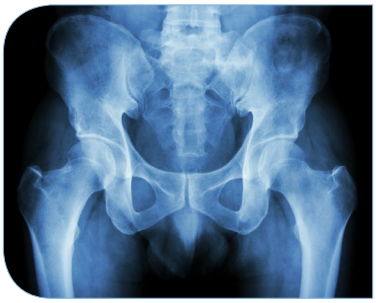


A Lifespan Approach to

Bone Health and Bone Fragility

Intermountain Canyons and Desert Regions

This document was collaboratively developed by the Bone Health and Bone Fragility team at Intermountain Health in partnership with Amgen. It serves as a summary of current clinical guidelines and medical literature, and offers expert advice on the prevention, screening, detection, and treatment of osteoporosis across the lifespan. The document aims to provide primary care clinicians with information and interventions that are known or believed to have a positive impact on bone health outcomes for patients of all ages.

Key Points

Bone mass attained during childhood and adolescence is the most important modifiable determinant of lifelong skeletal health.

- By age 18 years, approximately 90% of peak bone mass has been accrued.
- The most effective strategy to achieve optimal bone health in children and adolescents consists of regular weight-bearing activities, high calcium intake, and adequate vitamin D.

Screening for osteoporosis should be performed every 2 – 3 years in women ≥ 65, men ≥ 70, AND younger individuals with risk factors such as prior fractures, low body weight, high-risk medication use, or medical conditions associated with bone loss.

Screening for osteoporosis should include:

- DXA for bone mineral density (BMD) with or without a trabecular bone score (TBS). TBS is most useful for patients over 40 who are nearing the threshold for pharmacologic treatment and those with secondary causes for bone loss (e.g. glucocorticoid use or diabetes).[1] TBS is not useful in monitoring response to pharmacological therapy.
- Estimate risk of fracture (e.g., FRAX® or FRAX® adjusted for TBS)

Diagnosis of osteoporosis in adults includes any of the following:[2,3]

- T-score –2.5 or below at spine, hip, or 1/3 proximal radius.
- Fragility fracture (e.g. low-trauma spine or hip fracture, pelvis, wrist, or humerus).
- T-score between –1.0 and –2.5 **AND** FRAX score (± adjusted for TBS) with a ≥3% risk of hip fracture or ≥20% risk of major osteoporotic fracture.

In children / adolescents, the diagnosis of osteoporosis is never made based on bone mineral density alone. [13]

Pharmacotherapy and lifestyle changes can reduce fracture risk in people with of people with osteoporosis or osteopenia.

- In patients with severe osteoporosis (T-scores <3.0), anabolic agents, including teriparatide (Forteo), abaloparatide (Tymlos), and romosozumab (Evenity) have shown improved efficacy when used as first-line agents before bisphosphonates and denosumab. An early referral to endocrinology should be strongly considered for administration of anabolic agents.
- Bisphosphonate medications may require a drug holiday to allow for bone remodeling and reduce the risk of atypical femur fractures. For patients at modest risk, holidays can be considered after 3 years (IV) or 5 years (oral). A 2 – 5 year holiday is reasonable for most patients.[4]
- Falls are a leading cause of morbidity and mortality in those with osteoporosis. Exercise and other interventions significantly decreases fall risk.[14,15] See *Falls Prevention CPM*.

What's Inside?

Intermountain HEDIS and Stars Measures

- Screening rates for osteoporosis in women age 65 – 75
- Osteoporosis screening or pharmacotherapy within 6 months of fracture in women age 67 – 85

Supporting Evidence

American Association of Clinical Endocrinology/ American College of Endocrinology Clinical Practice Guidelines 2020

International Society for Clinical Densitometry: Indications for Bone Mineral Density Testing 2023

Intermountain Health

Bone Health in Children and Adolescents Age 0 – 18[5,6]

Screen for characteristics that may indicate increased risk for low BMD (A)

Does patient have ≥1 of the following and provider has clinical suspicion of bone fragility?

