Appendix 1: Data about reduction of fracture risk, Health Canada indications and Alberta Blue Cross eligibility criteria for the use of bisphosphonates in the treatment of postmenopausal osteoporosis

Etidronate/calcium

The data supporting the use of etidronate to treat osteoporosis in postmenopausal women are largely based on 2 relatively small studies (by current standards) with limited power to demonstrate a reduction in the risk of fracture.1–3 In neither study did the use of etidronate lead to significant reductions in vertebral fracture rates over a 3-year treatment period. The US Food and Drug Administration (FDA) considered the data insufficient, so etidronate was not approved for osteoporosis therapy in the United States.4,5 Through subgroup analysis in one study, it was shown that a high-risk subset of postmenopausal women had a statistically significant reduction in fracture risk.3–5 The FDA also rejected this analysis because it was done post hoc.4,5 Health Canada did not accept the drug for general use in treating postmenopausal osteoporosis but chose to approve etidronate/calcium for the specific and select group of postmenopausal women defined by the subgroup analysis.5 The Health Canada indication for the treatment of postmenopausal osteoporosis with etidronate/calcium is as follows:

“For the treatment of established postmenopausal osteoporosis diagnosed by means of objective measuring techniques such as bone densitometry (a bone mineral density of more than 2.67 standard deviations below the young adult mean) or by radiographic evaluation of the spine (> 2 vertebral fractures) in women at least 8 years postmenopause.”6

Subsequent studies of cyclical etidronate for the treatment of postmenopausal osteoporosis have also failed to demonstrate a reduction of vertebral fractures over 3 years.7–10 No study of etidronate/calcium has been of sufficient size to assess the effect of treatment on hip fractures. A recent meta-analysis of 7 etidronate trials (including both the treatment and prevention of postmenopausal osteoporosis) found no effect on nonvertebral fractures.10

There are no restrictions of the coverage of etidronate/calcium under the Alberta Prescription Drug Program.

Alendronate

Clinical studies with alendronate included much larger numbers of subjects, so the power to detect a reduction in the rate of fracture was substantially increased. Alendronate has been shown to reduce fracture rates in the vertebrae, hip and wrist by about 50%.11–13 It has also been shown to reduce painful fracture episodes, the number of days of bedrest, prolonged bedrest and the number of days of limited activity.14 Because of this larger body of efficacy data, evidence-based reviews of bisphosphonates favour alendronate over etidronate.15–18 In Canada, the approved indications for the use of alendronate in the treatment of postmenopausal osteoporosis are much broader than for etidronate/calcium, with fewer restrictions, and include:

"the treatment ... of osteoporosis in postmenopausal women.... Osteoporosis may be confirmed by the finding of low bone mass (e.g. at least 2.0 standard deviations below the premenopausal mean) or by the presence or history of osteoporotic fracture.”19

There exists a specific population of women who would meet the Health Canada indications for alendronate, but not the criteria for etidronate. This includes the following women:

- with a bone density T-score between −2.0 and −2.67 standard deviations (SD) of the
Eligibility criteria for alendronate under the Alberta Blue Cross formulary are as follows:

“For the treatment of osteoporosis in patients who have documented hip, vertebral or other fractures. Special authorization is granted to a maximum of twelve months. The patient would go on to etidronate/calcium therapy at the beginning of the second year.

For the treatment of osteoporosis in patients with documented evidence of intolerance or lack of response to etidronate (i.e. demonstrated as a > 2% loss in bone mineral density in one year).”

The first criterion is relevant to the discussion in this paper. It mandates switching a patient from alendronate to etidronate/calcium, even if the patient meets Health Canada criteria for alendronate but not for etidronate/calcium.

Risedronate

Risedronate is the most recently available bisphosphonate. It has been shown to reduce the rate of vertebral fractures by at least 50% and to reduce hip fractures by 40%.21–23

Health Canada indications for risedronate include the treatment of postmenopausal osteoporosis when “[o]steoporosis may be confirmed by the presence or history of osteoporotic fracture, or by the finding of low bone mass (for example, at least 2 SD below the premenopausal mean).”

The eligibility criteria under Alberta Blue Cross formulary coverage are identical to the criteria for alendronate.25 Because both the Health Canada indications and Alberta Blue Cross eligibility criteria are virtually identical for the use of risedronate and for the use of alendronate, the same situation is created for a person with a history of fracture who is prescribed either of these medications. Risedronate and alendronate will be reimbursed for only one year, then must be changed to etidronate/calcium, even if the patient does not meet Health Canada indications for the use of etidronate/calcium.

References


