

Recommendations and Reasons

Committee to Evaluate Drugs (CED)

Alendronate / Cholecalciferol

Product:

ALENDRONATE/CHOLECALCIFEROL
(Fosavance®) 70mg/140mcg tablet

Class of drugs:

Bisphosphonate

Indication:

Treatment of osteoporosis

Manufacturer:

Merck Frosst Canada Inc.

Highlights of Recommendation:

- ◆ Alendronate/cholecalciferol 70mg/140mcg is a product that combines a bisphosphonate with vitamin D to treat osteoporosis in men and post-menopausal women. This product is taken once a week and contains the equivalent of 5600 IU of Vitamin D. This equals 800IU of Vitamin D daily.
- ◆ The trial submitted by the manufacturer demonstrated that alendronate with the 140mcg of cholecalciferol was as well tolerated as the same combination product with 70mcg. There are no trials demonstrating that the combination product is more effective than alendronate alone.
- ◆ Alendronate/cholecalciferol 70mg/70mcg is already listed on the Ontario Drug Benefit Formulary.
- ◆ This combination product costs the same as generic alendronate 70mg tablet, meaning the vitamin D component is provided at no additional cost.
- ◆ **Overall, the CED recommended that alendronate/cholecalciferol 70mg/140mcg should be listed on the Formulary as a General Benefit as a replacement for alendronate/cholecalciferol 70mg/70mcg, since it would be cost-neutral and would provide a more suitable dose of Vitamin D.**

Background:

Osteoporosis is a disease commonly associated with aging. It results in a loss of bone mineral density. Osteoporosis is more common in women than in men, and may lead to fractures of the wrist, spine and hip.

To treat and prevent osteoporosis and their associated fractures, physicians advise patients to consume appropriate amounts of calcium and vitamin D, use weight-bearing exercise, stop smoking, consume limited alcohol, and avoid falls.

Secondary treatment involves a class of drugs called bisphosphonates, which includes drugs such as etidronate, alendronate and risedronate. All these drugs are currently listed on the Ontario Drug Benefit Formulary.

Third-line treatments (in women only) are raloxifene and hormone replacement therapy.

Alendronate/cholecalciferol combination products are indicated for the treatment of osteoporosis in both men and post-menopausal women.

CED Recommendation-

The CED recommended that alendronate/cholecalciferol 70mg/140mcg be listed as a General Benefit on the Ontario Drug Benefit (ODB) Formulary/CDI as a replacement of the alendronate/cholecalciferol 70mg/70mcg combination product, on the basis that it would be cost-neutral to the Ministry and would provide a more suitable dose of vitamin D than the 70mg/70mcg formulation of Fosavance that is already funded.

Executive Officer Decision

Based on the CED's recommendation and a subsequent listing agreement which addresses cost, the Executive Officer decided to list alendronate/cholecalciferol 70mg/140mcg (Fosavance®) on the ODB Formulary as a General Benefit.

Status

Funding available through the Ontario Public Drug Programs.

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Detailed Discussion:

- ◆ Alendronate/cholecalciferol 70mg/140mcg is taken once a week and contains the equivalent of 5600 IU of Vitamin D to provide 800 IU of Vitamin D per day. The currently listed combination product with alendronate/cholecalciferol 70mg/70mcg, also taken once a week, contains the equivalent of 2800IU of Vitamin D.
- ◆ According to the Canadian guidelines for osteoporosis (Brown JP and Josse RG. 2002 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada. CMAJ 2002;167 Suppl 10:S1-34), the recommended daily intake of vitamin D is 800 IU for men and women over the age of 50. However, the optimal daily allowance of Vitamin D has not been established and 1000 IU of Vitamin D daily has been recommended for all adults in northern latitudes (Vieth R, Fraser D. Vitamin D insufficiency: no recommended dietary allowance exists for this nutrient. CMAJ 2002;166 (12):1541-2).
- ◆ Although there are clinical trials demonstrating the efficacy of alendronate alone in the treatment of osteoporosis or in the prevention of fractures, there are no clinical trials to support any superiority of alendronate/cholecalciferol combinations. There are also no clinical trials demonstrating that the combination product is more effective or causes fewer side effects than when alendronate and cholecalciferol are taken separately.
- ◆ The only published trial with the alendronate/cholecalciferol 70mg/140mcg combination product is a 24-week extension of a 15-week randomized controlled trial (Binkley et al. *Bone* 2009). This trial evaluated the safety and tolerability of alendronate/cholecalciferol 70mg/140mcg versus alendronate/cholecalciferol 70mg/70mcg in men and women with post-menopausal osteoporosis. The trial concluded that patients previously treated with alendronate/cholecalciferol 70mg/70mcg combination for 15 weeks, that the addition of 70mcg cholecalciferol (given as alendronate/cholecalciferol 70mg/140mcg combination product) for 24 weeks did not produce hypercalcemia (high calcium levels in the blood) nor increase the risks of hypercalciuria (excessive calcium levels in the urine).
- ◆ Although Vitamin D is not listed on the ODB Formulary, the CED noted that Vitamin D 800IU is very inexpensive. The

manufacturer has set the price of alendronate/cholecalciferol 70mg/140mcg to be the same as generic alendronate 70mg.

- ◆ Since alendronate/cholecalciferol 70mg/140mcg could be prescribed instead of the alendronate/cholecalciferol 70mg/70mcg or alendronate 70mg, the addition of this product is expected to be cost-neutral to Ontario Public Drug Program.
- ◆ **Overall, the CED recommended that alendronate/cholecalciferol 70mg/140mcg be listed on the ODB Formulary as a General Benefit in place of alendronate/cholecalciferol 70mg/70mcg, since the new combination product would provide a more suitable dose of vitamin D to patients.**

CEDAC Recommendation:

(<http://www.cadth.ca/index.php/en/cdr/recommendations>)

The Canadian Expert Drug Advisory Committee (CEDAC) recommended that alendronate/cholecalciferol 70mg/140mcg be listed similar to other alendronate products.



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Ontario Public Drug Programs

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