- Characteristics that may indicate further investigation of BMD (A)
- Known condition associated with high-risk of low BMD. (B)
- Clinically significant fracture history. (C)

no → Continue to encourage conservative support measures (F) pg 3

yes

Perform DXA scan and test vitamin D levels

In children/ adolescents:
- DXA results are compared with expected values of those with similar age/sex to produce a Z-score.
- Densitometric criteria alone should not diagnose osteoporosis

Diagnosis[13]

Osteoporosis (*Any* of the following)	
• Vertebral compression fracture in absence of major trauma (regardless of Z-score) • ≥2 long bone fractures by 10 yrs old + Z-score ≤2.0 • ≥3 long bone fractures by 19 yrs old + Z-score ≤2.0	
Low bone mineral density for age	Z-score ≤2.0 w/out clinically significant fracture

Treatment Steps

Low vitamin D (serum 25-OH-D ng/ml)	
Insufficient (21–29 ng/ml)	Encourage dietary changes; see (D) pg 3
Deficient (<21 ng/ml)	Encourage dietary change; see (D) pg 3 Supplement with vitamin D2 or D3 (preferred) at 50,000 IU, 1 capsule weekly for 6 weeks OR vitamin D2 or D3 (preferred) at 2,000 IU per day for 6–8 weeks. Measure after treatment to ensure serum levels >21 ng/mL. (Common that second course of treatment needed). Once levels >21 ng/mL, give maintenance dose. Infants/ Toddler (400–1000 IU/day); Children/Adolescents (600–1000 IU/day)
Osteoporosis or low bone mineral density for age	
Documentation	Add low bone mineral density for age or osteoporosis to problem list.
Calcium	Emphasize dietary calcium which has better bioavailability. Supplements unlikely to significantly reduce fracture risk. (E)
Physical activity	Prescribe physical activity. For patients with movement disorder or prior exercise non-compliance, refer to PT.
Specialty referrals as needed	Osteogenesis imperfecta or other rare bone disease suspected, delayed puberty, or unexplained low BMD
Hormone therapy as needed	Estrogen or testosterone with endocrinology guidance; consider the effect of sex hormones on growth plates.
Drugs to AVOID	Limit use of systemic corticosteroids.

In those with low BMD or osteoporosis perform DXA scan every 2–3 years. Encourage conservative support measures (F) *pg 3*

(A) Characteristics that may indicate further investigation of BMD

- Low height/weight growth
- Low Physical Activity Vital Sign
- Low-dairy intake per day
- Family history of bone disease
- Signs of eating disorder
- Primary or secondary amenorrhea
- Delayed puberty

(B) Condition associated with low BMD in children/adolescents

Genetic Disease
- Osteogenesis imperfecta
- Hypophosphatasia
- Turner syndrome

Chronic Illness
- Chronic parenteral nutrition*
- Inflammatory bowel disease
- Chronic immobilization
- Childhood cancer
- Organ transplant
- Cerebral palsy
- Eating disorders
- Celiac disease

Endocrine Conditions
- Diabetes Mellitus
- Female athlete triad
- Cushing's Syndrome
- Hyperparathyroidism
- Hyperthyroidism
- Hypogonadism
- Growth hormone deficiency
- Transgender post-gonadectomy

Medications/Treatments
- Cyclosporine*
- Radiation*
- Anticoagulants (e.g. warfarin, heparin)*
- Chemotherapy*
- CY3P3A4 inducers (e.g. phenobarbital)*
- Loop diuretics (e.g. furosemide)*
- Anticonvulsants
- Ketogenic diet*
- Hormone replacement/suppression*
- Chronic glucocorticoids >3 mos.*
- Selective serotonin reuptake inhibitors
- Proton pump inhibitors
- Medroxyprogesterone-acetate (Depo-Provera)

*Major risk factor

(C) Clinically significant fracture history

- Vertebral compression fracture in absence of major trauma
- ≥2 long bone fractures by 10 yrs of age
- ≥3 long bone fractures by 19 yrs of age

Bone Health in Children and Adolescents Age 0 – 18

(D) Dietary sources of Vitamin D
• Fortified dairy, plant-based milk or orange juice • Fortified cereals • Salmon or Tuna

(E) Dietary sources of Calcium
• Dairy (cow, goat, sheep products) • Leafy greens (collard, mustard, turnip, kale, bok choy, spinach) • Almonds • Fortified plant-based milk or juice

