What are the effects of popular bone drugs?

Drug	What it does	Side effects	Concerns with long-term use
Bisphosphonates			
alendronate (Fosamax), risedronate (Actonel), ibandronate (Boniva), zoledronate (Zometa / Reclast), pamidronate (Aredia), etidronate (Didronel)	All bisphosphonate drugs affect the formation and survival of osteoclasts, the cells that break down bone, thus reducing bone breakdown activities. The drug molecules also attach to mineral surfaces in cortical and trabecular bone to increase mass	Stomach irritation, esophageal erosion, bone, joint, or muscle pain, atrial fibrillation (in women), osteonecrosis of the jaw	Heightened risk of esophageal cancer; oversuppression of bone turnover leading to brittle bones and unusual shaft fractures of the femur
Selective estrogen receptor modulators (SERMs)			
tamoxifen (Nolvadex), raloxifene (Evista) (others in this class are in development but not yet approved)	Binds to estrogen receptors in bone tissue to decrease the activity of osteoclasts; also reduces the risk of invasive breast cancer. Note that both drugs are only used for postmenopausal women and not men or premenopausal women. Tamoxifen is not FDA approved for osteoporosis.	**Tamoxifen:** blood clots, resumption of bone loss after discontinuing use of the drug. May increase risk of hip fracture in low doses. **Raloxifene:** Blood clots in veins, eyes, and lungs, strokes, hot flashes, leg cramps, leg swelling, shortness of breath, vision changes	Increased risk of venous thromboembolism and fatal stroke (more so with tamoxifen than raloxifene). Tamoxifen's benefit for reducing fractures is maintained only while the drug is in use.
Biologics			
Teriparatide (Forteo)	Utilizes a segment of human parathyroid hormone to mobilize osteoblast activity and thereby increase bone formation. Used in men and women at high risk of fracture.	Nausea, vomiting, constipation, low energy, muscle weakness, joint aches, leg cramps, dizziness, increased blood calcium	Possible increase in adrenal hormone release after >1 year of use; potential increased risk of osteosarcoma. Should not be used in persons with Paget's disease of bone, bone cancer, high blood calcium, or who have had kidney stones or radiation therapy.
Denosumab (Prolia)	Inhibits maturation of osteoclasts by binding to RANKL, a protein that is expressed by osteoclast precursors.	Low blood calcium levels, serious urinary and respiratory tract infections, skin rashes or inflammation, joint pain, osteonecrosis of the jaw	Possible slight increase to risk of cancer. Hypothetical risk to gut and immune system function, since RANKL also is expressed by T helper cells and controls differentiation of microfold cells in the intestinal epithelium.
Calcitonin (Miacalcin)	Binds to osteoclasts and inhibits bone resorption; delivered in both injectable and nasal spray forms	Nausea, vomiting, flushing (occurring more often with subcutaneous or intramuscular delivery than with nasal delivery), dry mouth, headache, joint or back pain, potential for allergic reaction	Few long term effects, but the drug also has only weak effects in building bone.
PTH-related peptide (PTHrP)	When administered as single dose intermittently, markedly increases BMD without causing hypercalcemia	Nausea, vomiting, altered hemodynamics, flushing, hypercalcemia. High doses activate 1,25 dihydroxyvitamin D production.	Best known as secretion of certain cancers that produces severe hypercalcemia (high calcium levels in the blood) and bone resorption.
Other (drugs not approved for use in the US by the FDA)			
Tibolone (Livial)	Mimics the action of estrogen to help preserve bone; inhibits bone resorption	Endometrial bleeding, increase in LDL cholesterol in postmenopausal women, increased risk of stroke	Doubles the risk of stroke in postmenopausal women within the first year and in women over 70. Effects of tibolone on endometrial morphology are as yet unknown. A possible association with increased risk of breast cancer recurrence has been noted.
Strontium ranelate (Protelos)	Increases osteoblast replication, differentiation, and activity while decreasing osteoclast differentiation and activity.	Nausea, diarrhea, headache, dermatitis, eczema	Possible slight increased risk of venous thromboembolism; rarely, DRESS syndrome has been observed in patients using this drug.
Ipriflavone	Not found to be effective in preventing bone loss or reducing bone resorption	Can suppress white blood cells in a significant number of users.	Low white blood cell counts increases risk of infection and serious complications.