GLIN IPA

2024

Clinical Care Pathway: Osteoporosis

Clinical Care Pathway: Osteoporosis

Purpose & Objective

This protocol provides evidence-based care recommendations in the screening and treatment of osteoporosis in the primary care setting. The protocol seeks to assist in early diagnosis and effective treatment of osteoporosis. The osteoporosis protocol should provide primary care physicians, family nurse practitioners, and physician's assistants with a guide that is evidence-based and cost effective.

Goals of Care

- Reduce bone loss
- Prevent fracture
- Control pain
- Prevent disability

Osteoporosis in Postmenopausal Women

As defined by the World Health Organization (WHO), osteoporosis is present when BMD is 2.5 SD or more below the average value for young healthy women (a T-score of $\leq$ -2.5 SD). A second, higher threshold describes "low bone mass" or osteopenia as a T-score that lies between (−1 and −2.5 SD).

Fracture Risk Assessment

- Evaluate all postmenopausal women aged 50 years and older at risk of osteoporosis
- Initial evaluation of osteoporosis includes:
  - Detailed history to determine potential risk factors
    - Age ≥65 years or if <65 years with one (1) or more risk factors (i.e. secondary osteoporosis, previous fracture, or parent with hip fracture history)
    - Low body weight (i.e. <127lbs)
    - Smoking (i.e. firsthand and secondhand smoking)
    - Early menopause (a loss of typical ovarian function before the age of 40)
    - Excessive alcohol intake (i.e. two (2) or more than drinks daily)
    - Excessive caffeine use
    - Medications (i.e. chronic glucocorticoid use – daily dose of 2.5mg prednisone or equivalent dosing, PPI, SSRI, anticonvulsants, anticoagulants, androgen deprivation agents, loop diuretics, or aromatase inhibitors)
    - Primary and secondary osteoporosis
    - Previous fracture (including low trauma-related fractures other than hip)
    - Height loss of kyphosis
    - Risk factors for falling (i.e. reduced functional mobility, recurrent falls, use of walking aids, dementia, frailty, use of sedatives)
    - Chronic medical diseases related to inflammation and malabsorption (i.e. rheumatoid arthritis, inflammatory bowel disease, celiac disease, cystic fibrosis, hyperthyroidism, sickle cell disease, diabetes, chronic kidney disease, vitamin D deficiency)
  - Physical exam
  - Clinical fracture risk assessment with risk assessment tool (FRAX)
- Complete bone mineral density (BMD) testing based on clinical fracture risk profile
  - Axial dual energy X-ray absorptiometry (DXA) measurement (lumbar spine and hip; 1/3 radius if indicated) should be used
- BMD is recommended for all women 65 years and older per the USPSTF, AACE, NOF, and ACOG guidelines
- BMD is also recommended as outlined in the following table (see next page)

Fracture Risk Assessment (continued)

Guideline	Recommendation
United States Preventive Services Task Force (USPSTF)	Postmenopausal women less than 65 at an increased risk for osteoporosis, as determined by a formal risk assessment tool (i.e. FRAX)
Association of Clinical Endocrinologistas (AACE)	• Any adult with a history of low-trauma fracture • Younger post-menopausal women with clinical risk factors for fracture
American College of Obstetrics and Gynecology (ACOG)	• Women under age 65 with additional clinical risk factors for fracture • Alternatively, women under age 65 with FRAX 10-year risk of major osteoporotic fracture of 9.3% or higher
American Academy of Family Physicians (AAFP)	Women age 60 years and older at increased risk for osteoporotic fracture
National Osteoporosis Foundation (NOF)	• Men age 70 years and older, regardless of clinical risk factors • Younger postmenopausal women, women in the menopausal transition, and men age 50 to 69 years with clinical risk factors for fracture • Adults who have fracture after age 50 years • Adults with a condition (i.e. rheumatoid arthritis) or taking a medication (i.e. glucocorticoids in a daily dose ≥5 mg prednisone or equivalent for ≥3 months) associated with low bone mass or bone loss
HEDIS Measure	• Women 67 to 85 years of age who suffered a fracture are recommended to have BMD or receive a prescription to treat osteoporosis within six (6) months of fracture

Low bone mineral density (BMD) is associated with an increased risk of fracture, regardless of the technique used for measurement. However, there are discrepancies in T-score values at different skeletal sites as well as with different technologies. T-scores derived from different skeletal sites with different technologies are not interchangeable. **DXA is the preferred measurement.**

In comparing measurement technology, differences between BMD results may simply reflect the inherent variability of the test measurement; thus, testing facilities must calculate the least significant change for relevant measurement sites to determine the magnitude of difference that represents a real change.

