

Figure 2: Approach to pharmacotherapy to prevent fractures. Note: Rec. = recommendation (see Tables 4, 6 and 7 for full recommendations).

\*Menopausal hormone therapy is a suggested alternative for females younger than 60 years or within 10 years after menopause who prioritize alleviation of substantial menopausal symptoms (Rec. 4.4). †Antiresorptive therapy includes bisphosphonates (alendronate, risedronate and zoledronic acid), denosumab, raloxifene and menopausal hormone therapy. ‡Raloxifene is suggested rather than no treatment for females who have contraindications or substantial intolerance to, or who choose not to take, other suggested therapies) (Rec. 4.7). §See Figure 1 for list of risk factors and Appendix 1, Supplementary Table 5, for causes of secondary osteoporosis.

Drug	Route and dosing	Potential adverse effects	Contraindications	Other considerations	Cost
Antiresorptive age	nts				
Bisphosphonates					
Alendronate	Oral: 70 mg weekly or 10 mg daily	<ul> <li>Esophageal or GI intolerance</li> <li>MSK discomfort</li> <li>Rare: AFF, ONJ</li> </ul>	<ul> <li>CrCl &lt; 30–35 mL/min</li> <li>Esophageal abnormalities</li> <li>Inability to be upright &gt; 30 min</li> <li>Hypocalcemia</li> </ul>	<ul> <li>Foods, drinks (except plain water), other drugs should be avoided for &gt; 30-60 min</li> <li>Minerals and dairy impair absorption if taken close together</li> </ul>	\$
Risedronate	Oral: 35 mg weekly or 150 mg monthly or 5 mg daily	<ul> <li>Esophageal/GI intolerance</li> <li>MSK discomfort</li> <li>Rare: AFF, ONJ</li> </ul>	<ul> <li>CrCl &lt; 30-35 mL/min</li> <li>Esophageal abnormalities</li> <li>Inability to be upright &gt; 30 min</li> <li>Hypocalcemia</li> </ul>	<ul> <li>Foods, drinks (except plain water), other drugs should be avoided for &gt; 30-60 min</li> <li>Minerals and dairy impair absorption if taken close together</li> <li>Delayed-release formulation available (taken with food)</li> </ul>	\$
Zoledronic acid	Intravenous: 5 mg yearly	<ul> <li>Transient flu-like symptoms</li> <li>Hypocalcemia</li> <li>Renal toxicity</li> <li>Rare: AFF, ONJ</li> </ul>	<ul><li>CrCl &lt; 35 mL/min</li><li>Hypocalcemia</li></ul>	<ul> <li>Inadequate vitamin D increases risk for hypocalcemia</li> <li>Less frequent dosing than yearly may be considered</li> </ul>	\$\$
RANK-ligand inhibit	tor (monoclonal antibod	y)			
Denosumab	Subcutaneous: 60 mg every 6 mo	<ul> <li>Hypocalcemia</li> <li>Dermatitis, infections</li> <li>MSK discomfort</li> <li>Rare: AFF, ONJ</li> </ul>	Hypocalcemia	<ul> <li>Inadequate vitamin D increases risk for hypocalcemia</li> <li>Caution warranted in severe renal impairment</li> <li>Rapid bone loss and risk of vertebral fractures if delayed dose or with discontinuation</li> </ul>	\$\$\$
Hormonal therapy					
Menopausal hormonal therapy	Multiple regimens	VTE, CVD, stroke Breast cancer	<ul> <li>VTE, CVD, stroke, estrogen- dependent tumours, abnormal vaginal bleeding, active liver disease</li> </ul>	Only in postmenopausal women	\$-\$\$
Raloxifene (SERM)	Oral: 60 mg daily	<ul> <li>VTE, CVD, stroke</li> <li>Vasomotor symptoms, leg cramps</li> </ul>	VTE, CVD, stroke, abnormal vaginal bleeding	Only in postmenopausal women	\$
Anabolic agents					
Parathyroid hormo	ne analog				
Teriparatide	Subcutaneous: 20 µg daily for 24 mo	<ul> <li>Orthostatic hypotension, nausea</li> <li>Hypercalcemia, hypercalciuria</li> <li>MSK discomfort</li> </ul>	<ul> <li>CrCl &lt; 30 mL/min</li> <li>Bone malignancy, Paget disease, previous skeletal radiation</li> <li>Hypercalcemia disorder</li> <li>Unexplained elevated ALP</li> </ul>	Caution warranted with active or previous kidney stone disease	\$\$\$\$
Sclerostin inhibitor	(monoclonal antibody)				
Romosozumab	Subcutaneous: 210 mg monthly for 12 mo	<ul><li> Myocardial infarction, stroke</li><li> Hypocalcemia</li><li> MSK discomfort</li></ul>	<ul><li>Previous myocardial infarction or stroke</li><li>Hypocalcemia</li></ul>	<ul> <li>Inadequate vitamin D increases risk for hypocalcemia</li> <li>Caution warranted in severe renal impairment</li> </ul>	\$\$\$\$

Note: AFF = atypical femoral fracture, ALP = alkaline phosphatase, CrCl = creatinine clearance, CVD = cardiovascular disease, Gl = gastrointestinal, MSK = musculoskeletal, ONJ = osteonecrosis of the jaw, RANK = receptor activator of nuclear factor  $\kappa$ - $\beta$ , SERM = selective estrogen receptor modulator, VTE = venous thromboembolism. \*Information in this table is not meant to be exhaustive and should not replace complete details provided by drug monographs (available in the Compendium of Pharmaceuticals and Specialties at myrxtx.ca). Further information on some medications available in selected references. \$^{15,43,46-51}\$ †Relative cost.