PHARMACOTHERAPY FOR THE TREATMENT OF OSTEOPOROSIS

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CONFLICTS OF INTEREST

- The presenters have no actual or potential conflicts of interest in relation to this presentation.

PHARMACIST LEARNING OBJECTIVES

1. Summarize the prevalence and impact of osteoporosis on patients, families, and communities
2. Compare and contract first and second line pharmacotherapy options for the treatment of osteoporosis
3. Formulate a plan that incorporates evidence-based recommendations, patient-specific factors, and decision aids for the treatment of osteoporosis

TECHNICIAN LEARNING OBJECTIVES

1. Summarize the prevalence and impact of osteoporosis on patients, families, and communities
2. Recognize medications used to treat osteoporosis
3. Describe how patients and families can use decision aids as part of the treatment plan process

BACKGROUND

- Most common bone disease
  - Low bone mass
  - Deterioration of bone tissue
  - Disruption of bone architecture
  - Results in lower bone strength and increased risk of fractures

PATHOGENESIS

HORMONAL CONTROL OF BONE RESORPTION

RISK FACTORS

- Old age
- Sex steroid deficiency
- Lipid oxidation
- Decreased physical activity
- Use of glucocorticoids
- Propensity to fall

RISK FACTORS FOR OSTEOPOROSIS

- Lifestyle factors
- Conditions and diseases
- Medications

IMPACT

- 1.5 million fractures yearly resulting in more than 500,000 hospitalizations
- Hip fractures are linked with 8-36% excess mortality within 1 year
- Approximately 20% of patients with hip fractures require long-term nursing home care
- Only 40% fully regain same level of independence
**LIFESTYLE FACTORS**
- Alcohol abuse
- Excessive vitamin A
- Frequent falls
- High salt intake
- Immobilization
- Inadequate physical activity
- Low calcium intake
- Smoking (active or passive)
- Underweight
- Vitamin D insufficiency

**CONDITIONS**
- AIDS/HIV
- Anorexia nervosa
- Central obesity
- Chronic obstructive lung disease
- Congestive heart failure
- Depression
- Diabetes mellitus (types 1 and 2)
- End-stage renal disease
- Epilepsy
- Gastric bypass
- Inflammatory bowel disease
- Parenteral history of hip fracture
- Parkinson’s disease
- Premature menopause (<40 years)
- Rheumatoid arthritis
- Stroke

**MEDICATIONS**
- Aluminum (antacids)
- Anticonvulsants
- Aromatase inhibitors
- Chemotherapy
- Glucocorticoids (long-term/high dose)
- Methotrexate
- Proton pump inhibitors
- Selective serotonin reuptake inhibitors
- Thiazolidinediones

**BONE MINERAL DENSITY (BMD)**
- Dual-energy X-ray absorptiometry (DXA) of hip and spine is used to measure BMD
- T-score: Compared to young-adult reference population of the same sex

<table>
<thead>
<tr>
<th>Classification</th>
<th>T-scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>T-score ≥ 1.0 or above</td>
</tr>
<tr>
<td>Low bone mass (osteopenia)</td>
<td>T-scores = -1.0 or -2.5</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>T-score ≤ -2.5</td>
</tr>
<tr>
<td>Severe or established osteoporosis</td>
<td>T-score ≤ -2.5 with one or more fractures (abuse of major trauma)</td>
</tr>
</tbody>
</table>

**RISK FACTORS FOR FALLS**
- Neurologic and musculoskeletal
  - Impaired mobility
  - Poor balance
  - Environmental
  - Low lighting
  - Slippery conditions
  - Medical
  - Decreased cognitive function
  - Osteoarthritis
  - Urinary incontinence
  - Vision
- Medicaions
  - Antipsychotics
  - Short and intermediate acting benzodiazepines
  - Tricyclic antidepressants
  - Selective serotonin reuptake inhibitors
  - Nonbenzodiazepine receptor agonist hypnotics
  - Anticonvulsants
  - Opioids

**QUESTION 1**
- Which of the following increases a patient’s risk of developing osteoporosis?
  A. Menopause at 45 years of age
  B. Prednisone 40 mg daily for 5 days
  C. T-score last month of – 0.5
  D. Zolpidem 5 mg at bedtime
TREATMENT STRATEGIES

LIFESTYLE CHANGES
- Fall prevention
- Limit alcohol consumption
- Weight-bearing exercises like walking, jogging, Tai Chi, and dancing
- Muscle-bearing exercises like weight training, yoga, and pilates
- Tobacco cessation