Fracture Risk Assessment (continued)

Measurement Technology	Clinical Utilization	Mechanism of Measurement	Pros	Cons
Dual-Energy X-ray Absorptiometry (DXA)	Preferred for diagnostic classification	Measures bone mineral content and bone area at clinically relevant skeletal sites by using two X-ray beams with different energy levels	• Precise and accurate • Used for diagnostic classification, input with FRAX, and monitoring response to therapy	• Large/Not Portable • More expensive • Uses ionizing radiation; in very low doses
Peripheral DXA (pDXA)	Use when DXA is not available	Measures peripheral sites forearm, calcaneus, or finger	• Portable • Low T-score values at peripheral sites have been associated with increased fracture risk	• Cannot be used for diagnostic classification • Confounded by technical differences databases of calculating T-scores • Cannot be used to monitor therapy, due to very slow clinical response and changes in peripheral sites
Quantitative Ultrasonography (QUS)	Use when DXA is not available	Measures the transmission of ultrasound through accessible limb bones or reflectance of the ultrasound waves from the bone surface	• Portable • Less expensive than DXA • Lack of radiation exposure	• Cannot be used for diagnostic classification • No studies showing reduction in fracture risk for patients selected for therapy based on measurements • Cannot be used to monitor response to therapy due to too slow of clinical response at measurement sites
Quantitative Computed Tomography	Use when DXA is not available	Measures volumetric BMD at spine and hip	• Can be clinically useful to monitor changes in BMD over time for some patients with structural abnormalities of the spine that preclude the use of DXA • Primarily used as a research tool	• Cannot be used for diagnostic classification • More expensive than DXA • Less reproducible than DXA • Higher radiation dose than DXA

Osteoporosis Diagnosis

- Presence of fragility fractures in the absence of other metabolic bone disorders and even with normal bone mineral density (T-scores)
  - DXA should be completed within six (6) months of fragility fracture date to assess osteoporosis severity and align treatment intensity
    - Fragility fracture is defined by those occurring spontaneously or from minor trauma, such as a fall from a standing height or less. Fragility fractures result from mechanical forces that would not ordinarily result in fracture.
- T-score -2.5 or lower in the lumbar spine (anteroposterior), femoral neck, total hip, or 1/3 radius (33% radius), even in the absence of prevalent fracture
- T-score between -1.0 and -2.5 and increased fracture risk using FRAX country-specific thresholds (i.e. a 10-year probability of hip fracture ≥ 3% or a 10-year probability of any major osteoporosis-related fracture ≥ 20% based upon the United States Adapted WHO algorithm)

Repeating DXA

For those patients who do not meet the criteria for osteoporosis, please consider follow up DXA based on T-score results

Category Bone Density Results	T- Score	Years to Next DXA
Normal	-1.0 or higher	10 to 15 years
Mild Low	Between -1.0 and -1.5	10 to 15 years
Moderately Low	Between -1.5 and -2.0	2 to 5 years
Borderline Osteoporosis	Between -2.0 and -2.5	2 years

Following Diagnosis of Osteoporosis

Evaluate causes of secondary osteoporosis including but not limited to

- Endocrine disorders
  - Acromegaly
  - Adrenal atrophy in Addison disease
  - Cushing syndrome
  - Eating disorders
  - Endometriosis
  - Gonadal insufficiency (primary or secondary)
  - Hyperparathyroidism
  - Hyperprolactinemia
  - Hyperthyroidism
  - Hypogonadism
  - Type 1 diabetes mellitus
  - Nutritional disorders
  - Tumor secretion of parathyroid hormone–related peptide

- Gastrointestinal disease
  - Alcohol-related liver diseases
  - Celiac disease
  - Chronic active hepatitis
  - Chronic cholestatic diseases
  - Gastrectomy
  - Inflammatory bowel disease
  - Jejunoileal bypass
  - Malabsorption syndromes
  - Pancreatic insufficiency
  - Parenteral nutrition
  - Primary biliary cirrhosis
  - Severe liver disease

- Genetic disorders
  - Hypophosphatasia
  - Osteogenesis imperfecta

- Marrow-related disorders
  - Amyloidosis
  - Hemochromatosis
  - Hemophilia
  - Leukemia
  - Lymphoma
  - Mastocytosis
  - Multiple myeloma
  - Pernicious anemia
  - Sarcoidosis
  - Sickle cell anemia
  - Thalassemia

- Organ transplantation
  - Bone marrow
  - Heart
  - Kidney
  - Liver
  - Lung

- Miscellaneous causes
  - Ankylosing spondylitis
  - Chronic obstructive pulmonary disease
  - Congenital porphyria
  - Epidermolysis bullosa
  - Hemophilia
  - Idiopathic hypercalciuria
  - Idiopathic scoliosis
  - Multiple sclerosis
  - Rheumatoid arthritis

- Evaluate for prevalent vertebral fractures

Lifestyle Modifications in Management of Osteoporosis in Postmenopausal Women

- Lifestyle Measures should be adopted universally to reduce bone loss in postmenopausal women.
- Counsel patients **at least annually** on the benefits of the following lifestyle modifications
  - **Calcium**
    - **Calcium supplementation is determined based on dietary intake**
      - Discuss dietary intake of calcium with patients to determine if supplementation is required
      - While dietary calcium intake is ideal, women with inadequate calcium intake should take supplemental elemental calcium 500 to 1000 mg/day, in divided doses at meal times to equal a total of 1200 mg/day with diet (limit to <300 to 500mg per dose) and supplementation for women age 50 years and older
      - Postmenopausal women who are getting adequate calcium from dietary intake alone (approximately 1,200 mg/daily) do **NOT** need calcium supplementation.
    - **Calcium formulation**
      - Calcium carbonate supplements should be advised to be administered with meals. Carbonate-based supplements tend to be the best value as they contain the highest amount of elemental calcium (~40% by weight).
      - Calcium citrate supplements should be advised to be administered without regard to meal times and may be taken on an empty stomach. Citrate-based supplements are more readily absorbed when taken with acid-reducing heartburn medications (i.e. proton pump inhibitors or H2-blockers).
      - Store-specific brands may offer similar options and at a lower out-of-pocket cost to the patient

