

Management Strategies for Osteoporosis

Jena L. Ivey, PharmD, BCPS
Clinical Assistant Professor, UNC School of Pharmacy
Clinical Pharmacist, Medication Management
Program for Older Adults
ivey@unc.edu

Objectives

- Discuss the clinical features, pathophysiology, and risk factors for osteoporosis
- Review nonpharmacological and pharmacological options for management
- Select an appropriate agent for the prevention/treatment of osteoporosis
- Discuss limitations of current treatment options

Osteoporosis

- “Silent disease” until complicated by fractures
- Most common bone disease in humans
- Characterized by:
 - Low bone mass
 - Microarchitectural deterioration
 - Compromised bone strength
 - Increased risk for fracture

Impact of Osteoporosis

- Affects enormous number of people and prevalence will increase as population ages
- In 2002, National Osteoporosis Foundation (NOF) estimated that 8 million women and 2 million men have the disease
- Additional 34 million have low bone mass
- In US, approx. half of women and one-fourth of men over 50 years of age will experience osteoporotic fracture within their lifetime
 - Important disease in men as well, although increased risk occurs about 5-10 years later

NOF. America's Bone Health: The State of Osteoporosis and Low Bone Mass In our Nation, 2002.

Impact of Osteoporosis

- Fractures and associated complications are relevant clinical sequelae of osteoporosis
- Most common fractures occur at the femur (hip), vertebrae (spine), and distal forearm (wrist)
- Hip fractures result in 10-20% excess mortality within 1 year
- One-third of patients who experience a hip fracture will fracture the opposite hip
- Up to 25% of hip fracture patients may require long-term nursing home care, only 40% fully regain their previous level of functioning

Impact of Osteoporosis

- Fractures can occur in absence of trauma or with minimal trauma
- Vertebral fracture complications include back pain, height loss, kyphosis, death
- Fractures can lead to decreased quality of life, depression, loss of self-esteem
- Projected annual direct costs of osteoporosis: \$25.3 billion by 2025, ~ \$50 billion by 2040

Pathophysiology

- Process of bone remodeling normal to maintain a healthy skeletal architecture
- Bone loss occurs when balance between bone removal and replacement is altered, resulting in greater bone removal
- Imbalance occurs with menopause and advancing age

Normal Bone vs Osteoporotic Bone

Bone strength = Bone density + Bone quality

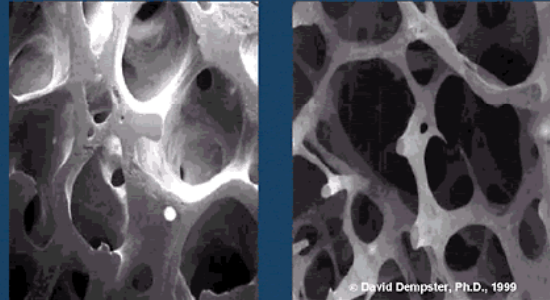


Photo source: Dempster DW, et al. *J Bone Miner Res.* 1986;1:15-21.

Risk Factors

Major

- History of fracture as an adult
- Fragility fracture in first degree relative
- Caucasian/Asian postmenopausal woman
- Low body weight (< 127 lb)
- Current smoking
- Use of oral corticosteroids > 3 mo.

Additional

- Impaired vision
- Estrogen deficiency at early age (< 45 YO)
- Dementia
- Poor health/frailty
- Recent falls
- Low calcium intake (lifelong)
- Low physical activity
- > 2 alcoholic drinks per day

Medical Conditions Associated with Increased Risk of Osteoporosis

- COPD
- Cushing's syndrome
- Eating disorders
- Hyperparathyroidism
- Hypophosphatasia
- IBS
- RA, other autoimmune connective tissue disorders
- Insulin dependent diabetes
- Multiple sclerosis
- Multiple myeloma
- Stroke (CVA)
- Thyrotoxicosis
- Vitamin D deficiency
- Liver diseases

