Medications for Osteoporosis: An Update

B.C. Provincial Academic Detailing (PAD) Service **June 2023**

Participants will have the opportunity to:

1. Apply current evidence to guide prescribing and deprescribing decisions for bisphosphonates, denosumab, raloxifene, teriparatide and romosozumab.
2. Incorporate fracture risk reduction and time-to-benefit estimates as part of shared-decision making with patients.
3. Compare the principal clinical considerations when choosing between bisphosphonates and denosumab, the most commonly prescribed osteoporosis medications in British Columbia.

Screening in primary care: See the Canadian Task Force on Preventive Health Care's 2023 recommendations on the primary prevention of fragility fractures.

Understudied populations in medication clinical trials: Premenopausal females, males, intersex persons, transgender persons, diverse racial or ethnic groups, residents of long term care, multimorbidity and polypharmacy, people taking glucocorticoids, participants defined by FRAX scores.

Brand Name	Generic Name
Fosamax®, Fosavance®	alendronate oral once a day or week
Actonel®, Actonel DR®	risedronate oral once a day or week or month
Aclasta®	zoledronic acid intravenous once a year
Prolia®	denosumab subcutaneous every 6 months
Evista®	raloxifene oral once a day
Forteo®, Osnuvo®	teriparatide subcutaneous once a day
Evenity®	romosozumab subcutaneous once a month

Osteoporosis medications: overview

Drug Administration		Contraindications, serious precautions	Important adverse events	Duration of therapy
alendronate **risedronate** antiresorptives	oral: *daily, weekly or monthly*	▪ hypocalcemia ▪ alendronate: CrCl < 35 mL/min ▪ risedronate: CrCl < 30 mL/min ▪ abnormalities of esophagus ▪ inability to sit/stand upright for 30 minutes	▪ osteonecrosis of the jaw ▪ atypical femoral fractures ▪ esophageal	▪ review for potential for stopping after 5 years of initial therapy
zoledronic acid antiresorptive	intravenous: *annual infusion*	▪ hypocalcemia ▪ CrCl < 35 mL/min ▪ risk factors for acute kidney injury ▪ inability to hydrate pre + post infusion	▪ osteonecrosis of the jaw ▪ atypical femoral fractures ▪ first dose infusion reactions	▪ review for potential for stopping after 3 years of initial therapy
denosumab antiresorptive	subcut: *every 6 months*	▪ hypocalcemia: significantly increased risk in renal impairment	▪ osteonecrosis of the jaw ▪ atypical femoral fractures ▪ infections, dermatologic reactions	▪ if stopping, transition to a bisphosphonate is recommended
raloxifene estrogen receptor modulator	oral: *daily*	▪ history or current VTE ▪ history of stroke or risk factors for stroke ▪ males and premenopausal females	▪ thromboembolism ▪ vasodilation (hot flushes) ▪ leg cramps	▪ review for opportunity to deprescribe or transition to another osteoporosis therapy
teriparatide anabolic	subcut: *daily*	▪ hypercalcemia ▪ CrCl < 30 mL/min	▪ orthostatic hypotension ▪ arthralgia, headache, muscle spasms	▪ after 24 months (total exposure), review for continuation or transition to an antiresorptive
romosozumab anabolic + antiresorptive	subcut: *once a month*	▪ hypocalcemia ▪ history of myocardial infarction or stroke	▪ possible increased risk of major cardiovascular events †	▪ after 12 months, transition to an antiresorptive is recommended

antiresorptive: inhibits resorption of bone (osteoclasts); **anabolic:** stimulates bone formation (osteoblasts); † US FDA 2019 advisory committee: additional data needed to better characterize risk

Osteoporosis medications: indications & basis of approval

Basis of regulatory drug approval for osteoporosis

1. Osteoporosis medications generally enter the market with an indication for use in postmenopausal females based on evidence of a reduction in the risk of radiographic vertebral fractures and, in some cases, clinical (symptomatic) fractures.
2. Subsequent population indications may be added by demonstrating that the medication increases bone mineral density (BMD) – estimates of drug effects (efficacy & safety) for these patient groups are less certain.

