Ms. B, a 72-year-old woman, presents with new-onset low back pain. A comprehensive workup is performed, and a radiograph reveals compression fractures of the L1 and L2 vertebral bodies. The patient recalls no trauma to account for her fractures. Dual-energy x-ray absorptiometry (DXA) is ordered; the results show evidence of osteoporosis. Ms. B asks about initiating long-term treatment.

Osteoporosis is a disease of significant public health concern.1 According to the NIH Osteoporosis and Related Bone Diseases National Resource Center, more than 53 million people in the United States either have osteoporosis or are at high risk for it.2 The total cost of osteoporosis-related fractures is expected to reach $25.3 billion by 2025.3 It is estimated that one in three women (and one in five men) older than 50 will sustain osteoporotic fractures.4 The morbidity and mortality associated with these fractures must be recognized by health care providers in all medical specialties. Appropriate preventive and treatment modalities should be employed when providing care to persons with or at risk for osteoporosis. Advances in medical science have yielded multiple options for the prevention and treatment of osteoporosis.

CASE CONTINUED Ms. B’s medical history includes hypertension and GERD, for which she uses twice-daily dosing of a proton pump inhibitor (PPI). At age 53, she was diagnosed with left breast cancer, which required surgical excision and radiation therapy. She took tamoxifen for a total of five years, and the cancer did not recur. She takes no OTC products, including vitamins. She has no history of systemic inflammatory conditions, kidney stones, or extended treatment with corticosteroids. No history of gastrointestinal surgeries is reported. Ms. B has never smoked cigarettes and has never consumed two or more alcoholic beverages a day. She has no family history of osteoporosis in first-degree relatives. She is otherwise healthy but is physically inactive, with no regular weight-bearing exercise routine. It is also notable that she experienced an uneventful early menopause at age 41 and did not take estrogen replacement therapy.

NONPHARMACOLOGIC OPTIONS
Regular weight-bearing exercise, adequate calcium and vitamin D intake, smoking cessation, avoidance of heavy alcohol use, and education in fall prevention are vital. Recommended calcium intake varies by age,
ranging from 1,000 mg/d to 1,200 mg/d in divided doses. Vitamin D intake is recommended at 600 IU/d until age 70; 800 IU/d after age 70; and additional units if deficiency is noted. Avoidance of medications that contribute to bone loss (eg, corticosteroids) is also encouraged, if possible. Patient education should include balance training and a home safety assessment.

**CASE POINT** Nonpharmacologic strategies should be encouraged for every patient to promote optimal bone health and to prevent or treat osteoporosis.

**PHARMACOLOGIC OPTIONS**

*Oral bisphosphonates* are considered first-line treatment for osteoporosis; currently available options include alendronate, risedronate, and ibandronate. Bisphosphonates work by inhibiting osteoclast function, thereby reducing bone resorption.

Oral bisphosphonates have been clinically available since the 1990s and have demonstrated their efficacy, safety, and cost-effectiveness. However, a thoughtful approach should be taken to their use in specific patient populations: those with esophageal disorders, chronic kidney disease, and/or a history of bariatric gastrointestinal procedures. Bisphosphonates of any form should be avoided in a patient with chronic kidney disease with a glomerular filtration rate ≤ 30 mL/min or ≤ 35 mL/min (based on the package insert for the specific product). Patients with a recent or upcoming tooth extraction should also avoid using bisphosphonates until they have healed, due to concerns for osteonecrosis of the jaw.

Administration of oral bisphosphonates requires special attention. Oral bisphosphonates must be taken first thing in the morning with water; for the next 30 to 60 minutes, the patient must stay upright and not have any food, drink, or additional medications by mouth. These specifications may affect patient adherence to treatment.

*Intravenous bisphosphonates.* Depending on the IV bisphosphate chosen—ibandronate and zoledronic acid are the currently available options—administration is recommended either every three or 12 months. A common adverse effect of IV bisphosphonates is flulike symptoms, which are generally brief in duration. Hypocalcemia has also been associated with IV administration, more so than with oral bisphosphonate use. Osteonecrosis of the jaw, while rare, must also be considered.

