Osteoporosis: “Bad to the Bone”

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Disclosure

- I, do not have a vested interest in or affiliation with any corporate organization offering financial support or grant money for this continuing education program, or any affiliation with an organization whose philosophy could potentially bias my presentation.
Objectives

Upon completion of this CE activity, the pharmacist should be able to:

- Discuss the prevalence of osteoporosis in women in 2018
- Identify genetic and lifestyle factors that contribute to osteoporosis
- Review treatment strategies, both pharmacological and non-pharmacological, for the management of osteoporosis
- Recall adverse effects, important drug interactions, and patient counseling pearls for patients treated for osteoporosis
- Discuss the role of the community and clinical pharmacy team in treatment and support of osteoporosis
Osteoporosis

- Porous bone

- Common, “silent” skeletal disease characterized by:
  - Low bone mass
  - Microarchitectural disruption
  - Skeletal fragility

- Increased fracture risk
  - Hip
  - Spine
  - Wrist

- Most commonly occurs in postmenopausal women
Osteoporosis

- Oversupply of osteoclasts
- Undersupply of osteoblasts
  - Bone resorption > bone formation
- Estrogen/androgen deficiency
  - Increased bone remodeling rate
  - Increased osteoclasts and osteoblasts
  - Increased resorption and formation
- Between menopause & age 75 years, women lose ~22% of total body bone mineral
  - 13.3% aging
  - 7.75% estrogen deprivation
Epidemiology

- Estimated 5.3 million people 50 years and older have osteoporosis at the hip
- By 2020, USPSTF predicts ~12.3 million people >50 years in the US are expected to have osteoporosis
- 71% of osteoporotic fractures occur among women
- 1 in 2 women vs. 1 in 4 men have osteoporosis-related fractures in their lifetime
- Women have higher rates of osteoporosis than men at any given age
- 21 - 30% of patients who experience a hip fracture die within 1 year
Risk Factors

- Age
- Sex
- Low body mass index (≤20 kg/m²)
- Parental history of hip fracture
- Previous fragility fracture, particularly of the hip, wrist and spine
- Smoking
- Excessive alcohol intake
- Prolonged immobility
- Frequent falling
- Vitamin D insufficiency
- High salt intake
- Low calcium intake
- Inadequate physical activity
- Excess vitamin A
- Glucocorticoid treatment = ≥5mg prednisone/day x ≥3 months
Fracture Risk Assessment Tool (FRAX)

Uses clinical risk factors to estimate 10-year risk of osteoporotic fracture

- Current age
- Sex
- Prior osteoporotic fracture
- BMD of femur neck
- BMI - weight & height
- Oral glucocorticoids
- Rheumatoid arthritis
- Parental history of hip fracture
- Smoking (current)
- Alcohol intake (≥3 drinks/day)
- Secondary causes of osteoporosis: Type-1 DM, early menopause <40 years, etc.

http://www.shef.ac.uk/FRAX
Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with BMD.

Country: US (Black)  Name/ID:  About the risk factors

Questionnaire:
1. Age (between 40 and 90 years) or Date of Birth
   Age:   Date of Birth:   Y:   M:   D:   
2. Sex
   Male   Female
3. Weight (kg)
4. Height (cm)
5. Previous fracture
6. Parent fractured Hip
7. Current Smoking
8. Glucocorticoids
9. Rheumatoid arthritis
10. Secondary osteoporosis
11. Alcohol 3 or more units/day
12. Femoral neck BMD (g/cm²)