Lifestyle Modifications in Management of Osteoporosis in Postmenopausal Women (continued)

Calcium Supplement	Elemental Calcium Content Per Tablet	Calcium Compound	Vitamin D
Caltrate 600 + D3 (including Soft Chews)	600 mg	Carbonate	800 units (20 mcg)
Caltrate Gummy Bites	250 mg	Tribasic calcium phoshate	400 units (10 mcg)
Caltrate 600 + D3 Plus Minerals Chewables	600 mg	Carbonate	800 units (20 mcg)
Caltrate 600 + D3 Plus Minerals Minis	300 mg	Carbonate	800 units (20 mcg)
Citracel Petites	200 mg	Citrate	250 units (6.25 mcg)
Citracel Maximum	315 mg	Citrate	250 units (6.25 mcg)
Citracel Plus Magnesium & Minerals	250 mg	Citrate	125 units (3.12 mcg)
Citracel + D Slow Release	600 mg	Citrate + carbonate blend	500 units (12.5 mcg)
Citracel Calcium Gummies	250 mg	Tricalcium phosphate	500 units (12.5 mcg)
Citracel Calcium Pearls	200 mg	Carbonate	500 units (12.5 mcg)
Os-Cal Calcium + D3	500 mg	Carbonate	200 units (5 mcg)
Os-Cal Extra + D3 or Chewable	500 mg	Carbonate	600 units (15 mcg)
Os-Cal Ultra	600 mg	Carbonate	500 units (12.5 mcg)
Tums	200 mg	Carbonate	-
Tums Extra Strength	300 mg	Carbonate	-
Tums Ultra Strength or Chewy Delights	400 mg	Carbonate	-
Viactiv Calcium plus D + K	650 mg	Carbonate	500 units (12.5 mcg)

- **Vitamin D**
  - Measure serum 25-hydroxyvitamin D (25[OH]D) in patients who are at risk of vitamin D insufficiency, particularly those with osteoporosis
  - Maintain serum 25-hydroxyvitamin D (25[OH]D) $\geq$ 40-50 ng/mL in patients with osteoporosis (preferable range 40 to 50 ng/mL)
  - Supplement with vitamin D3 if needed, with a daily dose of 1,000 to 2,000 IU to maintain a serum level of 40 to 50 ng/mL
  - Higher doses of vitamin D3 may be necessary in patients with present factors such as obesity, malabsorption, and older age
- **Exercise**
  - Women with osteoporosis should perform a weight-bearing exercise for 30 minutes 3-4 days a week

Lifestyle Modifications in Management of Osteoporosis in Postmenopausal Women (continued)

- **Avoid, if possible, drugs that increase bone loss or fractures**, such as long–term glucocorticoid and proton pump inhibitor utilization

Drug Class With Adverse Bone Effects	*Examples* Mechanism
Anticoagulants	*Heparin; LMWH* Decreasing bone formation, increasing bone resorption, both. *Warfarin* Inhibits osteocalcin interrupting calcium binding
Cyclosporine	Increase in bone resorption and bone loss; “high turnover” osteoporosis
Medroxyprogesterone acetate	Induction of estrogen deficiency when used at higher doses (doses 5-10 mg/day had no effect on bone density)
Vitamin A and synthetic retinoids	Inhibitsosteoblast activity, stimulates osteoclast formaion, counteracts Vitamin D’s effect to maintain calcium homeostasis (high doses > 1500 mcg/day)
Loop diuretics	Increased calcium loss by impaired resoption in the Loop of Henle
Aromatase inhibitors	Induced estrogen deficiency leading to suppressed osteoclast mediated bone resorption and net bone loss. Class effect of both steroidal and non-steroidal aromatase inhibitors; estimated incidence of osteoporosis with anastrozole is 11%, exemestane is 4.6%, and letrozole is 4.7-14.5%.
Methotrexate	Increased bone resorption and inhibition of bone formation; not seen at doses ranges used for rheumatic diseases
Anti-seizure medications	*Phenobartital; Phenytoin; Carbamazepine* Cytochrome P450 induction leading to increased catabolism of vitamin D and subsequent rise in PTH; increased mobilization of bone calcium stores and bone turnover
PPIs	Reduced absorption of insoluble calcium
Antidepressants	*TCAs; SSRIs* Risk is highest at start of therapy and diminished with time, so currently speculation is increased risk of postural hypotension increasing risk of falls