Not an inclusive list

Drugs Associated with Reduced Bone Mass

- Aluminum
- Anticonvulsants
- Cytotoxic drugs
- Glucocorticosteroids (oral/high dose inhaled)
- Immunosuppressants
- Gonadotropin-releasing hormone (e.g. Lupron)
- Lithium
- Heparin (chronic use)
- Supraphysiologic thyroxine doses
- Aromatase inhibitors
- Depo-Provera

Not an inclusive list

Glucocorticoids and Osteoporosis

- Glucocorticoids reduce bone formation, increase bone resorption
- Most common form of secondary osteoporosis
- Possible mechanisms:
 - Inhibitory effect on osteoblasts
 - Increase in osteoclast activity
 - Decrease in sex steroid production
- Also decrease intestinal calcium absorption, increase renal calcium excretion

Glucocorticoids and Osteoporosis

- Substantial increase in fracture risk in patients receiving glucocorticoid therapy
 - Appears within 3-6 months of initiating therapy
- Risk appears to be related to dose (oral and inhaled) and duration of therapy, but independent of BMD
- Evaluate BMD at hip, spine
- Use of FDA-approved medications
 - Bisphosphonates

Risk Factors: Men

- Genetics
- Physical activity/strength
- Smoking/alcohol
- Testosterone production
- Calcium intake
- Estrogen production
- Use of glucocorticoid therapy ≥ 7.5 mg of prednisone for > 3 mo

Risk Assessment/Diagnosis

- After menopause, all women should be evaluated clinically for osteoporosis risk to determine need for BMD testing
- 50-60% of men with osteoporosis have disorders known to reduce bone loss, such as hyperparathyroidism, intestinal disorders, malignancies, conditions resulting in immobilization
- BMD recommended in men with known risk factors and who have lost > 1.5 inches in height
- Diagnosis can be established in patients who have never had a fragility fracture by BMD measurement

World Health Organization Diagnostic Criteria

DIAGNOSIS	BMD CRITERIA*
• Normal	within 1 SD of a "young normal" adult (T-score at -1.0 and above)
• Osteopenia	between 1 and 2.5 SD below that of a "young normal" adult (T-score between -1 and -2.5)
• Osteoporosis	2.5 SD or more below that of a "young normal" adult (T-score at or below -2.5)
• Severe Osteoporosis	2.5 SD or more below that of a "young normal" adult and fracture(s)
• T-score is the number of SDs above or below the average BMD value for young, normal adults of the same sex	

BMD = Bone mineral density

SD = Standard deviation

*Measured at the hip, spine, or wrist

BMD Measurement

- Can be used to establish or confirm diagnosis, predict future fracture risk
- Measurement of BMD at any skeletal site predicts fracture risk
- Hip BMD best predictor of hip fractures and predicts fractures at other skeletal sites

Who Should be Tested?

- Decision to test based on individual risk profile, never indicated unless *results* influence *treatment* decision
- BMD testing should be performed on:
 1. All women 65 YOA and older regardless of risk factors*
 2. Younger postmenopausal women with one or more risk factors (other than being white, postmenopausal and female)
 3. Postmenopausal women who present with fractures (confirm diagnosis, determine disease severity)

*Medicare permits repeat BMD testing every 2 years.

BMD Testing Techniques

- Central machines (DXA) – Dual x-ray absorptiometry
 - Spine, hip, wrist
 - Used for diagnosis, predict future risk
- pDXA – Peripheral dual x-ray absorptiometry and single-energy x-ray absorptiometry (SXA)
 - Forearm, finger, heel
 - Used to identify patients at risk, predict risk for future fractures
- QCT – Quantitative computed tomography
 - Trabecular bone density in spine
- Ultrasound densitometry
 - Heel, tibia, patella, other peripheral sites where bones superficial

