

Alendronate/Cholecalciferol

Product:

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

Class of drugs:

Bisphosphonate

Indication:

Treatment of osteoporosis

Manufacturer:

Merck Frosst

CED Recommendation

The CED recommended that alendronate/cholecalciferol (Fosavance) not be listed on the Ontario Drug Benefit (ODB) Formulary, on the basis that this product is more expensive than generic alendronate. The additional Vitamin D can be purchased inexpensively.

Executive Officer Decision

Based on the CED's recommendation and a subsequent pricing agreement, the Executive Officer has decided to list alendronate/cholecalciferol (Fosavance) on the ODB Formulary.

Status

Funding available through the Ontario Public Drug Programs.

Highlights of Recommendation:

- ◆ Alendronate/cholecalciferol (Fosavance) is a combination product containing alendronate and cholecalciferol (Vitamin D). It is taken once weekly, similar to alendronate 70mg, for the treatment of osteoporosis.
- ◆ Alendronate/cholecalciferol (Fosavance) provides the equivalent of 2800 IU of Vitamin D weekly (or 400 IU daily). There is no evidence that this dose will reduce the risk of hip fracture. Recent large trials suggest that Vitamin D itself is not effective in preventing fractures and when given with recommended calcium supplements, increases the risks of kidney stones.
- ◆ Taking enough calcium and Vitamin D is considered important to help prevent osteoporosis, but is inadequate to treat osteoporosis.
- ◆ No trials were done with alendronate/cholecalciferol (Fosavance) to study its effect on preventing bone fractures. However alendronate alone has been demonstrated to prevent hip and spinal fractures. There is no comparative evidence that Fosavance improves clinically important outcomes, when compared to alendronate alone, in patients with osteoporosis.
- ◆ Alendronate/cholecalciferol (Fosavance) is more expensive than generic alendronate. Vitamin D is inexpensive and patients may buy it over the counter.
- ◆ **Overall, the Committee recommended that the ODB Formulary not list alendronate/cholecalciferol (Fosavance).**

Background:

Osteoporosis is a disease of aging that results in the loss of bone mineral density. More common in women than in men, advanced cases osteoporosis may lead to fractures of the spine and hip.

Optimal treatment and prevention of osteoporosis includes advising patients to consume enough calcium and Vitamin D, to strengthen muscles through weight-bearing exercise, to stop smoking, consume little or no alcohol, and to prevent falls.

Secondary treatment involves a class of drugs called bisphosphonates, which includes etidronate/calcium, alendronate and risedronate. All are currently listed on the ODB Formulary.

Third-line treatments (in women only) are raloxifene and hormone replacement therapy. Both are listed on the ODB Formulary.

Alendronate/cholecalciferol (Fosavance) contains alendronate 70mg and cholecalciferol 70mcg (Vitamin D3 2800 IU), and is indicated for the treatment of osteoporosis in men and postmenopausal women. Patients take alendronate/cholecalciferol (Fosavance) once a week.

Detailed Discussion:

- ◆ The manufacturer, Merck Frosst, asked the Ministry of Health and Long-Term Care to list alendronate/cholecalciferol (Fosavance) 70 mg tablets on the Ontario Drug Benefit Formulary.
- ◆ The effectiveness of the combination of alendronate and cholecalciferol in preventing bone fractures was not studied in the pivotal trial. The primary outcome measure of the pivotal trial was of Vitamin D insufficiency. The Committee noted this outcome measure was not useful. Measuring fracture prevention as the primary outcome would have provided the most relevant data.

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- ◆ Alendronate is widely accepted as an effective treatment for osteoporosis at the 70 mg weekly dose. Many of the trials of alendronate and other bisphosphonates compare the bisphosphonate in addition to calcium and Vitamin D at varying doses to the calcium and Vitamin D supplementation alone.
- ◆ No randomized controlled trials have compared alendronate/cholecalciferol (Fosavance) with both individual components. There is no evidence of synergistic effect on fracture prevention from alendronate/cholecalciferol (Fosavance) as compared with alendronate alone.
- ◆ The Committee is unaware of published evidence reporting that Vitamin D alone at a dose of 400 IU per day will affect the risk of clinically morbid fractures such as hip and vertebral fractures.
- ◆ The fixed dose combination of alendronate and cholecalciferol in Fosavance does not allow therapy to be individualized through dose titration of cholecalciferol. Supplementation with over-the-counter Vitamin D, which is available at many doses, is a convenient and inexpensive option.
- ◆ The CED also felt that there is a potential for medication errors if patients take extra Vitamin D as well as supplemental calcium. The WHI study (n=36,282 postmenopausal women) showed that Vitamin D 400IU daily added to calcium 1000 mg, increased the risk of renal stones by 17%. {Jackson RD et al. *NEJM* 2006; 354:669-83}
- ◆ The most common side effects with alendronate/cholecalciferol (Fosavance) are joint pain, bone pain and muscle pain.
- ◆ In October 2006, the price of generic alendronate 70mg was reduced to \$4.43, or \$17.70 per month, making it less expensive than alendronate/cholecalciferol (Fosavance).
- ◆ Overall, the Committee noted that alendronate/cholecalciferol (Fosavance) offers no therapeutic or economic advantages over generic alendronate. There is no evidence of a synergistic effect on fracture prevention from alendronate/cholecalciferol (Fosavance) compared with alendronate.

CEDAC Recommendation:

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

The Canadian Expert Drug Advisory Committee has recommended that alendronate/cholecalciferol (Fosavance) not be listed.



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