New Guidelines for the Management of Postmenopausal Osteoporosis

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Introduction

Over 200 million people worldwide currently suffer from osteoporosis, a silent and progressive disease in which the bones become less dense and more fragile. People that suffer from osteoporosis have a greatly increased risk of fractures, oftentimes with few to no symptoms that appear until the first fracture occurs.¹

Globally, among those over the age of fifty, one in three women and one in five men are at risk of a fracture due to osteoporosis; those that have already experienced an initial osteoporotic fracture are even more likely to sustain a new fracture. In addition to increasing mortality, fractures usually lead to decreased mobility, function, and overall quality of life.¹

In March 2019, the Endocrine Society published a new clinical practice guideline for the management of postmenopausal osteoporosis.² This article will address the new recommendations for osteoporosis management in postmenopausal patients as well as compare the new guidelines with existing guidelines.

2019 Recommendations

Postmenopausal women at high risk of fractures, especially those who have experienced a recent fracture, should be treated with pharmacological therapies without delay because the benefits outweigh the risks. A recent fracture is defined as having occurred within the past two years. In addition to treatment, patients should be counseled regarding adequate calcium and vitamin D intake, strategies for fall prevention, smoking cessation techniques, avoidance of excessive alcohol intake, strength conditioning, and balance training.²

Treatment is patient preference-driven and patient-specific factors, such as values, costs, resources, and needs, should be considered when choosing among the therapy options. The goal is to treat low bone mineral density (BMD) or osteoporosis in order to decrease the burden of major osteoporotic fractures.²

Therapy-specific recommendations from The Endocrine Society are described on the next two pages.
**Bisphosphonates**

Initial therapy with bisphosphonates (alendronate, risedronate, zoledronic acid, and ibandronate) is indicated for postmenopausal women at high risk of fractures. However, ibandronate is not recommended to reduce nonvertebral or hip fracture risk. Fracture risk should be reassessed after three to five years for postmenopausal women taking bisphosphonates. Women who remain at high risk of fractures should continue therapy and women who are at moderate to low risk of fractures should consider a "bisphosphonate holiday."²

**Denosumab**

Denosumab is an alternative initial treatment option for postmenopausal women with osteoporosis. In order to prevent a rebound in bone turnover, denosumab should not be delayed or stopped. Fracture risk should be reassessed after five to ten years. Women still at high-risk should either continue denosumab or consider other osteoporosis treatment therapies.²

**Teriparatide & abaloparatide**

Teriparatide and abaloparatide are recommended in postmenopausal women with osteoporosis at very high risk of fractures (severe or multiple vertebral fractures). Duration of treatment for up to two years with teriparatide and abaloparatide is recommended for the reduction of vertebral and nonvertebral fractures. Antiresorptive osteoporosis therapies are recommended in postmenopausal women who have completed a course of teriparatide or abaloparatide, in order to maintain density gains.²

**Selective estrogen receptor modulators (SERM)**

Raloxifene or bazedoxifene are recommended in postmenopausal women with osteoporosis at high risk of fractures with a low risk of deep vein thrombosis (DVT) and for whom bisphosphonates or denosumab are not appropriate, or who have a high risk of breast cancer. It is important to note that bazedoxifene is only licensed in the United States as a combination with conjugated estrogens, and the combination product has not been shown to reduce the risk of fractures.²

**Menopausal hormone therapy**

Postmenopausal women with high risk of fracture may use hormone therapy (estrogen only in women with hysterectomy) to prevent all types of fractures if they meet the following criteria:²

- Under 60 years of age or less than ten years past menopause
- Low risk of DVT
- Bisphosphonates or denosumab are not appropriate
- Bothersome vasomotor symptoms
- Additional climacteric symptoms
- No contraindications
- No prior myocardial infarction or stroke
- No breast cancer
- Willing to take menopausal hormone therapy
Nasal spray calcitonin
Nasal spray calcitonin is recommended for postmenopausal women at high risk of fractures who cannot tolerate bisphosphonates, estrogen, denosumab, abaloparatide, or teriparatide.\textsuperscript{2}

