Osteoporosis Clinical Practice Guidelines

Initial Evaluation for Osteoporosis

All postmenopausal women age ≥50 years of age should undergo clinical assessment for osteoporosis and a detailed history, physical exam, and clinical fracture risk assessment with Fracture Risk Assessment tool (FRAX®)

Note: FRAX age 40-90, Saudi FRAX in process of endorsement. Use USA white as per Saudi Osteoporosis Society SOS1) .Or the Kuwaiti FRAX (similar hip fracture incidence to Saudi Arabia) until the Saudi FRAX is available

History	Exam	FRAX Clinical risk factors in FRAX® www.shef.ac.uk/FRAX

• Prior osteoporosis-related fractures
• Prolonged steroid use
• Height loss > 6 cm historically
• Current smoking
• Excess alcohol≥ 3 units per day
• Parental hip fracture
• Falls in past 12 months
• Other high-risk conditions or medications
	• Height loss (>2cm prospectively)
	• Weight (BMI)
	  • Low <60 Kg
	  • Major loss (≥10% of weight since age 25)
	• Kyphosis
	• Rib to pelvis distance >2 FBs
	• Balance and gait, "Get up and Go" Test
		• age
		• Sex
		• body mass index (BMI)
		• smoking, alcohol use
		• prior fracture
		• parental history of hip fracture
		• use of glucocorticoids
		• rheumatoid arthritis
		• secondary osteoporosis
		• femoral neck BMD

Indications for BMD Testing *(1)*

Menopausal women, and men aged 50-64 years

Menopausal women, and men aged 50-64 years with clinical risk factors for fracture:

- All women ≥40 years who have sustained low-trauma fragility fracture
- Previous fragility fracture or maternal history of hip fracture .
- hypogonadism or premature menopause (< 45 years), Prolonged secondary amenorrhea (>1 year)
- Prolonged glucocorticoid use≥ 3 months cumulative use in the past year of prednisone-equivalent dose ≥ 7.5mg daily
- Other high-risk medication use (tamoxifen , thiazolidinedione , Empagliflozin, PPI and anticonvulsant)
- X-ray findings suggestive of osteoporosis such as vertebral fracture, osteopenia identified on X-ray, fragility fracture, loss of height, or thoracic kyphosis (clinical or radiological finding)
- Current smoking
- High alcohol intake
- Low body weight (< 60 kg) or major weight loss (>10% of weight at age 25 years)
- Rheumatoid arthritis
- Other disorders strongly associated with osteoporosis such as primary hyperparathyroidism, type 1 diabetes, osteogenesis imperfecta, uncontrolled hyperthyroidism, Cushing's, disease, chronic malnutrition or malabsorption, chronic inflammatory conditions (e.g., inflammatory bowel disease)

Routine Screening indicated by age

All women age ≥ 60 years in Saudi Arabia (expert opinion screen)

All men age ≥ 65 years

2020 AACE American Association of Clinical Endocrinologists Diagnosis of Osteoporosis in Postmenopausal Women *(2)*

1. T-score −2.5 or below in the lumbar spine, femoral neck, total proximal femur, or 1/3 radius
2. Low-trauma **spine or hip fracture** (regardless of bone mineral density)
3. T-score between −1.0 and −2.5 and a fragility fracture of **proximal humerus, pelvis, or distal forearm**
4. T-score between −1.0 and −2.5 and **high FRAX®** (or if available, TBS-adjusted FRAX®) 10-year probability for major osteoporotic fracture is ≥20% or the 10-year probability of hip fracture is ≥3% FRAX® = fracture risk assessment tool; TBS = trabecular bone score

For All Osteoporotic Patient Evaluate for Causes of Secondary Osteoporosis Before Start Treatment

- Serum chemistry: TSH calcium, phosphate, total protein, albumin, liver enzymes, alkaline phosphatases, creatinine, and electrolytes.
- Serum 25-hydroxyvitamin D Complete blood cell count
- SPE serum protein electrophoresis if vertebral fracture or suspect multiple myeloma
- X-ray lateral thoracolumbar screen for vertebral fracture if not available from DXA