- **Smoking cessation**
  - Smoking cessation is strongly recommended in all women with skeletal health concerns
- **Counsel on falls prevention**
- **Referral to physical therapy as clinically indicated**
- **Weight-bearing and muscle-strengthening exercise**
- **Avoid heavy alcohol use**
  - Limit alcohol intake to no more than two (2) drinks per day

Pharmacological Treatment for Osteoporosis in Postmenopausal Women

- Pharmacotherapy to be initiated, except where contraindications are present, in
  - Patients with osteopenia with low bone mass and a history of fragility fracture of hip or spine
  - Patients with a T-score of -2.5 or lower in the spine, femoral neck, total hip, or 1/3 radius
  - Patients with a T-score of -1.0 and -2.5 if the FRAX 10-year probability for major osteoporotic fracture is ≥20% or the 10-year probability of hip fracture is ≥3% in the U.S.
- Consider adjusting pharmacological therapy if
  - Recent fracture (i.e. within the past 12 months)
  - Fractures while on approved osteoporosis therapy
  - Multiple fractures
  - Fractures while on drugs causing skeletal harm (i.e. long-term glucocorticoids)
  - Very low T-score (i.e. less than -3.0)
  - High risk for falls or history of injurious falls
  - Very high fracture probability by FRAX (i.e. major osteoporosis fracture >30%, hip fracture >4.5%) or other validated fracture risk algorithm to be at very high facture risk
- Medications Used to Treat Osteoporosis
  - Approved agents with efficacy to reduce hip, non-vertebral, spine fractures include alendronate, denosumab, risedronate, and zoledronic acid for initial therapy in patients with **high** fracture risk/no prior fractures
  - Abaloparatide, denosumab, romosozumab, teriparatide, and zoledronic acid should be considered for patients unable to use oral therapy and as initial therapy at **very high risk** of fracture/prior fractures
  - Ibandronate or raloxifene may be appropriate initial therapy in some cases for patients requiring drugs with spine-specific efficacy

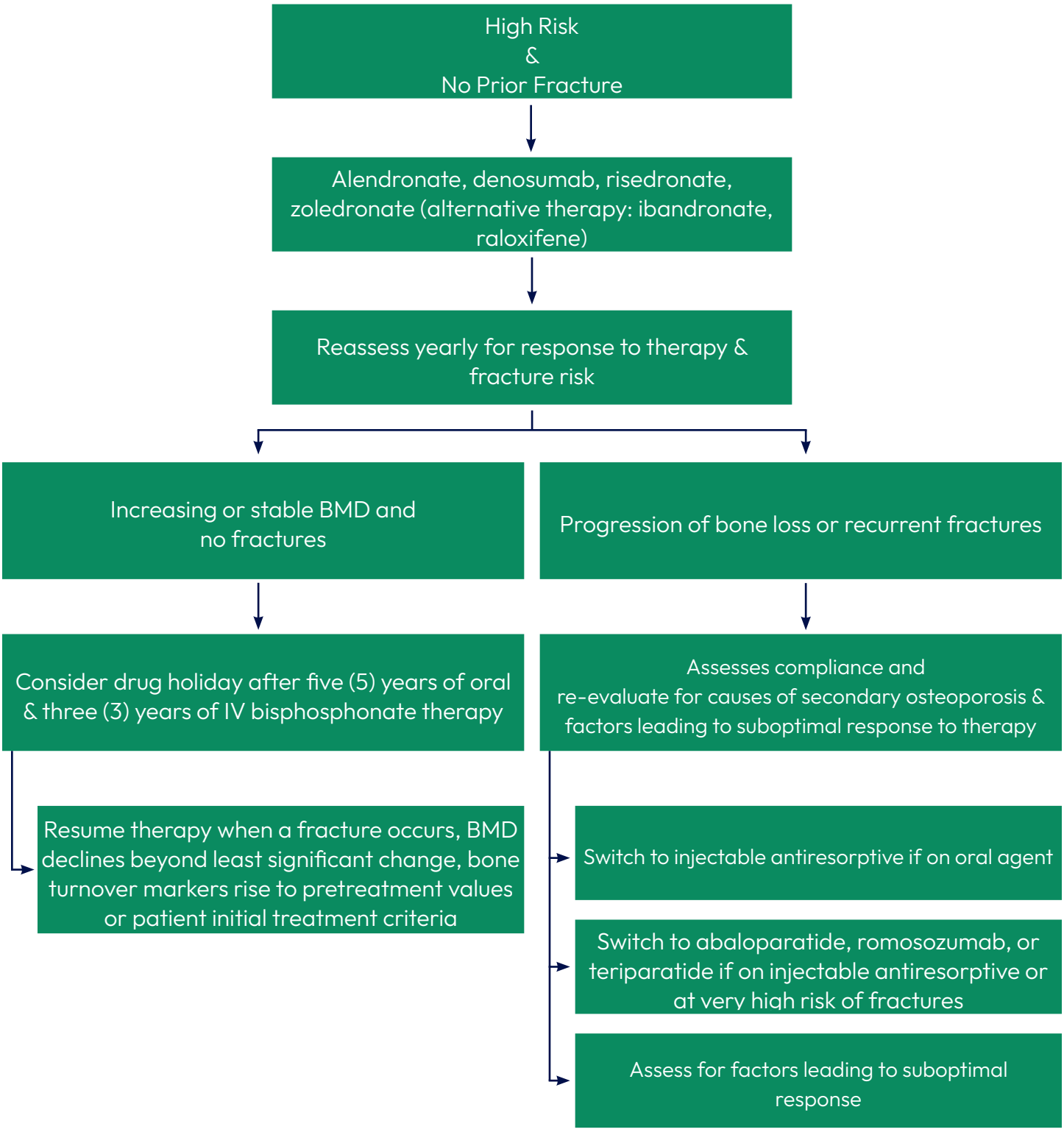
Pharmacological Treatment for Osteoporosis in Postmenopausal Women (continued)