F) Conservative Support Measures to Improve Bone Formation in Children and Adolescents [5,6]	
Breast-fed infants	Human milk contains inadequate amounts of vitamin D (unless lactating mother is taking supplements of approximately 6,400 IU/day) Breast-fed infants should be supplemented with 400 IU of vitamin D per day beginning the first few days of life and continue until the infant has been weaned and drinking vitamin D-fortified infant formula or cow's milk.
Calcium	Calcium-rich foods are preferred over supplementation. The RDA for calcium varies depending on age of child and is highest in 9–18 year old group. See *NIH recommended intakes .*
Vitamin D	RDA 600 IU daily. 5–15 minutes of sunlight exposure, 2–3 times per week produces ~3000 IU vitamin D; Lower rates of vitamin D production in pigmented skin. Sunscreen with SPF of ≥8 blocks vitamin D production. See Dietary sources of Vitamin D (D) and *NIH recommended intakes*.
Plant-based milk	If children/adolescents are drinking plant-based milk, see *guidance from AAP here .*
Activity	Children should experience 60 min. of moderate to vigorous physical activity (MVPA) per day (including bone loading) and avoid sedentary activity. A referral to physical therapy can help identify the best exercises for the child or adolescent.
Substance Use	Alcohol and tobacco use are associated with lower bone mass.
Carbonated beverages	Soda consumption is associated with lower intake of calcium and vitamin D.
Body weight and composition	Lean body mass is most strongly associated with bone mineral density.
Hormonal Status	Estrogen, testosterone, and growth hormone are positively associated with bone formation. Thyroid hormone excess is associated with an increase in bone resorption/breakdown and glucocorticoid excess is associated with bone resorption and impairs bone formation.

PATIENT EDUCATION FOR ADULTS

Helpful information for your adult patients.

- *Osteoporosis Treatment: What you should know (English/Spanish)*
- *Osteoporosis Eating Plan (English/Spanish)*
- *Fall Prevention (English/Spanish)*
- *Preventing Falls at Home: My action plan (English/Spanish)*
- *Bathroom Safety (English/Spanish)*
- *Improving and Maintaining Physical Activity as You Age (English/Spanish)*

Screening for Osteopenia / Osteoporosis in Adults

Females: ≥ 65 or < 65 with osteoporosis risk factors (A)
Males: ≥ 70 or 50 – 69 with osteoporosis risk factors (A)
Any person presenting with fracture: ≥ 50

↓

Perform DXA scan for BMD +/- TBS and perform fracture risk stratification (e.g.FRAX)

Use the *Radically Simple Tool* to talk with your adult patients about osteoporosis and fracture risk

Fracture Risk Assessment Tool (FRAX) Calculator

Diagnostic Criteria[1]

Category	T-score (spine, hip, or 1/3 proximal radius) + Clinical history
Normal	T-score –1.0 or above
Osteopenia	T-score between –2.5 and –1.0 with FRAX scores <3% risk of hip fracture and <20% risk of major osteoporotic fracture
Osteoporosis (ANY)	• T score –2.5 or below • Any fragility fracture • Osteopenia + FRAX score ≥3% risk of hip fracture or FRAX ≥20% risk of major osteoporotic fracture
Severe Osteoporosis	T-score –2.5 or below with fragility fracture OR T-score –3.0 or below

Normal → Recommend conservative support measures (B) Perform DXA scan every 2 – 3 years

Osteopenia → Recommend conservative support measures (B) Perform DXA scan every 2 – 3 years

Osteoporosis → See *Treatment of Osteoporosis in Adults pg 5*

Severe Osteoporosis → See *Treatment of Osteoporosis in Adults pg 5* AND consider referral to Endocrinology

(B) Conservative Support Measures to Prevent Bone Loss in Adults[1]

Diet	Consume diet high in fruits, vegetables, and calcium
Calcium	1000 mg daily (<50 years old), 1200 mg daily (>50 years old)
Vitamin D	Supplementation to achieve 30 – 50 ng/dL
Activity	Active lifestyle with weight-bearing exercise and balance training. A referral to PT can direct patient to best exercises.
Substance Use	Limit alcohol; females: <2 drinks/day ; males: <3 drinks/day
Fall Risk	Fall evaluation yearly: Ages ≥ 65 (consider earlier in females) [4,7]