Biochemical Markers of Bone Turnover

- Markers of bone formation and bone resorption
- Can indicate whether or not therapeutic intervention has slowed bone loss
- Cannot diagnosis osteoporosis
 - NTX, CTX, DPD, TRAP markers for bone resorption
 - BAP, OC, PINP, PICP markers for bone formation
- May be useful in predicting rates of future bone loss independent of BMD, monitoring therapy

Guidelines for Treatment

- American Association of Clinical Endocrinologists
- Scientific Advisory Council of the Osteoporosis Society of Canada
- National Osteoporosis Foundation
- National Institutes of Health Consensus Development Panel
- North American Menopause Society
- American College of Rheumatology*
- American Gastroenterological Association*

*For special populations

Universal Recommendations

- Adequate intake of calcium, vitamin D
- Weight-bearing and muscle-strengthening exercises to reduce risk of falls/fracture
- Provide strategies for fall prevention
- Avoidance of tobacco use
- Identification and treatment of alcoholism
- Treatment of other modifiable risk factors for fracture

NOF – Clinician's Guide to Prevention and Treatment of Osteoporosis

www.nof.org

- Released 2/21/08 (last update 2003)
- Guidelines include African-American, Asian, Latina and other postmenopausal women, also addresses men 50 years and older
- Will help identify people at high risk for developing osteoporosis/fractures and assure appropriate treatment
- Uses new algorithm FRAX[®] by the WHO, estimates 10-year fracture probability
 - <http://www.shef.ac.uk/FRAX/>

Adequate Intake of Calcium/Vitamin D

- Adequate intakes of dietary calcium and vitamin D, including supplements if necessary
 - Elemental calcium per day (> 50 YOA) = at least 1200 - 1500 mg
 - Vitamin D₃ per day (> 50 YOA) = 800 -1000 international units (IU)
- Vitamin D plays major role in Ca absorption
- Controlled clinical trials have demonstrated the combination reduces fracture risk
- Inexpensive, well-tolerated

Calcium and Vitamin D Supplementation

- Numerous OTC products with each calcium salt delivering a different proportion of elemental calcium
- Discourage herbal calcium supplements that may contain combination of Ca salts and other additional constituents (e.g. Coral calcium)
- Doses should be limited to 500 mg elemental calcium at a time for adequate absorption
- Food enhances absorption

Calcium/D Product Selection

Product (% elemental Ca)	Elemental Calcium (mg)	Vitamin D (units)	Comments
Calcium carbonate (40)			Requires acidic environment for dissolution and disintegration. Best to take with meals. Greater risk for constipation with carbonate form.
-Tums Ultra	400		
-Caltrate 600 Plus	600	200	
-Oscal Plus D	500	125	
-Viactiv Chews	500	100	
Calcium citrate (24)			Take without regard to meals. Serving size usually equals 2 capsules so label can be misleading to patients.
-Citracal Plus D	315	200	
-Citracal D Creamy Bites			
Vitamin D			
-Multivitamin (D ₃)	120-450	400	
-Vitamin D		100-400	

Vitamin D and Fall Risk

- In addition to its effect on BMD, may contribute to reduction in fracture risk
 - Improved muscle function
 - Reduction in risk for falls
- Meta-analyses of 5 clinical trials (≥ 60 YOA) showed significant reduction in risk for falling in those taking vitamin D plus calcium versus those taking placebo
- Vitamin D deficiency prevalent in older adult population
 - Inadequate sun exposure, use of sunscreen
 - Homebound, institutionalized
 - Northern latitudes
 - Maintain 25-hydroxyvitamin D₃ at least > 30 ng/mL
 - Treatment: 50,000 IU vitD weekly x 6-8 weeks, then assess need for chronic monthly therapy

Regular Weight-Bearing Exercise

- Defined as those in which bones and muscles work against gravity as feet and legs bear the body's weight
- Include walking, jogging, Tai-Chi, stair climbing, dancing, tennis, yoga
- Improve agility, strength, balance
- May increase bone density modestly, reduce fall risk, enhance muscle strength, improve balance