Medication Class	Available Prescriptions	Primary Fracture Reduction Benefit			Mechanism of Action
		vertebral	Hip	Non-vertebral	
Bisphosphonates	alendronate (Fosamax™, Binosto™)*	+	+	+	*Anti-resorptive* • Attaches to hydroxyapatite binding sites on bony surfaces undergoing active resorption; bisphosphonate released during osteoclastic bone resorption impairs formation of the ruffled border and production of the protons necessary for continued bone absorption • Reduces osteoclast activiy by decreasing osteoclast progenitor development and recruitment and promoting osteoclast apoptosis
	risedronate (Actonel™, Atelvia™)*	+	+	+	
	ibandronate (Boniva™)*	+	-	+/-	
	zoledronic Acid (Reclast™; IV only)*	+	+	+	
Rank-ligand inhibitors	denosumab (Prolia™)	+	+	+	*Anti-resorptive* A monoclonal antibody with affinity for RANKL; in binding to RANKL, it blocks the interaction between RANKL and RANK receptors on osteoclasts, and prevents osteoclast formation, leading to decreased bone resoption and increased bone mass in osteoporosis
PTH/PTH-related protein analogs	teriparatide (Forteo™) abaloparatide (Tymlos™)	+	+/-	+	*Anabolic* Stimulates osteoblast function, increases GI calcium absorption, and increases renal tubular calcium reabsorption
Sclerostin inhibitor	romosozumab (Evenity™)	+	+/-	+/-	*Anabolic* Inhibits sclerostin, a regulatory factor in bone metabolism that inhibits Wnt/Beta-catenin signaling pathway regulating bone growth

Pharmacological Treatment for Osteoporosis in Postmenopausal Women (continued)

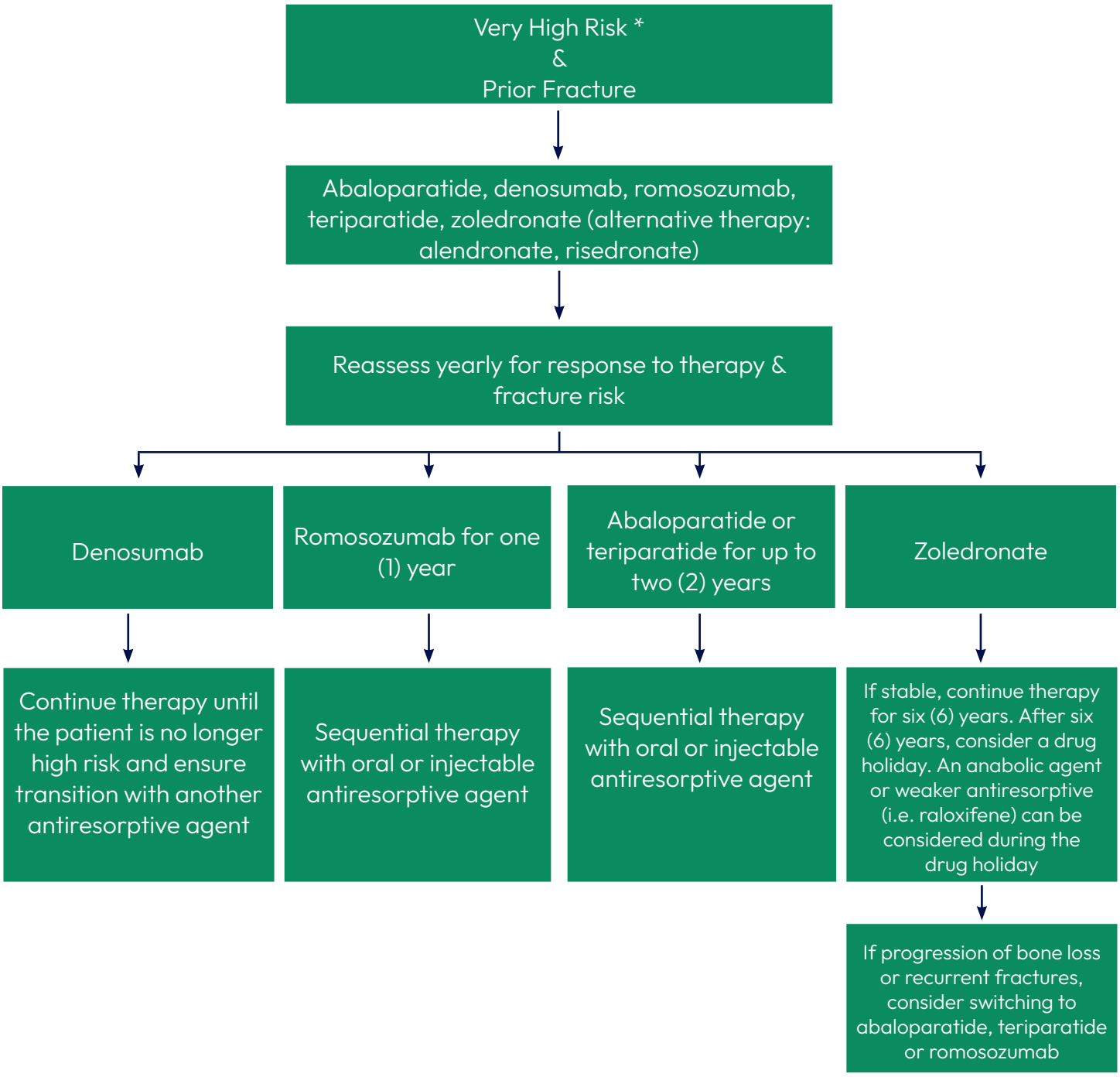
Medication Class	Available Prescriptions	Primary Fracture Reduction Benefit			Mechanism of Action
		vertebral	Hip	Non-vertebral	
Mixed estrogen agonists/ antagonists and tissue selective estrogen complexes	raloxifene (EvistaTM) bazedoxifene/ conjugated equine estrogen (Duavee™)	+	-	-	*Hormone Base* • selective binding activates estrogenic pathways in the bone and antagonizes estrogenic pathways to block some estrogen effects in the breast and uterine tissue • estrogen component of Duavee™ provides relief of vasomotor symptoms and maintenance of BMD in postmenopausal females with a uterus, while reducing the risk of endometrial hyperplasia observed with estrogen use alone
Calcitonin	salmon calcitonin (Miacalcin™)*	+/-	-	+/-	*Hormone Base* • antagonizes the effects of PTH • directly inhibits osteoclastic bone resorption • promotes the renal excretion of calcium, phoshate, sodium, magnesium, and potassium by decreasing tubular reabsorption • increases the jejunal secretion of water, sodium, potassium, and chloride • can be used for acute pain relief in patients who have sustained a vertebral fracture