**CASE POINT** Because of Ms. B’s GERD requiring PPI use, oral bisphosphonates are not the most ideal treatment for her osteoporosis; they could exacerbate her gastrointestinal symptoms. IV bisphosphonates are a potential option for her, as this method of administration would eliminate the gastrointestinal risk associated with oral bisphosphonates.

*Selective estrogen receptor modulators* (SERMs), which are administered orally, are another option for osteoporosis treatment for vertebral fractures. One medication in this class, raloxifene, selectively acts on estrogen receptors—it works as an agonist in bone estrogen receptors (preventing bone loss) and an estrogen antagonist in other tissue (eg, breast, uterine). SERMs are not considered first-line treatment for osteoporosis because they appear to be less potent than other currently available agents. However, a postmenopausal patient with a high risk for invasive breast cancer without a history of fragility fracture might consider this option, as raloxifene can reduce the risk for invasive breast cancer. SERMs have been associated with an increase in thromboembolic events and hot flashes.

*Calcitonin nasal spray* is used much less commonly now because its effect on bone mineral density is weaker than other currently available options. Calcitonin nasal spray is administered as one spray in one nostril each day. There has been some concern regarding calcitonin use and its association with malignancy.

**CASE POINT** Ms. B’s history of compression fractures suggests the need for potent pharmacologic options to treat her osteoporosis. SERMs and calcitonin nasal spray are felt to...
be less potent and therefore are not the preferred treatment recommendations for her.

**Parathyroid hormone analogs.** The availability of the parathyroid hormone analogs teriparatide and abaloparatide gives patients and health care providers another treatment option for osteoporosis. These potent stimulators of bone remodeling help reduce future fracture risk. Teriparatide and abaloparatide are considered anabolic bone agents, rather than antiresorptive medications. These medications are administered subcutaneously daily for no more than two years. Many health care providers use parathyroid hormone analogs for patients with severe osteoporosis (T score, ≤ −3.5 without fragility fracture history or ≤ −2.5 with fragility fracture history). The cost of these agents must be considered when recommending them to eligible patients.

Parathyroid hormone analogs do carry a black box warning because of an increased risk for osteosarcoma observed in rat studies. These products should therefore be avoided in patients with increased risk for osteosarcoma: those who have Paget disease of the bone or unexplained elevations of alkaline phosphatase; pediatric and young adult patients with open epiphyses; or those who have had external beam or implant radiation therapy involving the skeleton.

**CASE POINT** Because of Ms. B’s prior history of breast cancer requiring radiation treatment, parathyroid hormone analogs are not recommended.

**Denosumab** is a human monoclonal antibody, a RANKL inhibitor, that works by preventing the development of osteoclasts. This medication is administered subcutaneously every six months. There are no dosing adjustments recommended for hepatic impairment. The denosumab package insert does not specify a dosage adjustment for patients with renal impairment; however, clinical studies have indicated that patients who have a creatinine clearance < 30 mL/min or who are on dialysis are more likely to experience hypocalcemia with denosumab use. As with other newer osteoporosis treatments, cost considerations should be discussed with patients.

One unique consideration is that clinical trials have shown an increased fracture risk and the return of bone mineral density to predenosumab treatment levels within 18 months of discontinuing the medication. Health care providers should be prepared to recommend alternative treatment options if denosumab is discontinued.

**CASE CONCLUDED** After a discussion of the risks, benefits, and expectations associated with each of the available treatment options, Ms. B and her health care provider narrow down her options to use of an IV bisphosphonate or denosumab for her osteoporosis. She ultimately chooses denosumab, based on her preference for an injectable medication.

**CONCLUSION** The morbidity and mortality associated with osteoporosis can be improved with an appropriate balance of nonpharmacologic and pharmacologic approaches. The varying mechanisms of action, administration methods, and documented efficacy of the available medications provide an opportunity for patient education and informed decision-making when choosing treatment. For additional guidance, the American College of Physicians, the American Association of Clinical Endocrinologists, and American College of Endocrinology have published guidelines that can help in the decision-making process.

**REFERENCES**