Avoidance of Tobacco and Alcohol

- Tobacco products detrimental to skeleton, overall health
- NOF strongly encourages tobacco cessation programs as osteoporosis intervention
- Excessive alcohol intake also detrimental to bone health and requires treatment

Who Should Be Treated? NOF Recommendations – 2008

- Initiate therapy to reduce fractures in postmenopausal women/men > 50 with:
 1. BMD T-scores ≤ -2.5 at hip or spine
 2. Prior vertebral or hip fracture
 3. Low bone mass (T-scores -1.0 to -2.5 at hip or spine) when:
 - 10-year probability of hip fracture is $\geq 3\%$
 - 10-year probability of major osteoporosis-related fracture is $\geq 20\%$
 - Based on US-adapted WHO algorithm

www.nof.org

FDA-Approved Drugs for Osteoporosis

- **Bisphosphonates**
 - Alendronate, Alendronate plus D (Fosamax, Fosamax Plus D)
 - Risedronate, Risedronate with Calcium (Actonel®)
 - Ibandronate (Boniva®)
- **Calcitonin** (Miacalcin®, Fortical®, Calcimar®)
- **Parathyroid Hormone [PTH (1-34), teriparatide]**
 - Forteo®
- **Selective Estrogen Receptor Modulators (SERMs)**
 - Raloxifene (Evista®)
- **Estrogen/Hormone Therapy (ET/HT)**
 - Premarin®, Estrace®, Prempro®

Bisphosphonates – Antiresorptive Agents

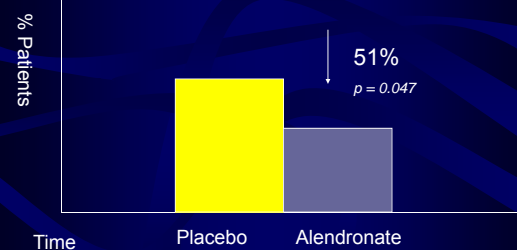
- Agents FDA-approved for:
 - Prevention and treatment of osteoporosis in postmenopausal women
 - Treatment to increase bone mass in men with osteoporosis
 - Treatment of glucocorticoid-induced osteoporosis in men and women receiving glucocorticoids
 - Treatment of Paget's disease of bone in men and women
- Mechanism: inhibits bone resorption by attaching to bony surfaces undergoing active resorption and inhibiting action of osteoclasts
 - Leads to increases in bone density and reduced fracture risk

Bisphosphonates – Clinical Efficacy

- Controlled clinical trials indicate over 3-4 year period, alendronate ↑ bone mass and ↓ incidence of vertebral, hip, and all non-vertebral fractures by 50%
- Controlled clinical trials indicate risedronate ↑ bone mass and ↓ risk of vertebral fractures by 40% and non-vertebral fractures by 30% over 3-year period
- Ibandronate has been shown in controlled clinical trials to ↑ BMD and reduce the risk of *vertebral* fracture by 50% over 3-year period
- Alendronate appears to be well tolerated and effective for at least ten years

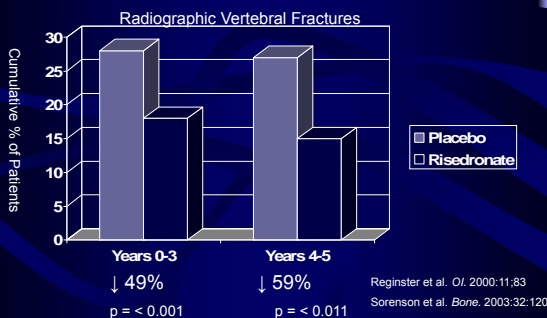
Risk Reduction in Hip Fracture at 3 Years in FIT 1 Trial

In patients with low FN bone density and prevalent vertebral fracture



Black DM, et al. *Lancet*. 1996;348(9041):1535

Reduction in Relative Risk of New Vertebral Fracture in Years 0-3 & 4-5 with Risedronate