Pharmacological Treatment for Osteoporosis in Postmenopausal Women (continued)



Pharmacological Treatment for Osteoporosis in Postmenopausal Women (continued)

*** Very High Risk is defined by patients with low bone density with advanced age, frailty, glucocorticoids, very low T-scores, or increased fall risk**



Pharmacological Treatment for Osteoporosis in Postmenopausal Women (continued)

- **Treatment Monitoring**
  - Obtain a baseline axial (lumbar spine and hip; 1/3 radius if indicated) DXA and repeat DXA in patients with osteoporosis every 1 to 2 years until findings are stable
  - DXA should be completed within 6 months of fragility fracture date to reassess osteoporosis severity and adjust treatment intensity
  - Consider 1/3 radius at alternative site when the lumbar spine/hip are not able to be evaluated, or as an additional site in patients with primary hyperparathyroidism
  - Monitor serial changes in lumbar spine, total hip, or femoral neck bone mineral density
    - If lumbar spine, hip or both are not able to be evaluated, monitoring with 1/3 radius site may be acceptable but is limited by a small area and a very large least significant change
  - Follow up of patients should ideally be conducted in the same facility with the same DXA system
  - Consider alternative therapy or reassessment for causes of secondary osteoporosis in patients who have recurrent fracture or significant bone loss while on therapy
    - A single fracture while on therapy is not necessarily evidence of treatment failure, consider two or more fragility fractures as evidence of treatment failure

Medication	Duration	Following Completion
denosumab	No limit on treatment duration	If denosumab therapy is discontinued, patients should be transitioned to another antiresorptive
abaloparatide	Two (2) years maximum	Start bisphosphonate or denosumab
teriparatide	Two (2) years maximum	Start bisphosphonate or denosumab
romosozumab	One (1) year maximum	Start bisphosphonate or denosumab
oral bisphosphonates	Consider a drug-holiday after five (5) years of treatment if fracture risk is no longer high (i.e. T-score of greater than -2.5 or the patient has remained fracture free)	• Continue treatment up to an additional five (5) years if fracture risk remains high • Consider a drug-holiday after six (6) to ten (10) years of stability in patients with very high fracture risk
zoledronic acid	Consider a drug-holiday after three (3) years in high-risk patients or until fracture risk is no longer high	Continue for up to six (6) years in very high risk patients

Pharmacological Treatment for Osteoporosis in Postmenopausal Women (continued)