Health Canada Indications	Postmenopausal females		Males with osteoporosis	Exposure to medications that increase fracture risk		
	Osteoporosis	Osteopenia		Glucocorticoid females, males	Aromatase Inhibitor non metastatic breast cancer	Androgen Deprivation non metastatic prostate cancer
bisphosphonates	radiographic vertebral & clinical fractures	BMD ⊕	BMD & radiographic vertebral fractures	BMD †		
denosumab ∗	radiographic vertebral & clinical fractures		BMD	BMD ††	BMD ⊕	BMD & radiographic vertebral fractures
raloxifene	radiographic vertebral fractures	BMD				
teriparatide ∗	radiographic vertebral & clinical fractures		BMD	BMD †††		
romosozumab ∗	radiographic vertebral & clinical fractures					

surrogate outcomes: radiographic vertebral factures and bone mineral density, used in osteoporosis medication clinical trials as a substitute for a direct measure of how a patient feels, functions or survives;
radiographic vertebral fractures: detected on scheduled imaging during the clinical trial, may not be symptomatic;
∗ high risk: indicated for those with a history of osteoporotic fracture or multiple risk factors for fracture; ⊕ postmarketing trial(s) demonstrate reduction in clinical fractures; † prednisone ≥ 7.5 mg per day equivalent irrespective of baseline BMD or fracture history; †† prednisone ≥ 7.5 mg per day equivalent plus prior fracture or low BMD; ††† prednisone ≥ 5 mg per day equivalent plus prior fracture or low BMD

Health Canada Drug Product Database; Health Canada Drug Health Product Register; US FDA Approved Drugs; US FDA 2015 public workshop osteoporosis drug development; US FDA table surrogate endpoints drug approval; KEHOE Br J Clin Pharmacol 2019; REID NEJM 2018 osteopenia zoledronic acid; B.C. Ministry of Health 2023 denosumab

B.C. PharmaCare coverage & annual drug cost

B.C. PharmaCare coverage criteria for osteoporosis indications Annual drug cost *approximate*			osteoporotic fracture clinically or radiographically documented	osteoporotic fracture *plus:*		glucocorticoid induced osteoporosis ++ 1 year coverage	aromatase inhibitor for breast cancer: fracture primary prevention 5 year coverage
				contraindication to oral bisphosphonate	intolerable side effects to oral bisphosphonate or unsatisfactory response +		
alendronate Fosamax, Fosavance	~ $100 ✱	Limited Coverage	✓			✓	
risedronate Actonel		Limited Coverage					
zoledronic acid Aclasta	~ $360 ◆	Limited Coverage		✓ †			
denosumab Prolia	~ $900 ■	Limited Coverage		✓ ††			✓
raloxifene Evista	~ $400	Limited Coverage			✓ postmenopausal females only		
teriparatide Forteo, Osnuvo	~ $8000 ■	non benefit					
romosozumab Evenity	~ $8500 ■	non benefit					

✱ approximate wholesale cost of weekly generic formulation (alendronate 70 mg, risedronate 35 mg); daily (alendronate 5 & 10 mg, risedronate 5 mg), monthly (risedronate 150 mg), delayed release (risedronate 35 mg DR) formulations are more costly; see **BC PAD Osteoporosis Drug Table** for doses, costs, coverage; ◆ excludes infusion costs and potential missed work hours for working patients; ■ Canada's Drug and Health Technology Agency (CADTH) Reimbursement Reviews: drug not cost effective at the time of review; † abnormalities of the esophagus such as stricture or achalasia; †† abnormalities of the esophagus such as stricture or achalasia *or* immune-mediated hypersensitivity reaction; **+** esophageal ulceration, erosion or stricture, lower gastrointestinal symptoms severe enough to cause discontinuation of bisphosphonates after ≥ 1 month trial *or* new clinically or radiographically documented osteoporotic fracture after 1 year of adherence to alendronate or risedronate; **++** patients receiving or expected to receive prednisone ≥ 7.5 mg per day equivalent for ≥ 90 consecutive days

