

## OSTEOPOROSIS MEDICATIONS

Drug	Dose	Metabolism	Efficacy	Interactions	Side Effects	Cost/Coverage
<b>BISPHOSPHONATES</b>						
<p>Alendronate Fosamax®</p> <p>Fosavance® 70mg/2800IU 70mg/5600IU (Alendronate/Vitamin D3)</p> <p>(Merck)</p>	<p><i>Prevention:</i> 5mg once daily</p> <p><i>Treatment:</i> 10 mg once daily, OR 70mg once weekly</p> <p><i>(1 hour prior to meals or other medications)</i></p>	Not metabolized by the liver; 50% excreted renally.	<p>↑BMD in lumbar spine, femoral neck, and trochanter in women with &lt;2.5SD below young peak adult bone mass with treatment dose over 3-4 years.</p> <p>↓risk of vertebral, hip and non-vertebral fractures by 35-50%</p> <p>Studied in HIV population (at 70mg dose + calcium/vitamin D)<sup>1,2,3</sup>. Benefit in ↑BMD at 48 weeks, but studies not powered to detect ↓ fractures.</p>	<p>↓ absorption with food, antacids, iron, calcium</p> <p>↑ GI side effects with NSAIDS, steroids</p>	Nausea, abdominal pain, acid regurgitation, headache, constipation, diarrhea, esophagitis, ulceration	<p>\$10.06/month (70mg weekly) to \$14.96/month (10 mg daily) ODB</p> <p>Blue Cross - special authorization (Fosavance® 70mg/2800 IU- not a benefit)</p> <p>NIHB-prior authorization</p>
<p>Etidronate Didrocal® (Warner Chilcott)</p>	<p>1 tablet daily (400 mg etidronate x14 days then calcium carbonate 500mg elemental x76 days)</p> <p><i>1 hour prior to meals or other medications</i></p>	Not metabolized by the liver; 50% of absorbed dose is excreted renally. Unabsorbed etidronate is reported to be excreted intact via the feces (up to 99%)	<p>↑BMD in the lumbar spine (1-2%) over 1 year</p> <p>↓risk of vertebral fractures</p>	↓ absorption with food, antacids, iron, calcium	Nausea, abdominal pain, acid regurgitation, headache, constipation, diarrhea, esophagitis, ulceration	<p>\$19.99/90 days (ODB)</p> <p>Blue Cross-regular benefit</p> <p>NIHB-regular benefit</p>
<p>Risedronate Actonel®</p>	<p><i>Prevention/treatment:</i> 5mg once daily, OR</p>	Not metabolized by the liver; up to	↑BMD (See Alendronate)	↓ absorption with food, antacids, iron, calcium	Nausea, abdominal pain, acid regurgitation,	\$9.96/month (35mg once

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(Aventis)	35mg weekly, OR 150mg once monthly  (1 hour prior to meals or other medications)	80% excreted in the urine.	↓risk of vertebral, hip and non- vertebral fractures by 35-50%		headache, constipation, diarrhea, esophagitis, ulceration	weekly), \$27.32/month (5 mg daily), \$43.15/month (150 mg once monthly), ODB  Blue Cross- special authorization (75mg/150mg not a benefit)  NIHB-prior approval (75mg/150mg not a benefit)
Zoledronic Acid Aclasta® (Novartis)	<i>Treatment:</i> 5mg IV infusion once yearly	Not metabolized by the liver; 39 ± 16% excreted in the urine.	↑BMD (See alendronate)  ↓risk of vertebral, hip and non- vertebral fractures by 40-70%  Studied in HIV population. <sup>4,5</sup> Benefit in ↑BMD at 12 months, but not powered to detect ↓ fractures.	<i>Theoretical interactions:</i> - ↓ serum calcium with loop diuretics, aminoglycosides - nephrotoxicity with NSAIDs and other nephrotoxins (ie. Tenofovir, although no documented interactions).	Within first 3 days of infusion: fever, myalgia, flu-like symptoms, arthralgia and headache (resolve thereafter) ? risk of atrial fibrillation – not a confirmed association	\$670.80/injection (\$55.90/month) ODB  Blue Cross- special authorization (only for Paget's disease)  NIHB-prior authorization (only for Paget's disease)
<b>ANABOLIC AGENTS</b>						
Teriparatide Forteo® (Eli Lilly)	<i>Treatment:</i> 20mcg SC once daily x24 months	Metabolized via nonspecific proteolytic hepatic enzymes (no specific CYP metabolism information)	↑BMD in lumbar spine, femoral-neck and whole-body  ↓risk of vertebral and non-vertebral fractures by 53-65%	↑ serum calcium with loop & thiazide diuretics  Use with caution in digoxin patients - ↑serum calcium may predispose to digitalis toxicity.	Nausea, headache, arthralgia, leg cramps, dizziness, pain at injection site  Transient hypercalcemia/	\$1400/month (not covered via ODB)  Blue Cross-not a benefit  NIHB-not a