- **Drug Holidays for Bisphosphonates**
  - Resuming a bisphosphonate after a drug-holiday should be based on individual patient circumstances such as
    - Increased fracture risk
    - Decreased bone mineral density beyond the least significant change of DXA machine
    - Increase in bone turnover markers
  - Drug-holidays are not recommended for non-bisphosphonates antiresorptive drugs and treatment should be continued for as long as clinically appropriate
- **Additional Considerations**
  - Combination pharmacologic therapy is not recommended for prevention or treatment of post-menopausal osteoporosis
  - Follow treatment with an anabolic agent (i.e. abaloparatide, romosozumab, teriparatide) with a bisphosphate or denosumab to prevent bone density decline and loss of fracture efficacy
  - Vertebroplasty and kyphoplasty are not recommend as first-line treatment for vertebral fracture, given unclear benefit on overall pain and a potential increased risk of vertebral facture in adjacent vertebrae
  - Recommend to delay initiation of bisphosphonate therapy for a few months until the jaw is healed following an invasive dental procedure (i.e. dental implant or extraction)
  - Recommend to continue bisphosphonates in patients undergoing dental procedures (i.e. dental implants or extractions) who have taken therapy for less than four (4) years and are at low risk of developing osteonecrosis of the jaw (ONJ)
  - Recommend to discontinue the bisphosphonate two (2) months prior to the dental procedure, if the patient has been on the bisphosphonate for greater than four (4) years or taking concomitant glucocorticoids
    - Bisphosphonates can be restarted once the bone has healed

- **Considerations for Referral to Endocrinologist or Other Osteoporosis Specialists**
  - Patients with T-score less than -3.0
  - Patients who experience new fragility fractures
  - Patients with normal BMD that sustain a fracture without major trauma
  - Patients with recurrent fractures or continued bone loss in a patient receiving therapy without obvious treatable causes of bone loss
  - Patients with BMD unexpectedly low or when osteoporosis has unusual features such as young age, unexplained artifacts or bone density, and unexplained laboratory studies, including high or low alkaline phosphatase and/or low phosphorous
  - Patients with endocrine or metabolic causes of secondary osteoporosis (i.e. hyperthyroidism, hyperparathyroidism, hypercalciuria, or elevated prolactin)
  - Patients with conditions that complicate management (i.e. decreased kidney function, hyperparathyroidism, or malabsorption)

Osteoporosis in Men

Fracture Risk Assessment

- All men 70 years and older are recommended to be screened for osteoporosis
- Men ages 50 to 69 years should be tested if they have a history of fracture or other risk factors including the following
  - Delayed puberty
  - Hypogonadism
  - Hyperparathyroidism
  - Hyperthyroidism
  - Chronic obstructive pulmonary disease
  - Use of glucocorticoids or GnRH agonists
  - Alcohol abuse or smoking

Osteoporosis Diagnosis

- Recommend the following men be diagnosed with osteoporosis and receive pharmacologic treatment
  - Men who had a hip or vertebral fracture without major trauma (fragility fracture)
  - Men who have not experienced a spine or hip fracture but whose BMD T-score of the spine, femoral neck, and/or total hip of -2.5 or lower
  - Men with a T-score between -1.0 and -2.5 in the spine, femoral neck, or total hip (low bone mass) if they 10-year risk of any fracture $\geq$ 20% or the 10-year risk of hip fracture is $\geq$ 3% using the FRAX risk calculator

Lifestyle Modifications in Management of Osteoporosis in Men

Counsel patients at least annually on the benefits of the following lifestyle modifications

- Smoking cessation
- Reduce alcohol intake to less than three (3) drinks per day
- Participate in weight-bearing activities for 30-40 minutes per session, three (3) to four (4) sessions per week
- Consume 1,000-1,200mg of calcium daily, ideally from dietary sources, with calcium supplements added if dietary calcium is insufficient (see Calcium Formulations – Osteoporosis in Postmenopausal Women above)
- If vitamin D levels are low (< 30 ng/mL), supplement vitamin D to achieve blood 25(OH)D levels of at least 30 ng/mL

Pharmacological Treatment for Osteoporosis in Men

- FDA Approved Treatments
  - Bisphosphonates: alendronate, risedronate, and zoledronic acid are FDA approved therapies
  - Denosumab
  - Teriparatide
  - Abaloparatide
- Select FDA approved treatment based on fracture history, severity of osteoporosis, comorbidities (i.e. peptic ulcer disease, gastroesophageal reflux, malabsorption syndromes, malignancy), cost
- Generic oral bisphosphonates alendronate or risedronate may be used as initial agents
  - Use caution if impaired kidney function (eGFR ≤30-35)
  - Use caution if history of osteonecrosis of jaw or atypical femur fractures with bisphosphonates
  - If unable to tolerate or respond adequately to bisphosphonates teriparatide or denosumab can be considered
- If upper or lower gastrointestinal problems, non-oral therapies such as zoledronic acid, denosumab or teriparatide may preferred
- If taking androgen deprivation therapy for prostate cancer, denosumab may be preferred
- If recent hip fracture, zoledronic acid is recommended
  - Zoledronic acid is contraindicated in patients with eGFR <35mL/min
  - Use caution if history of osteonecrosis of jaw or atypical femur fractures with bisphosphonates
- If high risk of vertebral fracture, teriparatide may be preferred
- If very high fracture risk, including those with a T-score of less than -3.0, a T-score of less than -2.5 with fragility fracture history, or severe or multiple prior vertebral fractures may consider abaloparatide