Osteoporosis medications: evidence overview

Postmenopausal females§	Hip fracture	Symptomatic vertebral fracture†	Symptomatic fracture††	Radiographic vertebral fracture†††	Serious adverse events	Withdrawals due to adverse events
bisphosphonate vs **placebo**; 3 – 4 yrs; meta-analysis baseline VF 0% – 100%	**ARR 0.6%** RRR 36%	**ARR 1.8%** RRR 62% ∗	**ARR 2.4%** RRR 21% ∗	**ARR 5.6%** RRR 51% ∗	NSS	NSS
denosumab vs **placebo**; 3 yrs; 1 RCT baseline VF 23%	**ARR 0.5%** RRR 40%	**ARR 1.8%** RRR 69%	**ARR 1.5%** RRR 20%	**ARR 4.9%** RRR 68%	NSS	NSS
raloxifene vs **placebo**; 3 yrs; meta-analysis baseline VF 37% – 56%	NSS	NSS	NSS	**ARR 2.8%** RRR 41%	NSS	**ARI 1.5%**
teriparatide vs **oral bisphosphonate**; 2 yrs; 1 RCT baseline VF 100%	NSS	**ARR 2.8%** RRR 71%	**ARR 4.6%** RRR 52%	**ARR 6.6%** RRR 56%	NSS	NSS
romosozumab vs **oral bisphosphonate**; 2 – 3 yrs; 1 RCT baseline VF or HF 100%	**ARR 1.2%** RRR 38%	**ARR 1.2%** RRR 59%	**ARR 3.3%** RRR 27%	**ARR 3.9%** RRR 50%	NSS	NSS

American College of Physicians 2023 Recommendations for Postmenopausal Females with Osteoporosis: bisphosphonates initial pharmacologic therapy (high certainty); denosumab second line (moderate certainty); romosozumab (moderate certainty) or teriparatide (low certainty) followed by a bisphosphonate in females at very high risk of fracture due to age and fracture history; raloxifene not recommended; **Males with Osteoporosis:** extrapolated from evidence for postmenopausal females: bisphosphonates initial pharmacologic therapy (low certainty); denosumab second line (low certainty)

§ primary osteoporosis: based on BMD or fragility fracture, not secondary to another medical condition or medication; **VF HF** proportion of participants with a vertebral or hip fracture at baseline; **†** clinically recognized, symptomatic; **††** symptomatic nonvertebral ± vertebral fractures excl. fractures not related to osteoporosis; **†††** detected on scheduled imaging, may not be symptomatic, radiographic criteria may vary between trials; **ARR** absolute risk reduction; **ARI** absolute risk increase; **RRR** relative risk reduction; **NSS** not statistically significantly different; **∗ bisphosphonates** heterogeneity in baseline fracture risk across RCTs & variability in estimates of drug effect; **teriparatide** 58% participants previously used a bisphosphonate; **romosozumab** sequential therapy romosozumab for 1 year followed by alendronate for 1 year; 6% participants previously used a bisphosphonate

ACP 2023 osteoporosis guideline & systematic review; FREEDOM NEJM 2009 denosumab; VERO Lancet 2018 & Osteo International 2020 teriparatide vs risedronate; ARCH NEJM 2017 romosozumab vs alendronate; US FDA 2019 romosozumab review; Health Canada 2019 romosozumab review; European Medicines Agency 2020 romosozumab review

