needed See conjugated estrogen therapeutic considerations

G-generics, IU-International Units

- A:** Prices are approximate retail cost, not including dispensing fee [as of December 2010]. Costs vary according to dose and choice of brand or generic product.
- B:** This is not an exhaustive list. Please review product monographs for complete details. Please review product monographs at http://webprod.hc-sc.gc.ca/dpd-bdpp/index_eng.jsp and regularly review current Health Canada advisories, warnings and recalls at: http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/index_e.html
- C:** PharmaCare coverage is available through Special Authority for 5 mg and 35 mg tablets but not 150 mg tablets.
- D:** Osteoporosis is not an approved indication for calcitonin injectable in Canada. In patients with postmenopausal osteoporosis, the suggested recommended dose of salmon calcitonin injection is 100 international units every other day, administered subcutaneously or intramuscularly. Common side effects include nausea, vomiting, and flushing. Consider skin testing prior to first dose. [reference Micromedex Healthcare Series Web site. <http://www.thomsonhc.com.azproxy.samford.edu/home/dispatch>. Accessed June 20, 2010]
- E:** Only estrogens with a Health Canada approved indication for the relief of menopausal symptoms AND prevention of osteoporosis are listed
- F:** Usual doses listed. Use lowest effective dose, for the shortest period of time.
- G:** Estrogen alone is associated with an increased risk of stroke and deep vein thrombosis; combination estrogen and progesterone is associated with an increased risk of coronary heart disease, stroke, breast cancer, and venous thromboembolism [this risk seems to be less in women 50 – 59 years of age]
- H:** PharmaCare coverage is available through special authority for 50 mcg and 100 mcg patches but not the 75 mcg patches.

PharmaCare Coverage Definitions

G: generic(s) are available.

regular coverage: also known as regular benefit; does not require Special Authority; patients may receive full coverage*

partial coverage: Some types of regular benefits are only partially covered* because they are included in the Low Cost Alternative (LCA) program or Reference Drug Program (RDP) as follows:

LCA: When multiple medications contain the same active ingredient (usually generic products), patients receive full coverage* for the drug with the lowest average PharmaCare claimed price. The remaining products get partial coverage.

RDP: When a number of products contain different active ingredients but are in the same therapeutic class, patients receive full coverage* for the drug that is medically effective and the most cost-effective. This drug is designated as the Reference Drug. The remaining products get partial coverage.

limited coverage: requires Special Authority for coverage. Patients may receive full or partial coverage* depending on LCA or RDP status. These drugs are not normally regarded as first-line therapies or there are drugs for which a more cost-effective alternative exists.

no coverage: does not fit any of the above categories; *coverage is subject to drug price limits set by PharmaCare and to the patient's PharmaCare plan rules and deductibles. See <http://www.health.gov.bc.ca/pharmacare/> for further information.