Pharmacological Treatment for Osteoporosis in Men (continued)

- **Treatment Monitoring**
  - Monitor BMD by DXA at the spine and hip every one (1) to two (2) years to assess treatment response
  - If BMD plateaus, the frequency of BMD measurements may be reduced
- **Treatment Duration**

Medication	Duration	Following Completion
denosumab	No limit on treatment duration	If denosumab therapy is discontinued, patients should be transitioned to another antiresorptive
abaloparatide	Two (2) years maximum	Start bisphosphonate or denosumab
teriparatide	Two (2) years maximum	Start bisphosphonate or denosumab
oral bisphosphonates	Consider a drug-holiday after five (5) years of treatment if fracture risk is no longer high (i.e. T-score of greater than -2.5 or the patient has remained fracture free)	• Continue treatment up to an additional 5 years if fracture risk remains high • Consider a drug-holiday after six (6) to ten (10) years of stability in patients with very high fracture risk
zoledronic acid	Consider a drug-holiday after three (3) years in high-risk patients or until fracture risk is no longer high	Continue for up to six (6) years in very high risk patients

- **Drug Holidays for Bisphosphonates**
  - Resuming a bisphosphonate after a drug-holiday should be based on individual patient circumstances such as
    - Increased fracture risk
    - Decreased bone mineral density beyond the least significant chance of DXA machine
    - Increase in bone turnover markers
  - Drug-holidays are not recommended for non-bisphosphonates antiresorptive drugs and treatment should be continued for as long as clinically appropriate

Pharmacological Treatment for Osteoporosis in Men (continued)

- **Considerations for Referral to Endocrinologist or Other Osteoporosis Specialists**
  - Patients with T-score less than -3.0
  - Patients who experience new fragility fractures
  - Patients with normal BMD sustain a fracture without major trauma
  - Patients with recurrent fractures or continued bone loss occur(s) in a patient receiving therapy without obvious treatable causes of bone loss
  - Patients with BMD unexpectedly low or when osteoporosis has unusual features such as young age, unexplained artifacts or bone density, and unexplained laboratory studies, including high or low alkaline phosphatase and/or low phosphorous
  - Patients with endocrine or metabolic causes of secondary osteoporosis (i.e. hyperthyroidism, hyperparathyroidism, hypercalciuria, or elevated prolactin)
  - Patients with conditions that complicate management (i.e. decreased kidney function, hyperparathyroidism, or malabsorption)

References

1. Endocrine Society. (2022, March 31). Osteoporosis treatment. Endocrine Society. Retrieved January 23, 2023, from https://www.endocrine.org/patient-engagement/endocrine-library/osteoporosis-treatment

2. Male osteoporosis. American Association of Clinical Endocrinology. (n.d.). Retrieved January 23, 2023, from https://pro.aace.com/disease-state-resources/bone-and-parathyroid/slide-library/male-osteoporosis

3. Management of postmenopausal osteoporosis. (2022). Obstetrics & Gynecology, 139(4), 698–717. https://doi.org/10.1097/aog.0000000000004730

4. Melissa A. Burmeister, P. D. A. P. D. of P. S. T. K. F. (2021, June 11). An overview of male osteoporosis. U.S. Pharmacist – The Leading Journal in Pharmacy. Retrieved January 23, 2023, from https://www.uspharmacist.com/article/an-overview-of-male-osteoporosis

5. Screening for osteoporosis: U.S. Preventive Services Task Force Recommendation Statement. (2011). Annals of Internal Medicine, 154(5), 356. https://doi.org/10.7326/0003-4819-154-5-201103010-00307

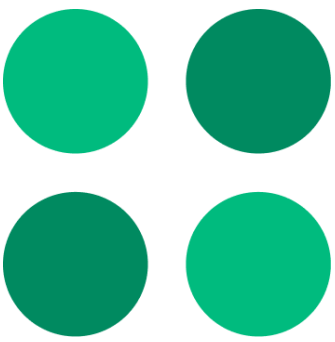
6. Shoback, D., Rosen, C. J., Black, D. M., Cheung, A. M., Murad, M. H., & Eastell, R. (2020). Pharmacological management of osteoporosis in Postmenopausal women: An endocrine society guideline update. The Journal of Clinical Endocrinology & Metabolism, 105(3), 587–594. https://doi.org/10.1210/clinem/dgaa048

7. Watts, N. B., Camacho, P. M., Lewiecki, E. M., & Petak, S. M. (2021). American Association of Clinical Endocrinologists/American College of Endocrinology Clinical Practice Guidelines for the diagnosis and treatment of postmenopausal osteoporosis—2020 update. Endocrine Practice, 27(4), 379–380. https://doi.org/10.1016/j.eprac.2021.02.001

8. Watts, N. B. (2013). Osteoporosis in men. Endocrine Practice, 19(5), 834–838. https://doi.org/10.4158/ep13114.ra

9. https://americanbonehealth.org/bone-density/how-often-should-i-have-a-bone-density-test/

GLIN.COM



For additional questions, please reach out to your assigned Practice Transformation Consultant.