Weight Conversion
Pounds  kg

Height Conversion
Inches  cm

00524229
Individual with fracture risk assessed since 1st June 2011
Secondary Osteoporosis

- Genetic diseases - CF, osteogenesis imperfecta, hemochromatosis, homocystinuria, hypophosphatasia
- Endocrine disorders - Cushing’s syndrome, diabetes mellitus, hyperparathyroidism, thyrotoxicosis, hypogonadism, premature menopause, hyperprolactinemia
- GI disorders - Celiac disease, gastric bypass, malabsorption syndrome, IBD, biliary cirrhosis, pancreatic disease, anorexia nervosa
- Hematological disorders - hemophilia, leukemia & lymphomas, SCD, multiple myeloma
- Neuro & musculoskeletal - epilepsy, MS, muscular dystrophy, PD, spinal cord injury, stroke
- Rheumatologic & immune diseases - RA, SLE, ankylosing spondylitis
- Other - HIV/AIDS, amyloidosis, COPD, CHF, chronic metabolic acidosis, ESRD, hypercalciuria, post-transplant bone disease
High Risk Medications

- Aluminum (in antacids)
- Anticoagulants
- Anticonvulsants
- Aromatase inhibitors
- Barbiturates
- Cancer chemotherapeutic drugs
- Cyclosporine A
- Depomedroxyprogesterone
- Glucocorticoids (≥5 mg/day prednisone or equivalent for ≥3 months)
- GnRH (gonadotropin-releasing hormone) agonists
- Lithium
- Methotrexate
- Parenteral nutrition
- PPIs
- SSRIs
- Tacrolimus
- Tamoxifen (premenopausal use)
- Thiazolidinediones
- Thyroid hormones (in excess)
Screening: Procedures

- **Central DXA** - gold standard
  - Bone mineral density (g/cm²)
  - T-score (postmenopausal)
  - Z-score (premenopausal)
  - Vertebral fracture assessment (VFA)

- **Peripheral DXA**

- **Quantitative ultrasound (QUS)**

- **Bone turnover markers (BTM)**
  - S-CTX
  - PINP
## World Health Organization (WHO) Classification

<table>
<thead>
<tr>
<th>Category</th>
<th>T-Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>≥ -1.0</td>
</tr>
<tr>
<td>Low bone mass (osteopenia)</td>
<td>-1.0 to &gt;-2.5</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>≤ -2.5</td>
</tr>
<tr>
<td>Severe or established osteoporosis</td>
<td>≤ -2.5 + fractures</td>
</tr>
</tbody>
</table>

*For postmenopausal women & men >50 years of age.*
Screening: USPSTF Recommendations

- Women ≥65 years of age
- Postmenopausal women <65 years of age at increased risk
- No recommendation in men
Screening: AACE Recommendations

All women ≥65 years of age

All postmenopausal women:
- With history of fracture(s) without major trauma
- With osteopenia identified radiographically
- Starting/taking long-term systemic glucocorticoid therapy

Secondary osteoporosis

Other peri- or postmenopausal women with risk factors of osteoporosis:
- Low body weight (<127lb or BMI <20kg/m2)
- Long-term systemic glucocorticoid therapy
- FH of osteoporotic fracture
- Early menopause
- Current smoking
- Excessive alcohol consumption
# Diagnosis

## AACE Diagnosis of Osteoporosis in Postmenopausal Women

1. T-score -2.5 or below in the lumbar spine, femoral neck, total hip, and/or distal one-third (33%) radius

2. Low-trauma spine or hip fracture (regardless of BMD)

3. Osteopenia or low bone mass (T-score between -1 and -2.5) with a fragility fracture of proximal humerus, pelvis, or possibly distal forearm

4. Low bone mass or osteopenia and high FRAX fracture probability
Prevention

“Bone healthy” lifestyle

- Adequate calcium & vitamin D intake
  - Vit D: ≥1000 IU daily for age ≥50 years, ULN 4000 IU daily
  - Ca: age + sex-specific

- Regular weight-bearing resistance exercise and balance-improving exercises
  - Walking, jogging, tai chi, stair climbing, dancing