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		available)			hypoparathyroidism  Although no reports in humans, potential risk of osteosarcoma	benefit
<b>ESTROGEN/SERMS</b>						
Conjugated Estrogen Premarin® (Wyeth-Ayerst)	0.3mg or 0.625mg once daily	Metabolized by CYP3A4 (30%), glucuronidation	<p>↑BMD in lumbar spine and hip over 2 years.</p> <p>↓risk of vertebral, hip and total osteoporotic fractures.</p> <p>Should only be used as symptomatic therapy for relief of menopausal symptoms. Should be used in the smallest dose for the shortest duration.<sup>6</sup></p>	<p>Avoid OC use if amprenavir, or unboosted fosamprenavir.</p> <p>In general, NNRTIs &amp; boosted PIs have the potential to decrease oral contraceptive (OC) effectiveness (ethinyl estradiol/ norethidrone acetate/ norgestimate) mostly through induction of CYP 3A4 and/or glucuronidation – resulting in ↓ Cmax/AUC and potential for ↓ OC efficacy<sup>7</sup>.</p> <p>ARVs which may ↓ AUC of OC: ritonavir<sup>8</sup>, lopinavir/r, nelfinavir, darunavir/r<sup>9</sup>, tipranavir/r, efavirenz<sup>10</sup>, nevirapine<sup>11</sup>, rilpivirine<sup>12</sup></p> <p>RTV &amp; NFV<sup>13</sup> can ↑estrogen metabolism by ↑ glucuronidation which may decrease effectiveness<sup>14,15</sup></p> <p>ARVs which may ↑ AUC and OC levels: atazanavir<sup>16</sup>, amprenavir, indinavir.</p> <p>Delavirdine, saquinavir<sup>17</sup> and tenofovir result in no OC level changes.<sup>18</sup></p>	Abdominal pain, amenorrhea, breast tenderness, depression, diarrhea, edema, fatigue, menorrhagia, pulmonary embolism, weight gain	<p>\$2.36/month (ODB)</p> <p>Blue Cross-regular benefit</p> <p>NIHB-regular benefit</p>

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				<p><b><u>Please refer to the Oral Contraceptive and ARV Drug Interactions chart for more details</u></b></p> <p>↓effect of warfarin Counteract effects of bromocriptine</p> <p>↓metabolism of cyclosporine, TCA antidepressants</p>		
Raloxifene Evista® (Eli Lilly)	60mg once daily	Extensive 1 <sup>st</sup> pass metabolism in the liver to glucuronide conjugates; No reported CYP metabolism	<p>↑BMD of several sites by ~2.5% over 1-2 years</p> <p>↓risk of vertebral fractures</p>	<p>No documented ARV interactions with raloxifene, however, caution when use.<sup>19-20</sup></p> <p>Cholestyramine ↓raloxifene absorption</p> <p>May alter the effects of warfarin (monitor INR)</p>	<p>Hot flashes, muscle cramps, weight gain, peripheral edema, myalgia, insomnia, breast tenderness, abdominal pain, vaginal bleeding</p> <p>↑ risk of deep vein thrombosis, and pulmonary embolism (not associated with ↑ CV risk)</p>	<p>\$27.51/month (ODB)</p> <p>Blue Cross-special authorization</p> <p>NIHB-prior approval</p>
<b>Monoclonal Antibody against RANKL</b>						
Denosumab Prolia® (Amgen)	60mg sc every six months (self-administered injection)	N/A	<p>↑BMD of several sites by 5.2-8.8% over 1-3 years</p> <p>↓ risk of vertebral, hip and non-vertebral fractures in postmenopausal women</p>	Interactions with other drugs have not been established.	<p>Back pain, musculoskeletal pain, rash, constipation, infection (ie cellulitis), hypercholesterolemia, hypocalcemia</p>	<p>\$450/dose (not covered via ODB)</p> <p>Blue Cross not a benefit</p> <p>NIHB not a benefit</p>

