Indian Health Service
National Pharmacy and Therapeutics Committee
Formulary Brief: ***Osteoporosis***
- May 2016 -

Background:
Osteoporosis affects over 10 million Americans, with another 34 million who have low bone mass. It is projected that from 2005 to 2025 the incidence of osteoporosis-related fractures will rise from 2 million to 3 million annually[1]. While there are many risk factors, the most at-risk segment of the population is post-menopausal women. In May 2016, the National Pharmacy & Therapeutics Committee (NPTC) undertook a comprehensive review of multiple pharmacologic classes approved for the prevention and/or treatment of osteoporosis. As a result of this review, **the NPTC retained the oral bisphosphonate, alendronate,** on the Indian Health Service National Core Formulary.

Discussion:
Beginning around age 30 years, there is an age-related decline in bone mass, affecting both trabecular and cortical bone[2].This decline is most pronounced among women following menopause. Other risk factors for osteoporosis include cigarette smoking, excessive alcohol intake, low body weight, previous fracture, family history and secondary causes such as rheumatoid arthritis or glucocorticoid use. All adults should undergo osteoporosis risk factor assessment as a part of routine preventive care. For those at high risk, an assessment of bone mineral density and a fracture risk assessment using the validated WHO FRAX risk calculator (available at http://www.shef.ac.uk/FRAX/) is warranted to facilitate an individualized treatment plan for the prevention of osteoporosis and osteoporosis-related fracture[3].

Adequate dietary or supplemental intake of calcium and vitamin D is essential to bone health but is not adequate to prevent osteoporosis or osteoporosis-related fracture. Osteoporosis treatment is generally indicated for those with one of the following; 1) History of osteoporotic hip or vertebral fracture, 2) T-score ≤-2.5 (DEXA) at the femoral neck or spine, after appropriate evaluation to exclude secondary causes, or 3) T-score between -1 and -2.5 (DEXA) at the femoral neck or spine, and a 10-year probability of hip fracture ≥3 percent or a 10-year probability of any major osteoporosis-related fracture ≥20 percent based upon the United States-adapted World Health Organization algorithm[4-5].

The NPTC reviewed the following medications and medication classes which are FDA approved for the prevention and/or treatment of osteoporosis; the bisphosphonates, denosumab, the selective estrogen receptor modulator raloxifene, the PTH analog teriparatide, and calcitonin. In a network meta-analysis of 116 trials, the bisphosphonates, teriparatide and denosumab were all found to be effective, with no significant differences. Raloxifene was found to be less effective than the other agents[6]. Among the bisphosphonates, ibandronate appears to have less efficacy for fracture prevention.

In 2013, the Institute for Clinical Systems Improvement published a guideline which included recommendations for the pharmacologic management of osteoporosis and which echoed similar previous guidelines published by other groups[3]. It noted that the use of bisphosphonates was associated with the strongest data showing risk reductions in vertebral, hip, and other non-vertebral fractures[3]. Teriparatide (PTH 1-34) is indicated for patients at the highest risk of future fracture, for whom it may be considered first-line therapy[3]. Meanwhile, nasal calcitonin is considered a third-line treatment for osteoporosis[3].

Regarding the duration of treatment, indefinite treatment is generally not recommended. The National Osteoporosis Foundation recommends that treatment duration decisions must be individualized[4]. The American Academy of Family Practitioners (AAFP) encourages clinicians to consider stopping bisphosphonate therapy after five years in women without a personal history of vertebral fractures[7]. They referenced the FLEX study which compared women taking alendronate for five years versus those taking alendronate for 10 years and showed no increased incidence in nonvertebral or hip fractures[8]. Furthermore, the AAFP noted that complications of bisphosphonates including osteonecrosis of the jaw and atypical femoral fractures are rare but are associated with longer duration of use. According to guidelines from the American Association of Clinical Endocrinologists, combination therapy with more than one agent is not recommended for the treatment of osteoporosis[1].

As with all pharmacologic interventions, medication non-adherence is associated with reduced efficacy. Non-adherence to oral bisphosphonate therapy has been associated with higher risk of fracture among those with osteoporosis. Clinicians should routinely review and address non-adherence factors.

Findings:
Osteoporosis is common and causes significant morbidity and mortality, particularly among post-menopausal women. Risk factor assessment is indicated for all adult patients as a component of routine preventive care. Treatment decisions are generally based on bone mineral density and fracture risk or prior history of fragility fracture. Lifestyle measures are an important component of osteoporosis prevention and treatment.

Conclusions:
Treatment decisions, including drug choice and duration of therapy, should be individualized based on unique patient needs and preferences. Alendronate, risedronate, zoledronic acid and denosumab may all be considered first-line therapy and likely offer similar efficacy however ibandronate is likely less efficacious. Bisphosphonates generally have the strongest data supporting their use in fracture risk reduction. Teriparatide is indicated for those at very high risk of fracture, particularly those who have failed bisphosphonate therapy. While not a first-line agent, raloxifene may offer unique benefits to women at high risk of breast cancer. Calcitonin is considered a third-line agent.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov. For more information about the NPTC, please visit the NPTC website.

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