Wyoming Drug Utilization Review

Osteoporosis and Pharmacological Therapies

Written by Lihan Deng, PharmD Candidate, 2020

Osteoporosis

Osteoporosis is a systemic skeletal disorder characterized by decreasing bone mass and deterioration of microarchitecture that leads to an increased risk for bone fracture (1,2). An estimated 54 million men and women in the United States have osteoporosis or low bone density. Among Americans older than 50, approximately 50% are at risk for osteoporotic fracture (2).

Some groups of patients are at higher risk for developing osteoporosis, including men (3) 70 years, women (3) 65 years, men or women (3) 50 years with a recent low-trauma fracture, and adult men or women taking chronic glucocorticoid therapy. These groups of patients should have BMD measured using dual-energy x-ray absorptiometry (DXA) and have the 10-year fracture risk calculated (3).

Other key risk factors for osteoporotic fracture include, but are not limited to, post-menopause for women, hypogonadism or premature ovarian failure, history of parental hip fracture, rheumatoid arthritis, current smoking, 3 or more alcohol drinks daily, low bone mineral density (BMD), vitamin D deficiency, and low calcium intake (2,3).

The treatment goal for osteoporosis is to prevent fractures and loss of bone density (4). Treatment regimens usually include pharmacological agents, supplementation, and lifestyle modifications (1,2).

Pharmacological Treatment

Bisphosphonates

Bisphosphonates are a class of antiresorptive drugs that decrease bone resorption by inhibiting osteoclasts (1,5). Bisphosphonates are generally considered first-line therapy in patients with osteoporosis or at high risk of fractures (2,4). The four bisphosphonates approved by the FDA are alendronate (Fosamax), ibandronate (Boniva), risedronate (Actonel), and zoledronic acid (Reclast), and all demonstrated antifracture benefit in large randomized controlled trials (1). The bisphosphonates differ in dose frequency, route of administration, and fracture type preventions, which are depicted in Table 1.1(3). For oral administration, to avoid reflux that could irritate the esophagus, patients are instructed to remain upright position for 30-60 minutes (1).

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Common adverse effects of oral bisphosphonates include heartburn, esophageal irritation, esophagitis, abdominal pain, and diarrhea(5). IV bisphosphonates have been associated with low-grade fevers, myalgias, and arthralgias after the first infusion (5). Occasionally, chronic use of bisphosphonates may cause osteonecrosis of the jaw and atypical femoral fractures (5,6).

Long-term bisphosphonate therapy after 5 years is not appropriate if the reassessment shows that the patient has a low risk of fracture, and a 'bisphosphonate holiday' is recommended until the next re-evaluation due to the long half-life and accumulation in bones (6). However, for high-risk patients (T-score < -2.5, prior vertebral fracture), the benefits outweigh the risks for use up to 10 years, while data beyond 10 years are limited (6).

Calcitonin

Salmon calcitonin (Miacalcin) is a peptide hormone that decreases bone resorption by inhibiting osteoclast function. It can be given intranasally, subcutaneously (SC) or intramuscularly (IM) (1,3). Calcitonin has been shown to reduce vertebral fractures and associated bone pain (1, 5). However, it is only recommended for women who are 5 years past menopause and when alternative treatments are not tolerated or suitable (1, 3, 4).

Common adverse effects of calcitonin include flushing and nausea with subcutaneous injection and local irritation with the nasal spray (1). Calcitonin use has also caused severe allergic reactions (3). There have been recent reports of an increased risk of prostate and liver cancer associated with long-term use of nasal calcitonin spray, and it has been withdrawn in both Canada and Europe (3,4).

RANKL inhibitor

Denosumab (Prolia) is a fully human anti-RANKL monoclonal antibody that inhibits osteoclast formation and reduces bone resorption (1,3). Denosumab was shown to increase bone mineral density (BMD) more than alendronate. It is administered by subcutaneous injection once every 6 months (1,5).

Common adverse effects of denosumab include hypocalcemia, rash, eczema, dermatitis, and increased risk of infections (3,4). Osteonecrosis of the jaw and atypical femoral fractures can also occur with denosumab use (3).

Long-term denosumab therapy after 5 years is not recommended if the reassessment shows that the patient has a low risk of fracture (6). For high-risk patients, the benefits outweigh the risks for use up to 10 years (6). However, a 'drug holiday' is not appropriate for denosumab due to the rapid reversal of bone turnover after discontinuation (3,6).