CALCIUM
- Dietary or supplemental calcium
  - Men 50 – 70 years: 1000 mg/day
  - Women 51 years and older and men 71 years and older: 1200 mg/day
- Estimate calcium in diet
  - 8 oz milk: 300 mg
  - 6 oz yogurt: 300 mg
  - 1 oz cheese: 200 mg
  - Add 250 mg for nondairy sources

- Calculate elemental calcium
  - Calcium carbonate: 40%
  - Calcium citrate: 21% (preferred with H2RA & PPIs)
- Recommend maximum of 500 mg elemental calcium at once
- Common adverse effects
  - Constipation
  - Flatulence

VITAMIN D
- Aim for 25(OH)D blood level ~30 ng/mL
  - May require 50,000 units weekly for 8-12 weeks followed by 1500-2000 units/day thereafter
- Common adverse effects
  - Lipid abnormalities

QUESTION 2
- Joanne Smith is a 68 year old female who presents for a comprehensive medication review. She is worried about her “bone health” and asks whether she should take a calcium supplement. You find out that she has a vegetarian diet and the only dairy she consumes is 6 ounces of yogurt and 8 ounces of milk daily. Her medications include lisinopril and omeprazole. She does not have any allergies. What do you recommend?

A. Increase dietary calcium by eating one serving of cheese daily
B. Add calcium carbonate 500 mg once daily
C. Add calcium citrate 800 mg twice daily
D. No additional calcium is needed
CONSIDERING PHARMACOLOGIC TREATMENT

- Hip or vertebral fracture
- T-score ≤ 2.5 at the femoral neck, total hip, or lumbar spine
- Low bone mass AND
  - 10-year probability of a hip fracture ≥ 3% OR
  - 10-year probability of a major osteoporosis-related fractures ≥ 20%

### BISPHOSPHONATES

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Dosage Forms</th>
<th>Frequency</th>
<th>Generic?</th>
<th>Selected Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alendronate</td>
<td>Fosamax</td>
<td>Tablet or solution</td>
<td>Daily or weekly</td>
<td>Yes</td>
<td>Prevention &amp; treatment of postmenopausal osteoporosis</td>
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<tr>
<td>Alendronate</td>
<td>Binosto</td>
<td>Effervescent tablet</td>
<td>Weekly</td>
<td>No</td>
<td>Treatment of male osteoporosis</td>
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<tr>
<td>Risedronate</td>
<td>Actonel</td>
<td>Tablet</td>
<td>Daily or weekly, or monthly</td>
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<td>Treatment of osteoporosis due to corticosteroids</td>
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<tr>
<td>Risedronate</td>
<td>Atelvia</td>
<td>Delay-release tablet</td>
<td>Weekly</td>
<td>Yes</td>
<td>Prevention &amp; treatment of postmenopausal osteoporosis</td>
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<tr>
<td>Zoledronic acid</td>
<td>Reclast</td>
<td>IV solution</td>
<td>Yearly</td>
<td>Yes</td>
<td>Prevention &amp; treatment of postmenopausal osteoporosis</td>
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<tr>
<td>Ibandronate</td>
<td>Boniva</td>
<td>Tablet</td>
<td>Daily or monthly</td>
<td>Yes</td>
<td>Prevention &amp; treatment of postmenopausal osteoporosis</td>
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</table>

### CALCITONIN

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<thead>
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<th>Selected Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcitonin</td>
<td>Fortical, Miacalcin</td>
<td>Nasal spray</td>
<td>Daily (1 spray) daily (alternate nostrils)</td>
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<tr>
<td>Calcitonin</td>
<td>Miacalcin</td>
<td>Injection</td>
<td>100 units IM/SubQ daily</td>
<td>No</td>
<td>Treatment of postmenopausal osteoporosis</td>
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### RALOXIFENE

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<tr>
<th>Generic Name</th>
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<th>Generic?</th>
<th>Selected Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raloxifene</td>
<td>Evista</td>
<td>Tablet</td>
<td>Daily</td>
<td>Yes</td>
<td>Prevention and treatment of postmenopausal osteoporosis</td>
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</table>

### ESTROGEN/HORMONE REPLACEMENT THERAPY (HRT)

<table>
<thead>
<tr>
<th>Generic Name</th>
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<th>Frequency</th>
<th>Generic?</th>
<th>Selected Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estradiol</td>
<td>Vivelle, Minivelle, Prempro, Premphase, Dioace</td>
<td>Oral tablet, Tablet, Tablet, Tablet, Tablet</td>
<td>Daily for 23 days of a 28-day cycle</td>
<td>Yes</td>
<td>Prevention of postmenopausal osteoporosis</td>
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<tr>
<td>Conjugated estrogens/medroxyprogesterone</td>
<td>Fortesta</td>
<td>Tablets</td>
<td>Daily</td>
<td>Yes</td>
<td>Prevention of postmenopausal osteoporosis</td>
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### TERIPARATIDE