Bisphosphonates, denosumab: patient population estimates

Secondary versus Primary Prevention: Alendronate, Denosumab					
Postmenopausal females		**Radiographic vertebral fracture†**			**Participant Demographics**
alendronate	secondary prevention previous vertebral fracture	**ARR ~7%**	3 years	placebo 15.0% → drug 8.0%	▪ ages 55 – 81; ambulatory; self rated health good to excellent ▪ BMD T score –2.0 or lower; mean age 71; 97% White
	primary prevention without previous fracture	**ARR ~2%**	4 years	placebo 3.8% → drug 2.1%	▪ ages 54 – 81; ambulatory; self rated health good to excellent ▪ BMD T score –1.6 or lower; mean age 68; 97% White
denosumab	secondary prevention previous vertebral fracture	**ARR ~9%**	3 years	placebo 13.6% → drug 4.6%	▪ ages 60 – 90; ambulatory; generally in good health ▪ BMD T score –2.5 to –4.0; mean age 72; 93% White ▪ excluding those who had taken a bisphosphonate for > 3 years or within the previous year
	primary prevention without previous fracture	**ARR ~4%**		placebo 5.2% → drug 1.7%	

Patient Populations: Bisphosphonates						
Population	**Radiographic vertebral fracture†**			**Hip fracture**		
postmenopausal females with osteoporosis	**NNT 20 (16 − 27)** baseline risk: ~10%	3 − 4 years	1205 events in 16,902 females	**NNT 143 (105 − 333) ∗** baseline risk: ~2%	3 − 4 years	263 events in 16,634 females
males with osteoporosis	**NNT 33 (26 − 125) ∗** baseline risk: ~5%	2 years	55 events in 1692 males	not estimable		∗ NNT estimate may include sufficient imprecision to impact clinical or patient decisions
people taking glucocorticoids	**NNT 30 (20 − 143) ∗** baseline risk: ~8%	1 − 2 years	77 events in 1343 people	not estimable		

† detected on scheduled imaging, may not be symptomatic; **ARR** absolute risk reduction; **baseline risk + estimates of drug effect** mean difference between drug and placebo for radiographic vertebral fractures varies by baseline risk (e.g., primary vs secondary prevention); this is less apparent for hip fractures where the drug effect varies minimally across trials; **NNT** number of people who need to take a bisphosphonate for one less person to experience a fracture with 95% confidence interval

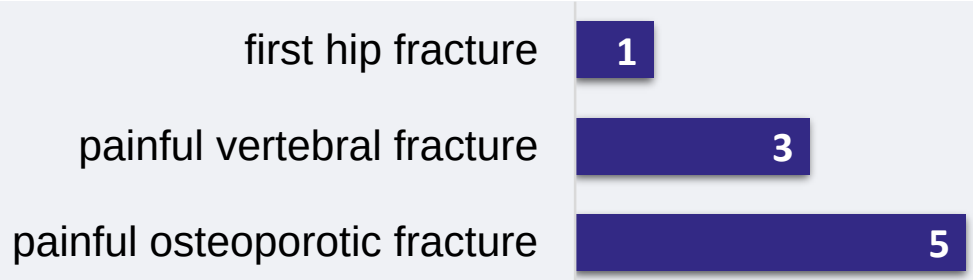
FIT 1 Lancet 1996 alendronate; FIT 2 JAMA 1998 alendronate; FREEDOM NEJM 2009 & J Bone Min Res 2012 denosumab; ACP 2023 osteoporosis guideline & systematic review; COCHRANE 2016 CD001347

Bisphosphonates: shared decision making

Preventing another fracture

You are a postmenopausal female in good health with osteoporosis and you've had a vertebral fracture[1]

number of people out of **100** estimated to benefit over **3 years**



Preventing another fracture

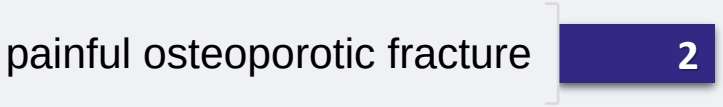
You are aged 50 or older and you have recently had surgery for an osteoporotic hip fracture[2]

number of people out of **100** estimated to benefit over **2 years**

Preventing a first fracture

You are a postmenopausal female in good health with osteoporosis and you've not had a fracture[3]

number of people out of **100** estimated to benefit over **4 years**



painful osteoporotic fracture: fracture of the vertebrae or another bone considered related to osteoporosis