(A) Risk factors of osteoporosis[1,2,4]

Lifestyle Factors

- Vitamin D insufficiency/deficiency
- Inadequate physical activity
- Smoking (active or passive)
- Low body weight; BMI <18.5
- Excessive vitamin A
- Low calcium intake
- Frequent falling
- High salt intake
- Immobilization
- Alcohol abuse

Hypogonadal States

- Premature menopause (<40 years)
- Surgical/chemo-induced menopause
- Androgen insensitivity
- Female athlete triad
- Hyperprolactinemia
- Panhypopituitarism
- Anorexia nervosa
- Hypogonadism

Endocrine Conditions

- Cushing's Syndrome
- Obesity
- Thyrotoxicosis
- Hyperparathyroidism
- Diabetes Mellitus

Medications

- Chemotherapy (aromatase inhibitors and androgen deprivation therapy)
- Aluminum containing antacids
- Proton pump inhibitors
- Thyroid replacement
- Thiazolidinediones
- SSRI's
- Depo-Provera
- Glucocorticoids

Miscellaneous conditions and diseases

- Renal disease (CKD III– CKD V/ ESRD)
- Chronic metabolic acidosis
- Congestive heart failure
- Bariatric surgery
- Idiopathic scoliosis
- Depression
- Hypercalciuria
- COPD
- Weight loss
- Amyloidosis
- Hyponatremia
- HIV/AIDS