- Tobacco cessation/abstinence

- Avoid high alcohol intake

- Eliminate risks factors for falling
## Recommended Calcium Intake

<table>
<thead>
<tr>
<th>Age</th>
<th>mg/day</th>
</tr>
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<tbody>
<tr>
<td>0 - 6 months</td>
<td>200</td>
</tr>
<tr>
<td>6 - 12 months</td>
<td>260</td>
</tr>
<tr>
<td>1 - 3 years</td>
<td>700</td>
</tr>
<tr>
<td>4 - 8 years</td>
<td>1,000</td>
</tr>
<tr>
<td>9 - 18 years</td>
<td>1,300</td>
</tr>
<tr>
<td>19 - 50 years</td>
<td>1,000</td>
</tr>
<tr>
<td>51 - 70 years (men)</td>
<td>1,000</td>
</tr>
<tr>
<td>51 - 70 years</td>
<td>1,200</td>
</tr>
<tr>
<td>71+ years</td>
<td>1,200</td>
</tr>
</tbody>
</table>
Fall Risk Factors

- Neurologic disorders
  - Parkinson disease
  - Seizure disorder
  - Peripheral neuropathy
  - Prior stroke
  - Dementia
  - Impaired gait and/or balance
  - Autonomic dysfunction with orthostatic hypotension
- Impaired vision
- Impaired hearing
- Frailty & deconditioning
- Proximal myopathy
- Sarcopenia

- Medications
  - Sedatives & hypnotics
  - Antihypertensive agents
  - Narcotic analgesics

- Environmental factors
  - Poor lighting
  - Stairs
  - Slippery floors
  - Wet, icy, or uneven pavement
  - Uneven roadways
  - Electric or telephone cords
  - Walking large dogs
  - Being tripped up by small dogs
  - Throw rugs
  - Positioning in a wet or dry bathtub
Treatment of Osteoporosis
Goals of Therapy

- Optimize skeletal development and maximize peak bone mass at skeletal maturity
- Maintain skeletal mass and prevent age-related bone loss
- Preserve the structural integrity of the skeleton
- Prevent falls and fractures
Non-Pharmacologic Therapy

- “Bone healthy” lifestyle modifications
  - Adequate calcium & vitamin D
  - Exercise
    - Caution in severe osteoporosis
  - Avoid tobacco
  - Avoid excessive alcohol consumption
- Physical therapy
- Limit caffeine intake to 1 - 2 servings/day
- Adequate protein intake (0.8 g/kg/day)
- Fall preventive measures
- Sunlight/UV exposure: 30 mins/day, 5 days/week
Fall Prevention

- Anchor rugs
- Minimize clutter
- Remove loose wires
- Use nonskid mats
- Install handrails in bathrooms, halls, and long stairways
- Light hallways, stairwells, and entrances
- Encourage patient to wear sturdy, low-heeled shoes
- Keep all items within reach and avoid using stepstools
Pharmacologic Therapy

Treat in postmenopausal women with:

- Osteopenia or low bone mass and history of fragility fracture of the hip or spine
- T-score ≤ -2.5 in the spine, femoral neck, total hip, or 33% radius
- T-score -1.0 to -2.5 in the spine, femoral neck, total hip, or 33% radius +
  - FRAX 10-year probability for major osteoporotic fracture is ≥ 20%
  - OR
  - 10-year probability of hip fracture is ≥ 3%
Pharmacologic Therapy

**Antiresorptive**
- Calcium + Vitamin D
- Bisphosphonates
- Denosumab
- Calcitonin

**Anabolic**
- Teriparatide
- Selective estrogen receptor modulators
- Hormone therapy
Treatment Algorithm

No prior fragility fracture or moderate fracture risk

Alendronate, denosumab, risendronate, ZA
Alternate therapy: ibandronate, raloxifene

Reassess at least yearly for response to fracture risk

Increasing or stable BMD + no fractures

Drug holiday after 5 years PO / 3 years IV bisphosphonate therapy

Resume therapy if fracture occurs, BMD declines beyond LSC, BTM’s rise to pretreatment values or patient initial treatment criteria

Progression of bone loss or recurrent fractures

Assess compliance, re-evaluate for secondary osteoporosis & factors for suboptimal therapy

Switch to injectable antiresorptive
Switch to teriparatide if on injectable or at very high risk for fractures
Treatment Algorithm