[1]FIT 1 NEJM 1996 alendronate, CADTH 2021; [2]HORIZON RFT 2007 zoledronic acid; [3]FIT2 JAMA 1998 alendronate, GATES Systematic Rev 2023 alendronate, moderate certainty

Older adults with frailty & multimorbidity

Representation of people with frailty and multimorbidity

- Mean age of participants across trials: 50 – 85 years
- People with multimorbidity, polypharmacy and persons in long term care are underrepresented in osteoporosis trials
- Canadian guideline pharmacotherapy recommendations on the prevention of fractures in long term care are extrapolated from ambulatory, community dwelling females with few or no comorbidities (Osteoporosis Canada 2015)
- A 2023 systematic review of osteoporosis medications did not find evidence for fracture related mortality, functionality or disability

Consider as part of medication decision making

1. **Time-to-benefit:** onset of symptomatic or hip fracture risk reduction and its relevance to people of advanced age or limited life expectancy
   - bisphosphonates: approximately after 12 months of treatment
   - denosumab: approximately after 6 – 12 months of treatment
2. **Administration instructions:** that make it difficult to provide medications safely
3. **Kidney function:** which may preclude medication use or increase the risk of adverse events

Administration		
alendronate	≥ 200 mL plain water	take on empty stomach upon arising for the day; contraindicated = inability to sit or stand upright for at least 30 minutes, abnormalities of the esophagus
risedronate	≥ 120 mL plain water	
zoledronic acid	≥ 500 mL of fluids before & after infusion	infusion not less than 15 minutes; check serum calcium before each dose
denosumab	subcutaneous injection: upper arm, upper thigh, abdomen	check serum calcium before each dose

Kidney	
alendronate	contraindicated: CrCl < 35 mL/min
risedronate	not recommended: CrCl < 30 mL/min
zoledronic acid	contraindicated: CrCl < 35 mL/min (C-G formula using actual body weight)
denosumab	significantly increased risk of hypocalcemia: CrCl < 30 mL/min

HANDEL BMJ 2023; ACP 2023 osteoporosis guideline & systematic review; Osteoporosis Canada 2015 guideline; GATES Systematic Rev 2023; DEARDORFF JAMA Int Med 2022; FIT 1 Lancet 1996 alendronate; HIP NEJM 2001 risedronate; HORIZON PFT & RFT NEJM 2007 zoledronic acid; REID NEJM 2018 zoledronic acid; FREEDOM NEJM 2009 denosumab; Health Canada Drug Product Database

Exit strategies & transitions

Persistence of effect

- Treatment effects of bisphosphonates may persist for years after treatment discontinuation
- Denosumab, teriparatide and romosozumab have a more rapid offset of effect following discontinuation

Bisphosphonates Concern:

longer treatment duration increases the risk of atypical femoral fractures and osteonecrosis of the jaw, although both are rare

- In postmenopausal females, if alendronate is continued for another 5 years after 5 years of initial therapy:
  - symptomatic vertebral factures: ARR 3%
  - atypical femoral fractures: ARI 0.1% – 0.4%
- American Association of Clinical Endocrinology 2020 recommends stopping oral bisphosphonate therapy after 5 years and zoledronic acid after 3 years if:
  - patient has remained fracture free, and
  - BMD T score is above (better than) –2.5
- Health Canada & US FDA: optimal duration of therapy has not been determined

Denosumab Concern:

discontinuing denosumab is associated with an increased risk of multiple vertebral fractures

- Rate of multiple vertebral fractures after stopping (≥ 7 months ago):
  - placebo: 3.2 per 100 patient years
  - denosumab: 4.2 per 100 patient years
- Consistency with the every 6 months dosing schedule is important
- Health Canada: consider transitioning to a bisphosphonate if denosumab is discontinued

