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RESTRICTED USE	Bisphosphonates (oral)	1 of 3		
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Bisphosphonates are indicated for the treatment and prevention of osteoporosis. They are most effective when used in combination with an adequate intake of calcium and Vitamin D. They must be taken on an empty stomach for maximal bioavailability, with a full glass of water. No other medications may be taken within 30-45 minutes of administration of the bisphosphonate. The resident must remain upright for 30-45 minutes after taking the dose. Bisphosphonates are also indicated for treatment of Paget's disease.

Individuals admitted to a care centre on a bisphosphonate must meet these criteria for continued use following admission.

Contraindications for use

1. Patients who are hypersensitive to this drug or to any ingredient in the formulation;
2. Abnormalities of the esophagus which delay esophageal emptying such as stricture or achalasia;
3. Inability to stand or sit upright for at least 30 minutes;
4. Hypocalcemia; and
5. Renal insufficiency with creatinine clearance <30 mL/min.

PROTOCOL 1 (weekly oral administration)

1. Prevention of osteoporosis in postmenopausal women. Fracture risk may be determined using the WHO FRAX™ 10-year risk model (see below) with or without bone mineral density measurement.
2. The treatment of osteoporosis in postmenopausal women. Osteoporosis may be confirmed by the presence or history of osteoporotic fracture, OR a WHO FRAX™ 10-year absolute risk of hip fracture of 3% or greater or 20% or more for any major osteoporotic fracture (hip, spine, humerus, or wrist), OR the finding of low bone mass (for example, at least 2.0 standard deviations below the premenopausal mean).
3. The treatment of osteoporosis in men to reduce the incidence of fractures; and
4. The prevention and treatment of glucocorticoid-induced osteoporosis [steroid equivalent to > 7.5 mg prednisone for >90 days].

PROTOCOL 2 - Paget's Disease (daily alendronate 40 mg tablets or risedronate 30 mg tablets)

Alendronate sodium in a dose of 40-mg daily for up to 6 months is approved for treatment of Paget's disease. The median time to normalization of the serum alkaline phosphatase with alendronate sodium is unknown. The manufacturer recommends that re-treatment not be undertaken for 6 months following the completion of the treatment course.

Risedronate in a dose of 30 mg daily for 2 months is approved for treatment of Paget's disease., Re-treatment may be considered (following post-treatment observation of at least 2 months) if relapse has occurred, or if treatment fails to normalize serum alkaline phosphatase. For re-treatment, the dose and duration of therapy are the same as for initial treatment. There are no data available on more than one course of re-treatment.

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WHO FRAX™ (WHO Fracture Risk Assessment Tool) <http://www.shef.ac.uk/FRAX/>

The FRAX® tool was developed by the WHO to evaluate fracture risk of patients. It is available both as an online calculator and in simplified paper version from the above website. The FRAX® algorithms give the 10-year risk of hip fracture as well as the 10-year probability of a major osteoporotic fracture (clinical spine, hip, shoulder or forearm).¹

The FRAX™ model can be used for men as well as women, and for 4 different ethnicities (Caucasian, Hispanic, Black, Asian). Simply select gender and ethnicity in the input fields.² It's database is also country specific. Since Canada is not an available selection, the current recommendation is that the UK database be used.

The FRAX model does not necessarily require a DXA bone density result; Since BMI is a reasonable surrogate for DXA, the FRAX model can yield a prediction score by using subject height and weight in place of DXA results.

This model does not account for osteoporosis treatment effects. Best estimates are that bisphosphonate therapy results in a 35% reduction in the risk of any of one of four fractures (spine, wrist, humerus, hip).^{3,4}

The risk thresholds of 3% for hip fracture and 20% for any of the four major osteoporotic fractures are based on American studies by Tosteson³ and Dawson-Hughes⁴.

¹ Kanis JA, FRAX® WHO Fracture Risk Assessment Tool, <http://www.shef.ac.uk/FRAX/> accessed 14 April 2009

² Frequently Asked Questions, Foundation for Osteoporosis Research and Education, <http://riskcalculator.fore.org/FAQ.htm> accessed 14 April 2009

³ Tosteson ANA, Melton II LJ, Dawson-Hughes B, Baim S, Favus MJ, Khosla S, Lindsay RL. Cost-effective osteoporosis treatment thresholds: the United States perspective. *Osteoporos Int* DOI 10:1007/s00198-007-0550-6.

⁴ Dawson-Hughes B, Tosteson ANA, Melton III LJ, Baim S, Favus ML, Khosla S, Lindsay RL. Implications of absolute fracture risk assessment for osteoporosis practice guidelines in the USA. *Osteoporos Int* DOI 10:1007/s00198-008-0559-5.

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For Consideration: Extended Use Bisphosphonates for Osteoporosis

As many long-term care clients are unable to take these medications safely as their chronic conditions progress (positioning, swallowing ability, timing of medication administered, etc.), it is reasonable to consider the risks of improper administration vs. the benefits of long-term use of bisphosphonates.

There is some evidence that the use of bisphosphonates may not provide any additional benefits after treatment length of five years. While some trials showed a decrease in bone-mass density (BMD) in placebo groups vs. bisphosphonate groups, the FLEX and HORIZON trials (assessing discontinuation of alendronate and zoledronic acid, respectively), showed there was little to no difference in risk of fractures over a period of 3-5 years in an aggregate 2,332 patients.

The only exception was a subgroup assessing clinical vertebral fractures, which did show an NNT of 36 with continued use of alendronate (2.4% vs. 5.3% placebo).

Bottom Line: There is no clear indication that bisphosphonates *should* be stopped after 5 years, but existing evidence seems to indicate that the fracture prevention effect may be limited (with the possible exception of those at higher risk of vertebral fracture). There is limited data for use in long-term, care clients, especially for clients who may be immobile, bed-bound, or near end of life.

Reference:

Kolber, M. Bisphosphonates: Forever or Five Years and Stop? ACFP Tools for Practice, updated Dec 2013. www.acfp.ca/wp.../tools-for-practice/1397764727_20140408_114438.pdf (accessed Oct 2, 2014)

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