Recommend pharmacologic therapy Education on lifestyle measures, fall prevention, benefits, & risks of medications

Treatment for Osteoporosis According to Fracture Risk

LOW RISK all of the following (4,5) :
No previous fracture, Osteopenia(T-score between −1.0 and −2.5)and low FRAX =10 year major osteoporotic fracture risk< 20% or hip fracture risk <3%

Exercise ,fall prevention Calcium and vitamin D

Reevaluate in 3-5 years

HIGH RISK any of :

- ❑ Previous osteoporotic fracture >12 months ago(3,6)
- ❑ Osteoporosis T score.-2.5(3,5)
- ❑ FRAX 10 year major osteoporotic fracture risk ≥ 20% or hip fracture risk ≥ 3%

First line Alendronate If can't tolerate oral bisphosphonate option of injectable bisphosphonate Zoledronate or Denosumab
Alternative is raloxifene

Reassess yearly for response to therapy and fracture risk DEXA after 1.5 -2 years

VERY HIGH RISK any of:

- ❑ Fracture within the past 12 months(3,6)
- ❑ Recurrent or multiple fractures(3,5)
- ❑ Fracture while on treatment for osteoporosis(3)
- ❑ Fracture while on glucocorticoids Or other bone harmful medication(3)
- ❑ Very low T scores <-3(5)
- ❑ FRAX 10 year major osteoporotic fracture risk ≥ 30% or hip fracture risk ≥ 4.5%
- ❑ advanced age, frailty, increased fall risk (2)
- ❑ secondary osteoporosis or decreased kidney function

referral to osteoporosis specialist

First line anabolic treatment (2):
Abaloparatide or **Teriparatide** for up to 2 years or **Romosozumab** for 1 year followed by Sequential therapy with oral or injectable antiresorptive agent **Alternative** treatment : **Denosumab** Continue therapy until the patient is no longer high risk and ensure transition with another antiresorptive agent. or **zoledronate** If stable, continue therapy for 6 years, Consider a drug holiday after 6 years of IV zoledronate. During the holiday, an anabolic agent or a weaker antiresorptive such as raloxifene could be used.• If progression of bone loss or recurrent fractures, consider switching to abaloparatide, teriparatide or romosozumab

Reassess yearly for response to therapy and fracture risk DEXA after 1.5 -2 years

Increasing or stable BMD and no fracture

Consider a drug holiday after 5 years of oral and 3 years of IV bisphosphonate therapy. Resume therapy when a fracture occurs, BMD declines beyond least significant change

Progression of bone loss or recurrent fractures

1. Assess compliance. Switch to injectable antiresorptive if noncompliant with oral agent
2. Re-evaluate for causes of secondary osteoporosis and factors leading to suboptimal response to therapy
3.Referral to osteoporosis specialist.