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<b>CALCITONIN</b>						
Calcitonin Calcimar® (Sanofi-Aventis), MiacalcinNS® (Novartis)	200IU intranasal once daily	Metabolized primarily in the kidneys and to a lesser extent in the blood and peripheral tissues	Stabilizes BMD in lumbar spine and hip  ↓risk of vertebral fractures, and pain associated with acute vertebral fractures	No significant drug interactions reported	Rhinitis, nasal dryness, epistaxis  Flushing, nausea, vomiting, dizziness (all usually subside spontaneously)	\$64.69/month (ODB EAP)  Blue Cross-special authorization (intolerant/failed etidronate)  NIHB-prior approval (intolerant/failed bisphosphonate and raloxifene)
<b>CALCIUM/VITAMIN D SUPPLEMENTATION</b>						
Calcium  Calcium carbonate: 500-1500mg (elemental calcium 200mg-600mg) (needs higher pH to be absorbed)  Calcium citrate (elemental calcium 200-300mg)	1000-1500 mg elemental calcium daily (in divided doses)  Note: use calcium citrate if patient on proton pump inhibitor.	Calcium is excreted renally. Unabsorbed calcium is excreted in the feces	↓bone loss ↑hip BMD & ↓fracture risk in combination with Vitamin D. <sup>6,21</sup>	↓absorption of bisphosphonates, phenytoin, tetracyclines, quinolones (space apart by >4 hours)	Constipation, flatulence, gastric distention	\$8.99/350 tabs (generic 500mg calcium tablet)  Blue Cross-not a benefit  NIHB-regular benefit (calcium 500mg tab; 20mg/mL liquid; calcium 500mg/vit D 400IU tab)
Vitamin D  200-1000 IU tablets 400IU/mL liquid 400IU or 1000IU drops	600-2000 IU/day >2000 IU/day on recommendation of health care professional only (option for prescription strength Vitamin D2)	Extensively metabolized by the kidney and liver. Excreted primarily in bile.	↑calcium absorption ↓bone loss ↑hip BMD & ↓fracture risk in combination with Calcium. ↓ risk of falls. <sup>6</sup>	Efavirenz may induce hepatic catabolism of 25(OH)D via the CYP450 system resulting in vitamin D insufficiency <sup>22</sup> . In one case, Vitamin D levels were decreased to below the limit	Metallic taste, in high doses can cause hypercalcemia or hypercalciuria	\$9.97/500 tabs (Vit D 1000 IU tab) \$7.99/bottle (Vit D 1000 IU/drop)

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50,000 IU capsule (D-Forte)	50,000 IU weekly x 8 weeks to treat low vitamin D levels)			<p>of detection (18nmol/L) after 18 months of treatment<sup>23</sup>.</p> <p>Tenofovir use may be correlated excessive renal phosphate and calcium losses and 1-hydroxylation defects of vitamin D<sup>24,25</sup></p> <p>Phenytoin and phenobarbital may ↓effects of vitamin D</p> <p>Cholestyramine, mineral oil may ↓absorption of Vitamin D</p>		<p>Blue Cross-not a benefit (except IFH-400IU tab regular benefit)</p> <p>NIHB-regular benefit (drops, liquid, 400/800/1000 IU tablet; 50,000IU D2 capsule))</p>

**Legend:** *BMD*=Bone mineral density; *CYP*=Cytochrome P450; *NSAIDS*=Non-steroidal anti-inflammatory drugs; *NIHB-Non-Insured Health Benefits (Indian Affairs)*; *ODB = Ontario Drug Benefit, IFH-Interim Federal Health*  
*Note: Blue Cross- includes AISH. SFI, IFH*

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