Rheumatologic and autoimmune disease

- Ankylosing spondylitis
- Rheumatoid arthritis
- Sarcoidosis
- Systemic lupus

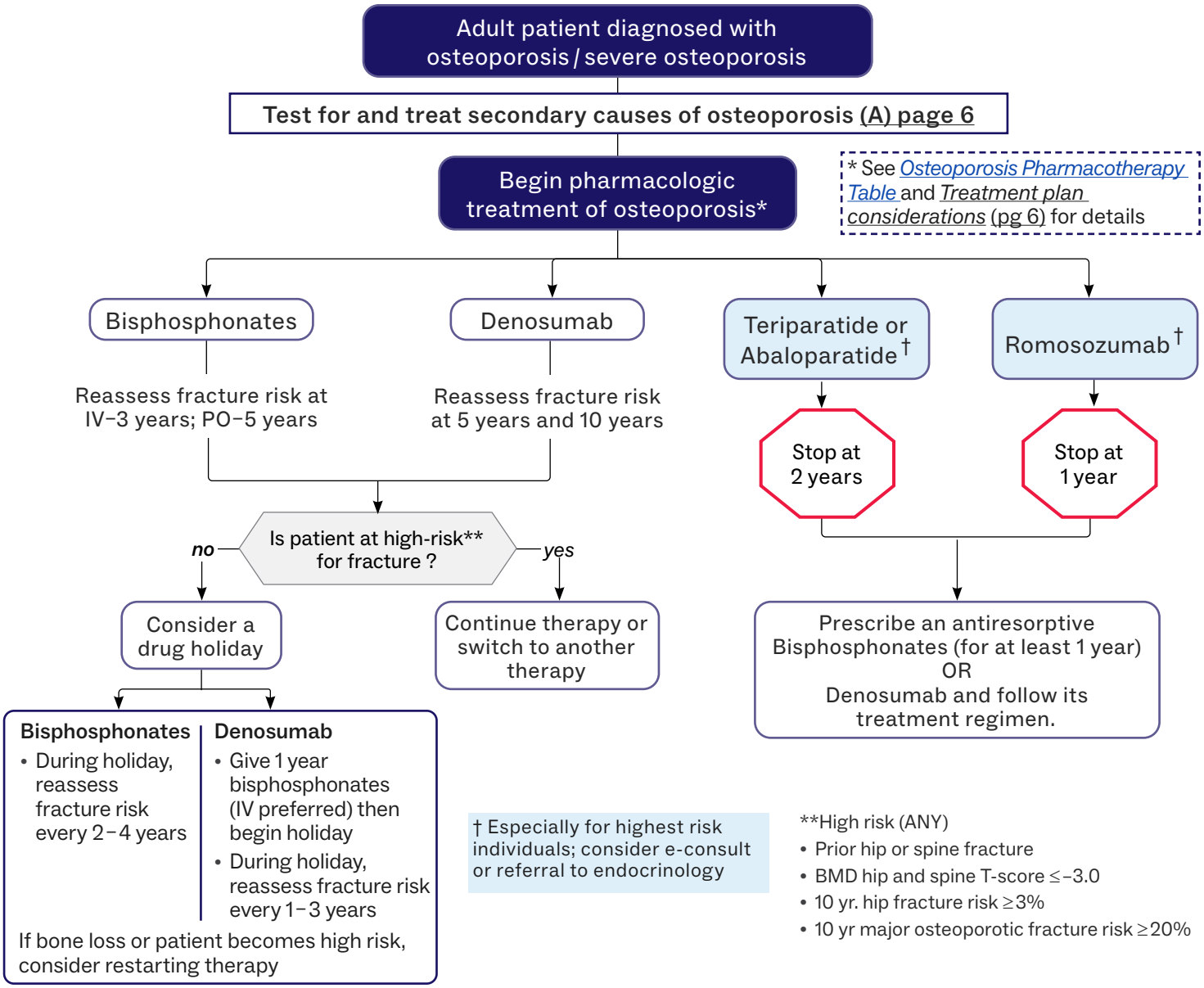
Gastrointestinal disorders

- Inflammatory bowel disease
- Malabsorption syndromes
- Primary biliary cirrhosis
- Gastrointestinal surgery
- Bariatric surgery
- Gastric bypass
- Celiac disease
- Pancreatic disease

Neurological/Muscular Disorders

- Muscular dystrophy
- Parkinson's disease
- Spinal cord injury
- Epilepsy
- Multiple sclerosis
- Stroke

Pharmacological Treatment of Osteoporosis in Adults [2,8]



† Especially for highest risk individuals; consider e-consult or referral to endocrinology

**High risk (ANY)
- Prior hip or spine fracture
- BMD hip and spine T-score ≤ –3.0
- 10 yr. hip fracture risk ≥ 3%
- 10 yr major osteoporotic fracture risk ≥ 20%

For those unable to tolerate the above drugs

Women age < 60 or < 10 yrs post-menopause

Consider (in order)
- Menopausal Hormone Therapy (see *NAMS guideline*)
- Selective estrogen receptor modulators (SERMs)
- Calcitonin
- Calcium + Vitamin D

Women age > 60

Consider (in order)
- Selective estrogen receptor modulators (SERMs)
- Calcitonin
- Calcium + Vitamin D
- Menopausal Hormone Therapy (see *NAMS guideline*)

Sequence Plan Examples [9,12]

- **Average risk:** PO Bisphosphonate (BS) → Drug holiday → PO BS → Drug holiday → PO BS
- **CKD progression to CKD 3/4:** PO BS → Drug holiday → PO BS → Drug holiday → if fracture risk high: Denosumab
- **Severe osteoporosis/high risk of fracture:** Anabolics (teriparatide, abaloparatide, or romosozumab) → Antiresorptive (bisphosphonates or denosumab) → Reassess

(A) Baseline labs prior to starting pharmacotherapy for osteoporosis[1,2]			
In all patients		**In select populations**	
• CBC • Albumin-adjusted calcium • Renal function • Phosphorus • Magnesium	• 25 (OH) Vitamin D • Parathyroid hormone • Calcium and creatine (24 hr. urine) • Liver function (including alk phos)	• Testosterone • Follicle-stimulating hormone (FSH), Luteinizing hormone (LH), Estradiol • Thyroid-stimulating hormone (TSH), Free thyroxine (FT4) • Anti-tissue transglutaminase antibody and IgA	• Prolactin • Tryptase • Serum protein electrophoresis, serum immunofixation, serum free kappa and lambda light chains • Urine protein electrophoresis • Urine free cortisol and creatinine