Teriparatide Concern:

risk of osteosarcoma in animal studies but postmarketing studies in humans do not find a clinical signal of osteosarcoma

- Transition to a bisphosphonate or denosumab typically considered after 24 months of teriparatide
- US FDA 2020 review: available evidence no longer supports a warning for osteosarcoma
- Health Canada & US FDA: continue beyond 24 months of lifetime exposure only if high risk for fracture

Romosozumab Concern:

effects on bone mineral density and bone formation markers wane after 12 months of treatment

- Transition to a bisphosphonate or denosumab typically considered after 12 months of romosozumab
- Health Canada & US FDA: limit treatment duration to 12 months

Health Canada Drug Product Database; US FDA Approved Drugs; AHRQ 2019 osteoporosis long term drug therapy; FLEX extension trial JAMA 2006 alendronate; BLACK NEJM 2020; HORIZON PFT extension trial J Bone Min Res 2012 zoledronic acid; AACE/ACE 2020 osteoporosis guideline update; CUMMINGS J Bone Miner Res 2018 extension trial denosumab; US FDA 2020 teriparatide review; US FDA 2019 romosozumab review; REID Lancet 2022

Bisphosphonates: clinical considerations

Contraindications

- oral: abnormalities of esophagus, inability to sit or stand upright for at least 30 minutes, inability to swallow ≥ 120 – 200 mL of water
- zoledronic acid: inability to appropriately hydrate pre and post infusion
- hypocalcemia
- CrCl < 35 mL/min: alendronate
- CrCl < 30 mL/min: risedronate
- CrCl < 35 mL/min: zoledronic acid

Calcium & Vitamin D

- zoledronic acid: check serum calcium before each dose – replete calcium and vitamin D if necessary
- hypocalcemia symptoms: muscle cramps or twitching, numbness or tingling mouth, fingers or toes

Acute kidney injury

- zoledronic acid: ensure adequate hydration (eat & drink normally including at least 500 mL of fluids) prior to and after administration – particularly in older adults, those receiving diuretics or nephrotoxic medications
- monitoring CrCl post dose: recommended in patients at risk
- infusion time: minimum 15 minutes

Infusion reaction

- zoledronic acid: ~25% of patients within 3 days of first infusion, less frequent on subsequent infusions
- symptoms: fever, chills, fatigue; musculoskeletal pain; pain & redness at infusion site
- acetaminophen or ibuprofen to prevent or manage symptoms

Gastrointestinal

- oral: may cause or worsen esophagitis, esophageal ulcers, esophageal erosions, stricture or perforation

Musculoskeletal

- bone, joint, muscle pain: possibly severe; also common infusion reaction symptoms

Ophthalmologic

- conjunctivitis, uveitis, episcleritis, scleritis: incidence ≤ 1%

Atypical femoral fractures

- subtrochanteric or proximal femoral shaft: 1/3 bilateral; may occur in absence of apparent trauma
- prodrome: patients should be counselled to report new or unusual thigh, hip, groin pain
- incidence: < 0.1% (0 – 5 years)
- additive risk factors: duration of therapy > 3 – 5 years, Asian descent, > 1 year of glucocorticoid use

Osteonecrosis of the jaw

- associated with invasive dental procedures such as tooth extraction: consider preventive dentistry/regular dental monitoring
- incidence: 0.02 – 0.15%
- additive risk factors: higher dose oncology regimens, duration of therapy > 2 – 3 years

See reference list

Denosumab: clinical considerations

Contraindications
hypocalcemia

Calcium & Vitamin D
hypocalcemia: rare if normal kidney function and adequate calcium and vitamin D intake
check serum calcium: before each dose (replete calcium and vitamin D if necessary), and within 2 weeks post dose in patients at risk for hypocalcemia
risk factors for hypocalcemia: hypoparathyroidism, thyroid or parathyroid surgery, excision of small intestine, malabsorption syndromes, CrCl < 30 mL/min or dialysis, previous hypocalcemia
hypocalcemia symptoms: muscle cramps or twitching, numbness or tingling mouth, fingers or toes