Bisphosphonates – Dosing

- **Alendronate***
 - Prevention
 - 5 mg PO daily
 - 35 mg PO weekly
 - Treatment
 - 10 mg PO daily
 - 70 mg PO weekly
 - 70 mg/2,800 IU vitamin D PO weekly
- **Risedronate**
 - Prevention/Treatment
 - 5 mg PO daily
 - 35 mg PO weekly
- **Ibandronate**
 - Prevention/Treatment
 - 2.5 mg PO daily
 - 150 mg PO monthly
 - Treatment
 - 3 mg IV every 3 months

*Alendronate also available in oral solution.

Bisphosphonates – Administration

- Must be taken *at least* one-half hour before the first food, beverage, or medication of the day with plain water only (1 hour prior for monthly ibandronate)
- Should only be taken upon arising for the day
- Tablet should be swallowed with a full glass of water (8 oz) and patients should remain upright, walking, standing, or sitting for at least 30 minutes (60 minutes for monthly ibandronate)
- Should supplement with calcium/vitamin D if dietary intake inadequate

Bisphosphonates – Adverse Effects

- Hypocalcemia (18%)
- Hypophosphatemia (10%)
- Musculoskeletal pain, cramps – recent FDA warning
- Gastrointestinal
 - Abdominal pain
 - Acid reflux
 - Dyspepsia
 - Esophageal ulcer
 - Gastritis
- Osteonecrosis of the jaw (IV bisphosphonates)
- Visual disturbances (rare)

Bisphosphonates – Missed Dose

- Once weekly alendronate, risedronate
 - Take on morning after remembering, then resume once weekly on regularly chosen day
- Once monthly ibandronate
 - If next dose > 7 days away, take dose the morning following the date remembered
 - Then return to original schedule
 - If next dose < 7 days away, wait until next scheduled dose
 - Must not take two 150 mg tablets within the same week

Intravenous Bisphosphonates

- Pamidronate, Zoledronic acid, Ibandronate
- Pamidronate (Aredia®)
 - Treatment of osteolytic bone metastases associated with multiple myeloma or metastatic breast cancer, hypercalcemia
 - Frequency of dosing variable (weekly to monthly)
- Zoledronic acid (Zometa®)
 - Approved for treatment of malignancy-associated hypercalcemia, documented bone metastases from solid tumors along with standard antineoplastic therapy, Paget's disease
 - Frequency of dosing variable (weekly to monthly)

Zoledronic Acid (Reclast®)

- Approved for treatment of osteoporosis in postmenopausal women in August 2007
- Single 5 mg infusion given IV over \geq 15 minutes
- Should still supplement with calcium/vitamin D
- May be ideal for those with GI contraindications to the oral formulations

Price Comparison

Drug	Price
Alendronate (Fosamax®) 10 mg once daily 70 mg once weekly 70 mg/2800 IU weekly	30 day supply: \$72.99 30 day supply: \$65.99 30 day supply: \$79.70
Risedronate (Actonel®) 5 mg once daily 35 mg once weekly	30 day supply: \$65.99 30 day supply: \$63.99
Ibandronate (Boniva®) 2.5 mg once daily 150 mg once monthly	30 day supply: \$65.99 30 day supply: \$75.99

www.drugstore.com

Bisphosphonates

- Very well tolerated in patients who adhere to proper administration techniques
- Proper patient counseling for correct administration is **KEY** to reduce risk of adverse effects and increase tolerability
- Place in Therapy: should be considered first-line for prevention/treatment of osteoporosis in patients with no contraindications