Treatment Plan Considerations	
Lifestyle modifications	Role to prevent excess bone loss but will NOT improve BMD in adults after mid–20s. Adequate calcium supplementation, Vit D level 30–50, weight-bearing exercise, and avoidance of tobacco products, excess caffeine (>2 soda/day), and alcohol (>2–3/day) help slow bone loss.
Treat underlying conditions that can worsen bone density	Hyperthyroidism, primary hyperparathyroidism, excess steroid exposure, celiac disease malabsorption, premature menopause/amenorrhea in women and severe hypogonadism (Testosterone <100 mg/dL) in men.
Anticipated duration	Osteoporosis/osteopenia are chronic conditions and should be treated long-term. Most patients with osteoporosis should be treated with 5 years of bisphosphonate (PO) before a holiday. After the holiday, resume medication. The treatment then holiday sequence can continue long term if a patient remains at risk. If fracture occurs consider escalation to anabolic.
First–line	For most patients, oral bisphosphonates – alendronate (Fosamax) and risedronate (Actonel) are most efficacious. If GERD or risk for esophageal/gastric ulcers, then annual IV zoledronic acid (Reclast) is recommended. In patients with severe osteoporosis or T scores <–3.0, anabolic agents, including teriparatide (Forteo), abaloparatide (Tymlos), and romosozumab (Evenity) have greatly improved efficacy if they are started as the first-line agent, prior to bisphosphonates and denosumab. Furthermore, they improve the efficacy of anti-resorptive medications that are used after them. Strongly consider referral to endocrinology for these medications. Cost may be a limiting factor. [9,10]
Escalation if fracture occurs after ≥12 months of treatment	Switch to IV zoledronic acid, denosumab, or anabolic therapies.
Premenopausal	Optimize lifestyle factors. If oligomenorrhea > 3 months, evaluate for hypogonadism and then prescribe estrogen (and progesterone if the patient has a uterus) via OCP, tablet, transdermal patch or vaginal ring. Avoid bisphosphonates and denosumab unless fracture has occurred. If the patient has a low-impact or fragility fracture, a referral to endocrinology is indicated.
Male osteoporosis	Treat hypogonadism if present. (AM testosterone <100 mg/dL contributes to bone loss). Men are more likely to have a secondary cause of osteoporosis.[11] Optimize lifestyle factors and recommend pharmacologic agent, as found in *Pharmacologic Treatment of Osteoporosis in Adults pg 5*
Drug holidays for bisphosphonates	The absolute risk of atypical femur fracture (AFF) is very low compared with the greater number of fractures effectively prevented by bisphosphonates. However, the risk of AFF increases significantly with the duration of bisphosphonate therapy. Bisphosphonate medications need a drug holiday to allow micro-stresses and injuries time to remodel and to prevent them from expanding into an AFF. A 2–5-year drug holiday is reasonable for most as AFF risk decreases 70% every year of a holiday. Resume treatment after a drug holiday.
Denosumab considerations	After denosumab discontinuation, risk is increased for multiple vertebral fractures which can be spontaneous and not related to falls. Longer durations of denosumab (>3 years) is correlated with a higher risk of these fractures. Following discontinuation, treatment with a potent antiresorptive should be prescribed beginning 6 mos. after the last denosumab injection. Both oral and IV bisphosphonates were protective against vertebral fractures, with IV zoledronic acid preferred. An exit strategy should be considered and risks discussed **before** denosumab is prescribed.
CKD 4-5 , GFR <20 or ESRD	**Strongly consider referral to endocrinology/osteoporosis specialist and nephrology before starting pharmacological therapy.** Osteoporosis must be differentiated from other forms of CKD-metabolic and mineral disease prior to treatment. Denosumab increases risk for severe hypocalcemia in CKD 4–5 patients, (re-check calcium levels 1 week after injection) and is *NOT* recommended for patients with ESRD/dialysis. Bisphosphonates are contraindicated.

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This CPM presents a model of best care based on the best available scientific evidence at the time of publication. It is not a prescription for every physician or every patient, nor does it replace clinical judgment. All statements, protocols, and recommendations herein are viewed as transitory and iterative. Although physicians are encouraged to follow the CPM to help focus on and measure quality, deviations are a means for discovering improvements in patient care and expanding the knowledge base. Send feedback to Betsy Batcher MD, Medical Director of Endocrinology, Canyons Region, Intermountain Health; *betsy.batcher@imail.org*

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