Prior fragility fractures or indicators of higher fracture risk

Denosumab, teriparatide, ZA
Alternate therapy: alendronate, risedronate

Reassess at least yearly for response to fracture risk

Denosumab

Continue therapy or consider adding teriparatide if progression of bone loss or recurrent fractures

Teriparatide for up to 2 yrs

Sequential therapy with oral or injectable antiresorptive agent

Zoledronic acid

If stable, continue therapy for 6 years. If progression of bone loss or recurrent fractures, consider switching to teriparatide.
Calcium Supplementation

- When unable to increase dietary calcium
- Ca intake should not exceed 1500 mg/day
- Should not exceed 500 - 600 mg per dose

**Calcium Carbonate**
- 40%
- Less pill burden
- Least expensive
- GI side effects
- Needs gastric acid
- Take with food

**Calcium Citrate**
- 21%
- More pill burden
- More expensive
- Less side effects
Vitamin D

Role
- Helps calcium absorption
- Increases BMD
- Enhances response to bisphosphonate therapy

Serum 25(OH)D
- Target: ≥30 ng/mL
- Insufficiency: 20-29 ng/mL
- Deficiency: < 20 ng/mL
Vitamin D

Vitamin D insufficient or deficient

Starting Dose
- 50,000 IU vitamin D2 or D3 once weekly for 8 - 12 weeks
- OR
- 5,000 IU vitamin D2 or D3 once daily for 8 - 12 weeks

Maintenance Dose
- Vitamin D3 1000 - 2000 IU daily (or as appropriate to reach target level)

Higher dose may be required for obesity, malabsorption, medications affecting vitamin D absorption.

Large bolus doses vitamin D3 ≥300,000 IU may rapidly correct deficiencies and improve vitamin D status for up to 3 months.
Bisphosphonates

- Alendronate (oral)
- Risedronate (oral)
- Ibandronate (oral, IV)
- Zoledronic acid (IV)

Mimic pyrophosphate

Decreased osteoclast activity

Decreased bone resorption & turnover
### Bisphosphonates

<table>
<thead>
<tr>
<th></th>
<th>Prevention</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alendronate (Fosamax®)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Tablet or liquid Plus D</td>
<td>5 mg PO daily 35 mg PO weekly</td>
<td>10 mg PO daily 70 mg PO weekly 70 mg + 2,800 or 5,600 IU Vit D₃ weekly</td>
</tr>
<tr>
<td><strong>Risedronate (Actonel®, Atelvia®)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Atelvia®: DR, weekly</td>
<td>5 mg PO daily 35 mg PO weekly 150 mg PO monthly</td>
<td>5 mg PO daily 35 mg PO weekly 150 mg PO monthly</td>
</tr>
<tr>
<td><strong>Ibandronate (Boniva®)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• IV: pre-filled syringe</td>
<td>2.5 mg PO daily 150 mg PO monthly</td>
<td>2.5 mg PO daily 150 mg PO monthly 3 mg IV Q3months</td>
</tr>
<tr>
<td><strong>Zoledronic acid (Reclast®)</strong></td>
<td>5 mg IV every other year</td>
<td>5 mg IV once yearly</td>
</tr>
</tbody>
</table>
Bisphosphonates

Class AE’s

• Irritation of upper GI mucosa (esophagitis, ulcers, and erosions)
• Hypocalcemia
• Diarrhea, abdominal pain
• Musculoskeletal pain
• Osteonecrosis of the jaw (ONJ) and atypical femoral fracture (AFF)

Zoledronic AE’s

• Pyrexia
• Myalgia
• Headache
• Arthralgia
• Flu-like illness
## Bisphosphonates