Chronic kidney disease
no dose adjustment required
insufficient evidence to evaluate fracture efficacy in patients with eGFR < 30 mL/min
risk of hypocalcemia increases as eGFR declines: 30 – 60 mL/min: < 1% 15 – 30 mL/min: 4% < 15 mL/min, dialysis: 24 – 42%

Infection
increase in serious infections leading to hospitalization: ENT, GI, cellulitis; absolute risk increase 0.6% over 1-3 years
caution: patients on glucocorticoids with active infection or history of recurrent or chronic infection

Stopping plan
discontinuing denosumab: associated with an increased risk of multiple vertebral fractures
Health Canada recommends if denosumab is discontinued, consider initiating a bisphosphonate to decrease the risk of rebound vertebral fractures

Musculoskeletal
bone, joint, muscle pain: reported by ~35% in both drug and placebo groups; case reports of severe pain

Dermatologic
rashes, dermatitis, eczema: uncommon; discontinue if severe

Atypical femoral fractures
subtrochanteric or proximal femoral shaft: 1/3 bilateral; may occur in absence of apparent trauma
prodrome: patients should be counselled to report new or unusual thigh, hip, groin pain
incidence: less well documented for denosumab compared to bisphosphonates

Osteonecrosis of the jaw
associated with invasive dental procedures such as tooth extraction: consider preventive dentistry/regular dental monitoring
incidence: 0.05 – 0.7% over 7 –10 years
additive risk factors: higher dose oncology regimens, longer duration of therapy

See reference list

Evidence for Practice

The fracture evidence for bisphosphonates and denosumab varies by patient population

- **Populations:** most osteoporosis medication clinical trials enroll community dwelling, ambulatory, postmenopausal females – evidence for other populations is more limited
- **Postmenopausal females:** bisphosphonates and denosumab reduce the risk of hip, other clinical, and vertebral fractures
- **Comparisons between bisphosphonates and denosumab:** indirect comparisons find that denosumab reduces the risk of radiographic vertebral fractures compared to bisphosphonates but not other clinical or hip fractures – however there isn't a large fracture trial comparing the two directly
- **Females receiving aromatase inhibitors:** denosumab reduces the risk of clinical fractures
- **Males receiving androgen deprivation therapy**: denosumab reduces the risk of radiographic vertebral fractures
- **Males with osteoporosis and people taking glucocorticoids:** bisphosphonates may reduce the risk of radiographic vertebral fractures but estimates of effect are imprecise
- **Time-to-benefit:** incorporate time to benefit estimates when sharing decisions with people of advanced age or limited life expectancy

Develop the exit strategy or transition plan at the time of medication initiation

- **Bisphosphonates:** review oral bisphosphonates after 5 years of treatment and zoledronic acid after 3 years: incorporating fracture history, bone mineral density, patient preference
- **Denosumab:** Health Canada recommends that if denosumab is discontinued, consider initiating a bisphosphonate to decrease the risk of rebound vertebral fractures
- **Teriparatide:** approved for a maximum of 24 months of use for most people, guidelines recommend subsequent treatment with a bisphosphonate or denosumab
- **Romosozumab:** approved for a maximum of 12 months of use, guidelines recommend subsequent treatment with a bisphosphonate or denosumab
- **Optimal sequence of osteoporosis medications:** there is limited evidence examining the optimal sequence of medications on fracture outcomes

Reference list is available upon request. Materials are designed to be used in conjunction with an academic detailing session provided by a PAD pharmacist.

For more information, or to schedule an academic detailing session, please contact: BC Provincial Academic Detailing Service Email: PAD@gov.bc.ca Web: www.bcpad.ca

v. June 15, 2023