CALCIUM Premenopausal, men <50 years and pregnant women (1000 mg/d), Postmenopausal, men >50 years (1500 mg/d)	Instructions: Calcium should be taken with meals for better absorption. Calcium should not be taken with iron (absorption may be adversely affected when given concurrently)
	Caution in patient with hypercalcemia and patients with history of renal stones
VITAMIN D Premenopausal, men <50 yr and pregnant women (600 IU/d) Postmenopausal, men >50 yr (1000 IU/d)	Instructions: Expose to sun for 10-15 min 2-3 times/wk
	Caution in patient with hypercalcemia and patients with history of renal stones
ALENDRONATE 70 mg once weekly Antiresorptive oral Consider drug holiday after 5 years	**Instructions:** should be taken as soon as patient wakes up in the morning, before eating, or drinking anything. - Tablet should be swallowed as a whole with a large glass (8 ounces) of plain water only (not mineral water, coffee, juice, or any other liquid). - Patient should not lie down on their back, eat, or drink for at least 30 min after taking alendronate.
	SE :1) Hypocalcemia 2) atypical fracture of the femur 3) osteonecrosis of the jaw defer initiation or hold if Invasive dental procedures **Contraindicated:** 1) Should not be prescribed for patients with active esophageal abnormalities or peptic ulcer disease. And inability to remain upright for at least ½ hour after the dose 2) In pregnancy, women who plan to be pregnant. 3) In patients with creatinine clearance below 30 mL/min.
zoledronate 5 mg IV once yearly Antiresorptive Intravenous Consider drug holiday after 3 years	One infusion per year over minimum of 15 min. Good hydration before receiving the medication. *Correct hypocalcemia before starting treatment.*
	SE: Hypersensitivity, flu-like reaction, Risk of atypical fracture, ONJ, Arterial fibrillation **Contraindicated:** in pregnancy, women who plan to be pregnant, and in patients with creatinine clearance below 30 mL/min
Denosumab (Prolia) 60 mg SC every 6 months Antiresorptive SC injection	60 mg denosumab in 1 mL solution in a single-use prefilled syringe or vial Subcutaneous injection every 6 months
	SE: Eczema, cellulitis, low calcium **Contraindicated:** 1) In pregnancy, women who plan to be pregnant. 2) Risk of atypical fracture, ONJ, Dose adjustment for renal impairment is not necessary. CrCl ≥ 30 ml/min risk of sever hypocalcemia if CrCl <30 ml/min
RALOXIFEN 60 mg/d oral SERMS (Evista)	Stop in periods of prolonged immobilization (surgery, long flight, cholestyramine intake)
	SE: premenopausal women worsening of hot flashes, leg cramps, increase risk of deep vein thrombosis. Increased risk of thromboembolic events Risks needs to be weighed against benefits, especially in patients with or at risk of CHD (in whom treatment reduces vertebral fracture and breast cancer risk at the same absolute rate that it increases the VTE and fatal stroke risk)

Recommend: Education on lifestyle measures, fall prevention, benefits and risks of medications

Exercise type /benefits	Frequency	Comment
Posture exercises keep you standing tall, not stooped.	Daily 10 mint	Pay attention to your posture posture when you stand and sit, do back exercises that extend your spine.
Balance exercises help you be more stable on your feet. You can walk more easily. Good balance helps prevent falls.	Daily 20 mint	walk heel to toe, reduce base of support, shift your weight, respond to things that upset your balance.
Strength exercises keep you strong and fit.	2 times per week	Exercise for leg ,arm ,chest shoulder and back. Use body weight against gravity ,band and weights *
Aerobic physical activity (moderate to vigorous intensity) improves your overall health. It can reduce your risk of disease. It may improve your bone strength.	150 minutes per week	Do aerobic physical activity for about 20 to 30 minutes per day. Exercise for at least 10 minutes at a time. In total, do 150 minutes or more per week.* If you are new to exercise or if you have had a spine fracture, start at low to moderate intensity — 3 to 6 on the scale*
*Refer to physical therapy for advice for proper exercise for each patient		

Give patient medication card when starting the treatment this is essential for collaborative medical care between specialist and primary care example: Abaloparatide or Teriparatide taken once in life time for up to 2 years and need to be followed by antiresorptive treatment. Moreover, it is essential to know when the patient can go for drug holiday.

Medication: _____

Calcium: Dietary sources: _____ mg Supplements: _____ mg

Vitamin D:

_____

Exercise: _____ minutes daily / weekly

Fall Prevention advice _____

Follow up DXA / labs in _____ months. Return visit in _____ months

References:
1. 2015 Guidelines for Osteoporosis in Saudi Arabia: Recommendations from the Saudi Osteoporosis Society Ann Saudi Med 2015;35(1):1-12
2. AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS/ AMERICAN COLLEGE OF ENDOCRINOLOGY CLINICAL PRACTICE GUIDELINES FOR THE DIAGNOSIS AND TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS— 2020 UPDATE Endocr Pract. 2020;26(Suppl 1)
3. Camacho et al. Endocr Pract. 2020.26.564-570
4. Shoback et al. J Clin Endocrinol Metab, 2020, 105(3), 1-8
5. Eastell et al. J Clin Endocrinol Metab. 2019, 104, 1595-1622
6. Kanis et al. Osteoporosis Int. 2020, 31, 1-12