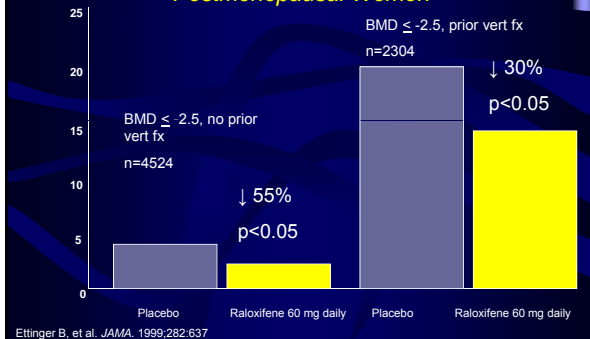
SERMs – Raloxifene

- FDA-approved for:
 - Prevention and treatment of osteoporosis in postmenopausal women
- Mechanism: tissue-selective activity, acts as an estrogen agonist on bone
 - Estrogen antagonist on breast, uterus

Raloxifene – Clinical Efficacy

- Reduces risk of vertebral fracture by 30% in patients with previous spinal fracture, 55% in patients without prior spinal fracture over 3 years
- Increases BMD at all skeletal sites and reduces total and LDL cholesterol
- Less potent antiresorptive agent than bisphosphonates, although direct comparison studies lacking

Raloxifene: Effect on Radiographic Vertebral Fractures (MORE) Postmenopausal Women



Raloxifene

- For prevention and treatment
 - 60 mg PO once daily
- Should supplement with calcium/vitamin D if dietary intake inadequate
- Adverse effects
 - Hot flashes
 - DVT
 - Leg cramps
 - Small increase in risk of fatal stroke
- Price
 - 30-day supply = \$86.99
 - No generic available

Raloxifene

- Place in Therapy: considered first-line in women who cannot tolerate bisphosphonates and have no contraindications to therapy
- Combination therapy (usually a bisphosphonate with a non-bisphosphonate) can provide additional small increases in BMD when compared to monotherapy
- Impact of combination therapy on fracture rate unknown

Estrogen/Hormone Therapy (ET/HT)

- FDA approved for:
 - Prevent osteoporosis
 - Treatment of moderate/severe vasomotor symptoms of menopause
 - Treatment of moderate/severe symptoms of vulvar and vaginal atrophy associated with menopause
 - Consider topical preparations to treat vaginal symptoms rather than oral ET/HT

FDA Recommendations – ET/HT

- When prescribing medications for osteoporosis, physicians should consider all non-estrogen therapies first
- When prescribing ET/HT, use smallest dose for shortest amount of time to achieve treatment goals
- Prescribe ET/HT products only when benefits believed to outweigh risks for a specific patient

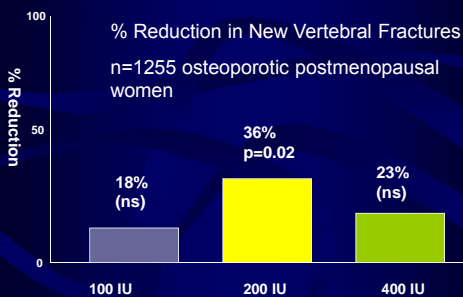
Calcitonin

- FDA-approved for:
 - Treatment of osteoporosis in women who are ≥ 5 years postmenopausal
 - Treatment of Paget's disease of bone
 - Adjunctive therapy for hypercalcemia
- Mechanism:
 - Peptide composed of 32 amino acids which binds to osteoclasts and inhibits bone resorption
 - Promotes the renal excretion of calcium, phosphate, sodium, magnesium and potassium by decreasing tubular reabsorption

Calcitonin – Clinical Efficacy

- Has been shown to increase spinal bone mass and may decrease risk of vertebral fracture
- Conflicting data on efficacy of calcitonin at sites other than the spine
- Less effective than bisphosphonates in treatment of osteoporosis
- Beneficial, short-term effect on acute bone pain after osteoporotic fracture (vertebral)

Nasal Calcitonin: Efficacy at the Spine (PROOF: 5 year analysis)