<table>
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<tr>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alendronate</strong></td>
</tr>
<tr>
<td>• Taken 30 minutes prior to food, beverage, or other medication upon rising for the day</td>
</tr>
<tr>
<td>• Do not lie down for 30 minutes after taking</td>
</tr>
<tr>
<td>• Caution with NSAIDs (GI irritation)</td>
</tr>
<tr>
<td><strong>Risedronate</strong></td>
</tr>
<tr>
<td><strong>IR</strong></td>
</tr>
<tr>
<td>• Same as alendronate</td>
</tr>
<tr>
<td><strong>DR</strong></td>
</tr>
<tr>
<td>• Swallow whole</td>
</tr>
<tr>
<td>• Take in the AM immediately AFTER breakfast</td>
</tr>
<tr>
<td>• Drink at least 4 oz. of water</td>
</tr>
<tr>
<td>• Remain upright</td>
</tr>
</tbody>
</table>
## Bisphosphonates

<table>
<thead>
<tr>
<th>Considerations</th>
<th>Ibandronate</th>
<th>PO</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>• Swallow tablet whole with 6 to 8 oz. plain water</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Take at least 60 minutes prior to food, beverage, or other meds</td>
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<tr>
<td></td>
<td></td>
<td>• For missed doses of monthly formulation, do not take more than 150 mg within 7 days</td>
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<tr>
<td></td>
<td></td>
<td>IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Inject over 15 - 30 seconds</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Zoledronic acid</th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>• Ensure adequate hydration</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Single-dose IV infusion over ≥15 minutes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Flush line with 10 mL of NS after complete</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Pre-medication to prevent acute-phase reaction</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• APAP given 1-2 hours before treatment</td>
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</tr>
</tbody>
</table>
Bisphosphonates

Contraindications

- Active upper GI diseases
- Inability to remain upright for 30-60 min
- Anatomic or functional esophageal abnormalities (achalasia, stricture, etc.)
- Vitamin D deficiency
- Hypocalcemia
- Hypersensitivity to drug

Caution

- Kidney failure
  - GFR <30 mL/min for risedronate & ibandronate
  - GFR <35 mL/min for alendronate & zoledronic acid
Denosumab (Prolia®)

**Mechanism of Action**
- Fully human monoclonal antibody
- Binds & inhibits RANKL
- Reduces differentiation of precursor cells into mature osteoclasts
- Decreases function and survival of activated osteoclasts
**Denosumab**

Indicated for treatment of:

- Postmenopausal women at a *high risk* for fracture
- Patients who have failed or are intolerant to other available osteoporosis therapies
- To increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer
Denosumab

Prior to use:
- Correct calcium and vitamin D deficiencies
- Rule out pregnancy

Dosing
- 60 mg subcutaneously in upper arm, upper thigh, or abdomen every 6 months by healthcare professional

Adverse Effects
- Back pain, musculoskeletal pain
- Cystitis (PM women)
- Dermatitis, skin rashes
- Hypocalcemia
- Serious skin infections
- ONJ and AFF
Raloxifene (Evista®)

- Selective estrogen receptor modulator (SERM)
  - Only agent in its class approved for prevention and treatment of postmenopausal osteoporosis
- Estrogen agonist/antagonist
  - Agonist in bone tissue
- Also approved for reduction in risk of invasive breast cancer in postmenopausal women
  - With osteoporosis
  - At high risk for invasive breast cancer
Raloxifene

Dosage
- 60 mg PO daily

Adverse Effects
- Hot flashes, sweating
- Leg cramps
- Swelling of legs
- Flu-like syndrome
- Joint pain

Black Box Warnings
- Increased risk of VTE
- Increased risk of death from stroke

Drug Interactions
- Cholestyramine
- Warfarin
- Highly protein-bound drugs
Raloxifene

Contraindications
- History of VTE
- Pregnancy

Caution
- Hepatic impairment
- CrCl <50 mL/min
- Hypertriglyceridemia with previous estrogen treatment

Not Recommended
- Premenopausal women
- Concomitant systemic estrogens
Duavee®

- Bazedoxifene (SERM) + conjugated estrogen
- BZA 20 mg + CEE 0.45 mg per day
- Approved for postmenopausal women with a uterus
  - For prevention of osteoporosis
  - To reduce moderate to severe hot flashes
Duavee®