<table>
<thead>
<tr>
<th>Generic Name</th>
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<th>Frequency</th>
<th>Generic?</th>
<th>Selected Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teriparatide</td>
<td>Forteo</td>
<td>SubQ injection</td>
<td>Daily</td>
<td>No</td>
<td>Treatment of postmenopausal osteoporosis with high risk of fracture</td>
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<tr>
<td>Teriparatide</td>
<td>Forteo</td>
<td>SubQ injection</td>
<td>Daily</td>
<td>No</td>
<td>Treatment of osteoporosis in men</td>
</tr>
<tr>
<td>Teriparatide</td>
<td>Forteo</td>
<td>SubQ injection</td>
<td>Daily</td>
<td>No</td>
<td>Treatment of osteoporosis due to corticosteroids</td>
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DENOSUMAB

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<thead>
<tr>
<th>Brand Name</th>
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<th>Frequency</th>
<th>Generic?</th>
<th>Selected Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolia</td>
<td>SubQ injection</td>
<td>Every 6 months plus calcium 1000 mg and vitamin D 400 units daily</td>
<td>No</td>
<td>Treatment of postmenopausal osteoporosis with high risk of fracture</td>
</tr>
</tbody>
</table>

Post-menopausal women

- Bisphosphonate (any)
- Raloxifene
- Estrace/ERT
- Conjugated estrogens/bazedoxifen

Men

- Bisphosphonates
- Alendronate
- Risedronate
- Zoledronic acid
- Teriparatide
- Denosumab

Post-menopausal women

- Bisphosphonate (any)
- Calcium
- Raloxifene
- Teriparatide
- Denosumab

Treatment of osteoporosis in men

- Bisphosphonates
- Alendronate
- Risedronate
- Zoledronic acid
- Teriparatide

EFFICACY OF AGENTS AT PREVENTING FRACTURES

<table>
<thead>
<tr>
<th>Medication</th>
<th>Vertebral fracture</th>
<th>Hip fracture</th>
<th>Nonvertebral fracture</th>
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</thead>
<tbody>
<tr>
<td>Bisphosphonate therapy</td>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>Alendronate</td>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>Risedronate</td>
<td>A</td>
<td>A</td>
<td>A</td>
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<tr>
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<td>A</td>
<td>A</td>
<td>A</td>
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<td>Teriparatide</td>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
</tbody>
</table>

QUESTION 3

TL is a 71-year-old female with a history of Parkinson’s disease, GERD, COPD, and gout. She was recently diagnosed with osteoporosis. Of note, she lives with her daughter who is her primary caregiver. Which of the following medications do you recommend?

A. Alendronate 70 mg once weekly
B. Denosumab 60 mcg subQ every 6 months
C. Estradiol 0.025 mg/day patch once weekly
D. Teriparatide 20 mcg subQ once daily

ADDITIONAL THERAPY CONSIDERATIONS

- Combination of therapy
- May be appropriate to use teriparatide with bisphosphonate for very severe osteoporosis
- Bisphosphonate with ERT or raloxifene if the patient is experiencing active bone loss (short term)
- Duration of therapy
- Effects of medications other than bisphosphonates quickly wane after discontinuation
- Products containing estrogen lowest dose for shortest amount of time
- Teriparatide: limit to 2 years over lifetime
- Bisphosphonates: limit to 3-5 years unless patient is at high risk for fracture

GAPS IN CARE

- Under-diagnosis
- Under-prescribing
- Early nonadherence
- Late nonadherence
- Long-term adherence

PHARMACISTS’ ROLES

At the point of prescribing/prescribing
- Drug selection
- Drug discontinuation

At the point of dispensing
- Ensure safe administration (oral bisphosphonates)
- Promote long-term adherence

Both
- Support adequate calcium and vitamin D intake by:
  - Assessing dietary intake
  - Determining appropriate dose for supplementation
  - Product selection

ROLES

Osteoporosis

- Very involved
- Involved
- Little involved
- Not at all involved

Falls

- Very involved
- Involved
- Little involved
- Not at all involved

BARRIERS

- Lack of awareness
- Lack of clinical trials
- Lack of reimbursement
- Lack of adherence
- Lack of communication
- Lack of knowledge about osteoporosis
- Lack of education
- Other
- Patients generally have more urgent medical conditions
- Patients are not interested in prevention activities
- Osteoporosis is not a serious medical condition

