CEDAC FINAL RECOMMENDATION and REASONS for RECOMMENDATION

ALENDRONATE/CHOLECALCIFEROL
(Fosavance® 70/5600 – Merck Frosst Canada Ltd.)
Indication: Osteoporosis

Description:
Fosavance 70/5600 is a fixed dose combination of alendronate, a bisphosphonate that inhibits bone resorption, and cholecalciferol (vitamin D_3). Fosavance 70/5600 is approved by Health Canada for the treatment of osteoporosis in men and postmenopausal women. CEDAC previously reviewed Fosavance (referred to as Fosavance 70/2800 in this document), which contains alendronate 70 mg and 70 µg cholecalciferol, and recommended that it not be listed (see Fosavance Notice of CEDAC Final Recommendation on September 27, 2006).

Dosage Forms:
Supplied as tablets containing alendronate 70 mg and cholecalciferol 140 µg (5600 IU vitamin D_3). The recommended dose is one tablet taken once weekly.

Recommendation:
The Canadian Expert Drug Advisory Committee (CEDAC) recommends that Fosavance 70/5600 be listed similar to generic alendronate.

Reasons for the Recommendation:
1. Fosavance 70/5600 offers no advantage over generic alendronate since there is no evidence that it improves clinically important outcomes such as bone fractures in patients with osteoporosis.
2. The manufacturer has requested that the submitted price of Fosavance 70/5600 remain confidential pursuant to the Confidentiality Guidelines of the Common Drug Review. The price submitted by the manufacturer was an important consideration in the Committee making the recommendation. The price of Fosavance 70/5600 is [redacted] the cost of generic alendronate and [redacted] the cost of Fosavance 70/2800.
3. Fosavance 70/5600 provides a weekly dose of cholecalciferol (equivalent to 800 IU vitamin D daily) consistent with national recommendations on vitamin D dosing for osteoporosis prevention.

Summary of Committee Considerations:
The Committee considered the results of two bioequivalence studies, P226 and P253, and the results of a 24-week extension phase of Study 227 (N=652). In Study P226, 70 mg alendronate was compared with

70 mg alendronate co-administered with 70 µg cholecalciferol; in Study P253, 70 mg alendronate was compared with 70 mg alendronate co-administered with 140 µg cholecalciferol.

Fosavance 70/5600 met Health Canada requirements for establishing bioequivalence to its individual components based on the results of Study P226 and Study P253.

In Study P227, a 15 week trial which compared the combination of Fosavance 70/2800 to alendronate 70 mg, patients were re-randomized to either Fosavance 70/2800 plus placebo or Fosavance 70/2800 plus 70 µg cholecalciferol in a 24 week extension phase. The primary outcome measure for the extension phase was the proportion of patients with hypercalciuria. The extension study demonstrated a significant reduction in the risk of vitamin D_3 insufficiency (when defined as a serum vitamin D_3 level < 20 ng/mL) in older patients with osteoporosis receiving the total dose of vitamin D_3 5600 IU but was too short to assess clinically important outcomes such as fracture risk.

Fosavance 70/5600 provides a greater dose of vitamin D_3 compared with Fosavance 70/2800, which contains only 400 IU daily of vitamin D_3. Fosavance 70/5600 provides 800 IU daily of vitamin D_3 which is consistent with the current national guidelines on vitamin D for the prevention of osteoporosis.

Fosavance 70/5600 has a [redacted] price of [redacted] per tablet which is [redacted] the cost of generic alendronate ($4.43) and [redacted] the price of Fosavance 70/2800 ($9.76).

Of Note:

1. Both published and unpublished data were reviewed and taken into consideration in making this recommendation.
2. This document has been edited to remove confidential information at the manufacturer's request in conformity with the CDR Confidentiality Guidelines.

Background:

CEDAC provides formulary listing recommendations to publicly funded drug plans. Recommendations are based on an evidence-based review of the medication's effectiveness and safety and an assessment of its cost-effectiveness in comparison to other available treatment options. For example, if a new medication is more expensive than other treatments, the Committee considers whether any advantages of the new medication justify the higher price. If the recommendation is not to list a drug, the Committee has concerns regarding the balance between benefit and harm for the medication, and/or concerns about whether the medication provides good value for public drug plans.

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