Calcium and vitamin D
Calcium and vitamin D are recommended in postmenopausal women who have low BMD and are at high risk for fractures as an adjunct to other osteoporosis therapies. Calcium and vitamin D are also recommended in patients who cannot tolerate bisphosphonates, estrogen, selective estrogen response modulators, denosumab, tibolone, teriparatide, or abaloparatide to prevent hip fractures.\textsuperscript{2}

Romosozumab
Romosozumab is indicated for the treatment of osteoporosis in postmenopausal women at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or who have failed or are intolerant to other osteoporosis therapies. The use of romosozumab should be limited to twelve total monthly doses as its anabolic effect wanes after this time; if there is still a need for osteoporosis therapy, an anti-resorptive agent should be considered. Due to its approval date, romosozumab’s place in therapy is not addressed in any of the current guidelines; however, the Endocrine Society guideline does mention that significant reductions in vertebral and non-vertebral fractures were associated with its use in clinical studies.\textsuperscript{2,3}

Monitoring
In postmenopausal women with low BMD at high-risk of fractures, to assess treatment response, a BMD via dual-energy X-ray absorptiometry (DEXA) at the spine and hip should be monitored every one to three years. In patients with poor response to therapy, bone turnover markers (BTMs) (serum C-terminal crosslinking telopeptide for antiresorptive therapy or procollagen type 1 N-terminal propeptide for bone anabolic therapy) should be monitored.\textsuperscript{2}

Previously published guidelines for the treatment of postmenopausal osteoporosis include those published by the Association of Clinical Endocrinologists (AACE) and the American College of Physicians (ACP) in 2016 and 2017, respectively. The AACE guidelines focus on postmenopausal osteoporosis only while the ACP guidelines focus on treatment of osteoporosis in both men and women.\textsuperscript{4,5} Key differences between the guidelines are highlighted in the table on the next page.

Conclusion
The 2019 guidelines from the Endocrine Society outline the pharmacological management of osteoporosis in postmenopausal women. There are many options available for postmenopausal osteoporosis treatment and fracture prevention. Previous guidelines were published by AACE and ACP and had some key differences in recommendations compared to the Endocrine Society guidelines. In the end, treatment should be patient preference-driven and patient-specific factors, such as values, costs, resources, and needs, should be considered when choosing among the therapy options.
Abaloparatide is recommended in postmenopausal women with osteoporosis at very high risk of fractures (severe or multiple vertebral fractures) for up to 2 years. “Bisphosphonate holiday” AACE recommends considering a “bisphosphonate holiday” after 5 years in moderate-risk patients. AACE recommends considering a “bisphosphonate holiday” after 6 to 10 years in high-risk patients. Patients who are at low-to-moderate risk after 3 to 5 years should consider a “bisphosphonate holiday”. Patients who remain at high risk after 3 to 5 years should continue bisphosphonate therapy. Calcitonin Nasal spray calcitonin is recommended for postmenopausal women at high-risk of fractures who cannot tolerate bisphosphonates, estrogen, denosumab, abaloparatide, or teriparatide. Menopausal hormone therapy (HT) ACP recommends against estrogen therapy with or without progestogen therapy or raloxifene for menopausal women with osteoporosis. HT is recommended in patients with specific characteristics. Treatment monitoring AACE recommends obtaining a baseline DEXA at the spine and hip and should be monitored every 1 to 2 years, or less frequently depending on clinician. ACP recommends against BMD monitoring in women with osteoporosis during the 5-year drug therapy. DEXA at the spine and hip should be monitored every 1 to 3 years.

Table. Differences between AACE, ACP, and Endocrine Society guidelines for the treatment of osteoporosis.2,4,5
References