Calcitonin – Dosing/Administration

- Intranasal
 - 200 units (1 spray) alternating nares daily
 - Store unopened bottles in refrigerator, protect from freezing
 - Can store open bottles at room temperature for up to 35 days
 - Activate pump of new bottles until full spray produced (allow to reach room temperature before priming)
 - Each bottle contains at least 30 doses
- IM/SQ
 - 100 units/every other day (minimum effective dose not well-defined)
 - Should perform skin test prior to initiating therapy
- Should supplement with calcium/vitamin D if dietary intake inadequate

Calcitonin

- Adverse effects:
 - Nasal spray: rhinitis (12%), irritation of nasal mucosa (9%), epistaxis (3.5%), sinusitis (2.3%), back pain, arthralgia, headache
 - Injection: nausea (10%), flushing (2-5%), headache
- Temporarily withdraw use of nasal spray if ulceration of nasal mucosa occurs
- Price per month
 - 200 units/mL (2): \$42.08
 - 200 units/ACT (3.7): \$81.59

Calcitonin

- Valid option for treatment of established osteoporosis, especially when accompanied by fracture pain
- Place in therapy: because of cost, adverse effects, inconvenience of nasal administration, recommend using calcitonin until pain is no longer a problem and then switching to a bisphosphonate for long-term therapy

Parathyroid Hormone [PTH (1-34)] *Anabolic agent*

- FDA-approved for:
 - Treatment of osteoporosis in postmenopausal women at high risk for fracture
 - previous osteoporotic fracture, multiple risk factors for fracture, extremely low BMD (< -2.5), or failed/intolerant to previous treatment
 - Treatment of primary or hypogonadal osteoporosis in men at high risk of fracture
- Mechanism: recombinant formulation of endogenous parathyroid hormone (PTH)
 - stimulates osteoblast function, increases gastrointestinal calcium absorption, increases renal tubular reabsorption of calcium
 - Enhances bone turnover by initiating greater bone formation

PTH (1-34) – Clinical Efficacy

- Shown to decrease the risk of new vertebral fractures by 65% and nonvertebral fractures by 53% versus placebo after median exposure of 19 months
- Increases lumbar spine BMD as well as at the femoral neck, total hip, and total body
- Safety, efficacy of PTH (1-34) has not been demonstrated beyond 2 years of treatment

PTH (1-34) – Dosing/Administration

- 20 µg SQ once daily for treatment of osteoporosis
 - Thigh or abdominal wall
- Forteo® prefilled pen contains 28 daily doses
- Important to read Medication Guide and User Manual before starting and each time medication refilled
- Should be administered initially under circumstances where the patient can immediately sit or lie down, in the event of orthostasis (dizziness, palpitations are transient)
- Should supplement with calcium/vitamin D if dietary intake inadequate

PTH (1-34) – Adverse Effects

- Most common
 - Dizziness, rash, nausea, headache, leg cramps, arthralgia, rhinitis, transient hypercalcemia
- S/s of hypercalcemia: nausea, vomiting, constipation, low energy, or muscle weakness
- Most adverse effects in the clinical trials were mild and generally did not lead to the discontinuation of the drug
- Osteosarcoma risk in animals
 - Lead to black box warning by FDA

PTH (1-34) – Warnings/Precautions

- Increased risk of osteosarcoma (rats) – clinical relevance unknown (no excess reports in humans)
- Avoid in:
 - Paget's disease of bone
 - Prior radiation therapy to skeleton
 - Bone metastases
 - Hypercalcemia
 - History of skeletal malignancy
 - Pregnant/nursing

PTH (1-34) – Price

- One-month supply \$539.99
- Lilly offers Forteo® Patient Assistance Program for Medicare-eligible (LillyMedicareAnswers) and non-Medicare eligible patients
- LillyMedicareAnswers intended for patients who are enrolled in any Medicare Part D prescription drug plan and who meet certain eligibility requirements
 - Expected to start early 2007
- For non-Medicare patients, application process includes paper application and income restrictions
- Call 1-877-795-4559 or visit www.lilly.com for more details