**BBW**

- Increased risk for endometrial cancer with unopposed estrogens
  - Do not take additional estrogens
  - Not recommended if unusual vaginal bleeding
- Increased risk of probable dementia in postmenopausal women \( \geq 65 \) years of age

**Drug Interactions**

- Estrogens - 3A4
- BZA - UGT
Duavee®

Contraindications
- Abnormal uterine bleeding
- Breast cancer
- Estrogen-dependent neoplasia
- VTE
- Arterial thromboembolism
- Hypersensitivity
- Hepatic impairment
- Thrombophilic disorders
- Pregnancy
Calcitonin

- Miacalcin® (synthetic calcitonin salmon) injection
- Fortical® (recombinant calcitonin salmon) nasal spray

**Mechanism of Action**
- Peptide hormone released from thyroid gland when serum calcium is elevated
  - Salmon calcitonin more potent/longer lasting
- Inhibits bone resorption by osteoclasts

- Indicated for treatment of postmenopausal osteoporosis, >5 years postmenopause
Calcitonin

Dosage
- Intranasal: one 200 IU spray daily
  - Alternate nostrils daily
- IM/SC: inject 100 IU daily

Adverse Effects
- Hypersensitivity/allergic reaction (salmon allergy)
- Intranasal: rhinitis, epistaxis
- IM/SC: nausea, arthralgia, injection site reaction

Drug Interactions:
- Lithium
Teriparatide (Forteo®)

- Recombinant human PTH(1-34)
- Increases bone formation, bone remodeling rate, and osteoblast number/activity
- Approved for initial treatment of women with postmenopausal osteoporosis who are at high risk of fracture or have failed or been intolerant of previous osteoporosis therapy
Teriparatide

Dosage
- 28-day prefilled pen: 20 mcg SC once daily
  - Thigh or abdomen
- No more than 2 years duration

Adverse Effects
- Orthostasis (typically within 4 hours of injection)
- Nausea, arthralgia
- Hypercalcemia

BBW: Osteosarcoma
- Not recommended in Paget’s/unexplained ALP elevations or prior external beam or implant radiation
Abaloparatide (Tymlos®)

- U.S. approval 2017
- Human parathyroid hormone related peptide [PTHrP(1-34)] analog
- Indicated for treatment of postmenopausal women with osteoporosis at high risk for fracture

**Dosage**

- 80 mcg SC once daily
  - 2000 mcg/mL pre-filled pen delivers 30 daily doses

- Similar SE profile as teriparatide
Pharmacist’s Role

**Educate**
- Educate patients on the benefits of early detection, the dangers of osteoporosis and poor bone health, and the qualities of a “bone healthy” lifestyle.

**Recognize**
- Recognize need for osteoporosis screenings, risk factors for bone loss, falls and fractures, and need for management.

**Provide**
- Provide personalized care and clinical intervention to patients at risk of falls and fractures.

**Evaluate**
- Evaluate non-pharmacological and pharmacological therapies to properly manage osteoporotic patients.
A postmenopausal woman presents for DXA follow-up. Which of the following T-scores confirms a diagnosis of osteoporosis?

A. -1.5
B. -2.7
C. -0.8
D. -2.0
E. -2.2
Which of the following is only indicated for treatment of osteoporosis?

A. Alendronate
B. Raloxifene
C. Zoledronic acid
D. Ibandronate
E. Denosumab
While counseling, your patient tells you she takes her alendronate while laying in bed. Which SE is most likely to occur?

A. Esophagitis
B. Hypercalcemia
C. Hypocalcemia
D. Diarrhea
E. Headache
After a year of alendronate therapy, BMD has not changed. Which of the following is an appropriate recommendation for switch in therapy?

A. Zoledronic acid  
B. Denosumab  
C. Calcitonin  
D. Teriparatide  
E. No change
After a year of alendronate therapy, BMD has worsened. Which of the following is an appropriate recommendation for switch in therapy?

A. Zoledronic acid
B. Denosumab
C. Calcitonin
D. Teriparatide
E. No change
References