ROLES IN DIFFERENT SETTINGS

INEFFECTIVE INTERVENTIONS

- Ambulatory care pharmacist recommending DEXA screening to PCP
- Managed care pharmacist contacting patients or PCP after fracture to encourage antiresorptive therapy
- Community pharmacist recommending antiresorptive therapy for chronic steroid patients to PCP
- Community pharmacist providing FRAX data to PCP to promote antiresorptive prescribing

- Pharmacists watch duration of therapy and evaluate for drug holiday/discontinuation
- Technicians in ambulatory care can support RPh roles in RPh-driving osteoporosis clinic
- Community RPh can improve adherence with antiresorptive therapy
- Ambulatory care RPh can improve inappropriate underprescribing and HEDIS indicators
- Community RPh can improve self-care among patients (Ca + D intake, exercise)

EFFECTIVE INTERVENTIONS

- Murphy-Menezes M. Clinical Therapeutics. 2015.

- Simplification of dosing regimens
- Decision aids
- Electronic prescription
- Patient education (maybe)


Medical providers tend to over-estimate benefits of treatment
- Patients tend to over-estimate side effects of treatment
- Adherence with treatment can be compromised when patients are passive in decision-making
- Shared decision-making can occur when more than one treatment option is available


ADDRESSING NONADHERENCE

SHARED DECISION MAKING

ADDRESSING NONADHERENCE

SHARED DECISION MAKING

EFFECT ON DECISION AND SHORT- AND LONG-TERM ADHERENCE

Pharmacists in a variety of healthcare settings can support non-pharmacologic and pharmacologic treatment strategies for osteoporosis and low bone mass, which are common conditions that significantly impact older adults, the community, and the healthcare system.

**Osteoporosis and low bone mass are common conditions that significantly impact older adults, the community, and the healthcare system.**

**Non-pharmacologic and pharmacologic treatment strategies exist to prevent and treat osteoporosis.**

Pharmacists in a variety of healthcare settings can support appropriate care for patients at risk for and with osteoporosis.

**REFERENCES**

- Harrison's Principles of Internal Medicine, 19e
- AHRQ on-line interactive tool
- AHRQ on-line interactive tool
- Mayo Clinic pdf documents for low, elevated and high risk for fracture
- Mayo Clinic on-line interactive tool
- AHRQ on-line interactive tool
- AHRQ on-line interactive tool
- AHRQ on-line interactive tool
- American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults.
- Pharmacists in a variety of healthcare settings can support non-pharmacologic and pharmacologic treatment strategies for osteoporosis and low bone mass, which are common conditions that significantly impact older adults, the community, and the healthcare system.

**CONCLUSION**

- Osteoporosis and low bone mass are common conditions that significantly impact older adults, the community, and the healthcare system.
- Non-pharmacologic and pharmacologic treatment strategies exist to prevent and treat osteoporosis.
- Pharmacists in a variety of healthcare settings can support appropriate care for patients at risk for and with osteoporosis.

**DECISION TOOLS**

- Mayo Clinic on-line interactive tool
- Mayo Clinic pdf documents for low, elevated and high risk for fracture
- FRAX calculator to determine 10-year risk for osteoporotic fracture
- Mayo Clinic on-line interactive tool

**DECISION AID**

- http://effectivehealthcare.ahrq.gov/ehc/decisionaids/osteoporosis/index.cfm?module=LM1&restartModule=1&urlName=LM1
- http://www.shef.ac.uk/FRAX/
- http://shareddecisions.mayoclinic.org/decision-aid-information/decision-aids-for-chronic-disease/other-decision-aids/
- https://osteoporosisdecisionaid.mayoclinic.org/

**EFFECT ON DECISION AND LONG-TERM ADHERENCE**

**QUESTION 4**

SP is an 83 year old female with hypertension, hypothyroidism, history of falls, and osteoporosis (without fracture).

- She was prescribed alendronate in January 2015, and you notice that she has not refilled it for the past 6 months.

**Which of the following is a reasonable course of action?**

A. It is OK to stop alendronate because it is not indicated (she is not falling)

B. It is OK to stop alendronate because she is due for a drug holiday

C. Promote adherence by educating her on risks of untreated osteoporosis and instructions for administration

D. Promote adherence by using a decision aid to revisit the decision to take bisphosphonate