PTH (1-34)

- Due to safety concerns, PTH treatment should be limited to those most severely affected and for a maximum of two years
- Combination therapy with a bisphosphonate not recommended as effects do not appear additive
- Cost, daily SQ injection may be prohibitive for some patients

PTH (1-34)

Place in Therapy:

- Recommend PTH for women or men with severe osteoporosis (low bone mineral density [T-score < -2.5] and at least one fragility fracture) who are refractory to or unable to tolerate bisphosphonate therapy
- In patients considered to be bisphosphonate "failures," PTH may be started approximately 3 months after bisphosphonates are discontinued
- Antiresorptive therapy may be considered after discontinuation of PTH to maintain gains in BMD acquired with PTH alone in those at high risk for subsequent fracture

Approaches to Monitoring Therapy

- Always important to ask patients about adherence, encourage continuation of therapies to reduce fracture risk
- Monitoring of therapy should be considered, as up to 1/6 of women taking effective therapies continue to lose bone, especially if they smoke
- May measure bone mineral density at a single site after one year of therapy, but results may be misleading
- Drugs may decrease a patient's risk for fracture even when there is no apparent increase in BMD

Monitoring Therapy

Option 1 — Bone density measurement can be repeated after one year of therapy

- If BMD stable or improving, evidence for treatment response
- If BMD declines at one year, adherence with drug, calcium and vitamin D should be verified, and evaluation for secondary causes should be performed
- If patient healthy and well, and taking the drug and supplements correctly, correct action is controversial

Monitoring Therapy

Option 2 — Repeat measurement of bone mineral density after two years of therapy

- Problem with this approach is it may delay detection of poor response

Option 3 — Combines measurement of biochemical markers of bone turnover with measurement of bone mineral density

- Bone mineral density and marker of bone turnover measured at baseline, followed by repeat measurement of the marker in six months
- If the marker falls significantly (>50% for urine NTX and >30% for serum CTX), evidence that the drug having desired effect, and BMD can be repeated after two years

Monitoring Therapy

Option 4 — Monitoring for effectiveness of antiresorptive therapy is unnecessary

- No evidence that we can improve outcomes in those who do not respond well to therapy
- Questions?
 - Do not know if they are best served by increasing the dose of the antiresorptive agent
 - Switching therapy altogether
 - Adding a second antiresorptive agent
 - Continuing therapy, assuming they would lose more bone mass if therapy was stopped

Questions Left Unanswered

- How can we better identify and assess patients at high risk for fracture?
- What strategies should be implemented to identify and modify risk factors for falling?
- How effective are pharmacotherapeutic agents in preventing fractures in patients with moderately low bone mass?

Questions Left Unanswered

- How long should antiresorptive therapies be continued?
- Are combination therapies useful and if so, which are the useful combos and when should they be used?
- Can we identify agents to significantly increase bone mass and return bone structure to normal?

References

- Actonel® Prescribing Information (www.actonel.com)
- Ann Intern Med 1990;112:352
- Ann Intern Med 2006;144:753
- Boniva® Prescribing Information (www.boniva.com)
- Clinical Reviews in Bone and Mineral Metabolism 2004;2(4):291
- Evista® Prescribing Information (www.evista.com)
- Forteo® Prescribing Information (www.forteo.com)
- Fortical® Prescribing Information (www.fortical.com)
- Fosamax® Prescribing Information (www.fosamax.com)

References

- JAMA 2004;291(16):1999
- J Clin Densitom 2004;7(1):1-6
- J Am Acad Orthop Surg 2006;14:347
- Miacalcin® Prescribing Information (www.miacalcin.com)
- Reclast® Prescribing Information (www.reclast.com)
- National Osteoporosis Foundation (<http://www.nof.org>)
- NEJM 2003;348:1187
- NEJM 2004;350(12):1189-99
- Osteoporosis Int 1998;8:1