Parathyroid hormone (PTH) analogs

Teriparatide (Forteo) and abaloparatide (Tymlos) are distinct anabolic treatments for osteoporosis that stimulate osteoblastic activity that leads to bone formation (1,3). They are the recombinant or synthetic analog of the human parathyroid hormone-related peptide (1). PTH analogs are administered as once daily SC injections and can be only used up to 2 years due to the incidence of osteosarcoma with high-dose treatment (1-4). PTH analogs are recommended for patients with a very high risk of fracture, including those with severe or multiple vertebral fractures (4).

PTH analogs can cause hypotension and tachycardia with the first few doses, which can be corrected by reducing calcium intake (3). Other common side effects include nausea, dizziness, muscle cramps, and infrequent hypercalcemia (1,3). BMD decreases quickly after discontinuation; therefore, it is important to follow on with an antiresorptive agent after discontinuing PTH analogs (1,2,4).

Selective estrogen receptor modulators (SERM)

Raloxifene (Evista) has estrogen-like effects on bones and antiestrogen effects on the uterus and breast. It was approved by the FDA for the prevention and treatment of postmenopausal osteoporosis (3). In addition to reducing vertebral fractures, SERMs can reduce the risk of invasive breast cancer (1,3,4). However, bisphosphonates are more effective in preventing nonvertebral and hip fractures than raloxifene (3). As a result, SERMs are more suitable for younger women who have an increased risk of breast cancer, and for those with a low risk of thrombosis and when bisphosphonates or denosumab are not appropriate (1,4). Common adverse effects of SERMs include hot flashes, leg cramps, and peripheral edema. Raloxifene also increases the risk of venous thromboembolic events and stroke (3).

Sclerostin inhibitor

Romosozumab (Evenity) is a newly FDA-approved monoclonal antibody that inhibits sclerostin, which increases bone formation and decreases bone resorption (7). It is the second class of drugs that builds bone. Romosozumab therapy should only be continued for 12 months due to a decrease in effect on bone formation after one year. A follow-on therapy is recommended after romosozumab treatment is completed (7). The most common side effects of romosozumab are arthralgia and headache. Other reported severe adverse effects are atypical femoral fractures, jaw osteonecrosis, and increased risk of cardiovascular events (7).

Table 1: Pharmacological treatment for osteoporosis (1,6,7)			
Medication	Route/Frequency	Fracture Prevention	Avoid in
Bisphosphonates			
Alendronate (Fosamax, Binosto)	Tablet or solution: 10 mg/d, 70 mg/wk	Vertebral, Hip	Cannot remain upright for at least 30 min.
Ibandronate (Boniva)	Tablet or solution: 2.5mg/d, 150 mg/mo, 3mg/3 mo	Vertebral	
Risedronate (Actonel, Atelvia)	Tablet: 5 mg/d, 35 mg/wk, 150 mg/mo	Vertebral, Hip	
Zoledronic acid (Reclast)	Intravenous: 5mg/y	Vertebral, Non-Vertebral	Hypocalcemia, Renal Insufficiency (CrCl <30)
Calcitonin			
Calcitonin	Nasal Spray: 200 IU/d, SC/IM: 100 IU/every other day	Vertebral	Allergy to calcitonin-salmon
RANKL inhibitor			
Denosumab (Prolia)	SC: 60 mg/6 mo	Vertebral, Hip	Hypocalcemia
Parathyroid Hormone			
Teriparatide (Forteo)	SC: 2 ug/d	Vertebral, Non-Vertebral	Hypersensitivity to PTH analogs (angiodema and anaphylaxis)
Abaloparatide (Tymlos)	SC: 80 ug/d		
SERM			
Raloxifene (Evista)	Tablet: 60 mg/d	Vertebral	Venous thromboembolism, Pregnancy, women who may become pregnant, nursing mothers
Sclerostin Inhibitor			
Romosozumab (Evenity)	SC: 210 mg/mo	Vertebral, Non-Vertebral, Hip	MI or stroke within the previous year.

References

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P&T Committee Meeting Update

The P&T Committee met for its quarterly business meeting on February 13, 2020.

Highlights of this meeting include:

- The new provider enrollment system is set to go live in July. All pharmacies will be enrolling through the central provider at that time.
- Showing no evidence of a difference in safety or efficacy against existing agents, Secuado and Talicia will be referred to the Department of Health for cost analysis and PDL placement.
- Trikafta will be limited to indication.

The proposed prior authorization criteria will be posted for public comment at **www.uwyo.edu/DUR**. Comments may be sent by email to **alewis13@uwyo.edu** or by mail to: **Wyoming Drug Utilization Review Board, Dept. 3375, 1000 E. University Avenue, Laramie, WY 82071**. Comments should be received prior to April 30, 2020.

The next P&T Committee meeting will be held May 14, 2020 in Cheyenne. An agenda will be posted approximately two weeks prior to the meeting.

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