

3 December 2009

## Proposal to amend the alendronate Special Authority

### *Proposal summary*

PHARMAC is seeking feedback on a proposal to amend the Alendronate for Osteoporosis Special Authority applying to alendronate +/- cholecalciferol (Fosamax and Fosamax Plus).

The proposed amendment would clarify that T-Scores must be derived using dual-energy x-ray absorptiometry (DXA). It is proposed that the Special Authority be amended from 1 April 2010.

Further details of the proposal and background information can be found below and on the following pages.

### *Feedback sought*

PHARMAC welcomes feedback on this proposal. To provide feedback, please submit it in writing by **4 pm on Thursday 11 February 2010** to:

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All feedback received before the closing date will be considered by PHARMAC's Board (or Chief Executive acting under delegated authority) prior to making a decision on this proposal.

### *The details of the proposal*

It is proposed that from 1 April 2010 the Alendronate for Osteoporosis Special Authority for subsidy for alendronate sodium tab 70 mg (Fosamax) and alendronate sodium tab 70 mg with cholecalciferol 2800 iu or 5600 iu (Fosamax Plus) in Section B of the Pharmaceutical Schedule is amended as follows (additions in bold, deletions in strikethrough):

Initial application – (Underlying cause - Osteoporosis) from any relevant practitioner. Approvals valid without further renewal unless notified for applications meeting the following criteria:

Any of the following:

- 1 History of one significant osteoporotic fracture demonstrated radiologically and documented bone mass density (BMD)  $\geq 2.5$  standard deviations below the mean normal value in young adults (i.e. T-Score  $\leq -2.5$ ) (**see Note**); or
- 2 History of one significant osteoporotic fracture demonstrated radiologically, and either the patient is elderly, or densitometry scanning cannot be performed because of major logistical, technical or pathophysiological reasons. It is unlikely that this provision would apply to many patients under 75 years of age; or

- 3 History of two significant osteoporotic fractures demonstrated radiologically;  
or
- 4 Documented T-Score  $\leq -3.0$  (**see Note**); or
- 5 A 10-year risk of hip fracture  $\geq 3\%$ , calculated using a published risk assessment algorithm (e.g. FRAX or Dubbo) which incorporates BMD measurements (**see Note**).

Initial application – (Underlying cause - glucocorticosteroid therapy) from any relevant practitioner. Approvals valid for 1 year for applications meeting the following criteria:

Both:

- 1 The patient is receiving systemic glucocorticosteroid therapy ( $\geq 5$  mg per day prednisone equivalents) and has already received or is expected to receive therapy for at least three months; and
- 2 Either:
  - 2.1 The patient has documented BMD  $\geq 1.5$  standard deviations below the mean normal value in young adults (i.e. T-Score  $\leq -1.5$ ) (**see Note**); or
  - 2.2 The patient has a history of one significant osteoporotic fracture demonstrated radiologically.

Renewal – (Underlying cause was, and remains, glucocorticosteroid therapy) from any relevant practitioner. Approvals valid for 1 year where the patient is continuing systemic glucocorticosteroid therapy ( $\geq 5$  mg per day prednisone equivalents).

Renewal – (Underlying cause was glucocorticosteroid therapy but patient now meets the 'Underlying cause – osteoporosis' criteria) from any relevant practitioner. Approvals valid without further renewal unless notified for applications meeting the following criteria:

Any of the following:

- 1 History of one significant osteoporotic fracture demonstrated radiologically and documented bone mass density (BMD)  $\geq 2.5$  standard deviations below the mean normal value in young adults (i.e. T-Score  $\leq -2.5$ ) (**see Note**); or
- 2 History of one significant osteoporotic fracture demonstrated radiologically, and either the patient is elderly, or densitometry scanning cannot be performed because of major logistical, technical or pathophysiological reasons. It is unlikely that this provision would apply to many patients under 75 years of age; or
- 3 History of two significant osteoporotic fractures demonstrated radiologically;  
or
- 4 Documented T-Score  $\leq -3.0$  (**see Note**); or
- 5 A 10-year risk of hip fracture  $\geq 3\%$ , calculated using a published risk assessment algorithm (e.g. FRAX or Dubbo) which incorporates BMD measurements (**see Note**).

Notes:

**a) T-Score must be derived using dual-energy x-ray absorptiometry (DXA). Quantitative ultrasound and quantitative computed tomography (QCT) are not acceptable.**

**a) b)** Evidence used by National Institute for Health and Clinical Excellence (NICE) guidance indicates that patients aged 75 years and over who have a history of significant osteoporotic fracture demonstrated radiologically are very likely to have a T-Score  $\leq -2.5$ , and therefore do not require BMD measurement for treatment with bisphosphonates.

**b) c)** Osteoporotic fractures are the incident events for severe (established) osteoporosis, and can be defined using the WHO definitions of osteoporosis and fragility fracture. The WHO defines severe (established) osteoporosis as a T-score below  $-2.5$  with one or more associated fragility fractures. Fragility fractures are fractures that occur as a result of mechanical forces that would not ordinarily cause

fracture (minimal trauma). The WHO has quantified this as forces equivalent to a fall from a standing height or less.

⇒ **d)** In line with the Australian guidelines for funding alendronate, a vertebral fracture is defined as a 20% or greater reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body, or a 20% or greater reduction in any of these heights compared to the vertebral body above or below the affected vertebral body.

### **Background information**

The above changes were recommended by the Osteoporosis Subcommittee of the Pharmacology and Therapeutics Advisory Committee (PTAC) at its August 2009 meeting. The relevant excerpt from the minutes of that meeting is as follows:

#### **Bone density scanning**

- 3.1 The Subcommittee reviewed a request for advice from PHARMAC staff around the suitability of quantitative ultrasound to derive T-scores to satisfy the requirements of the alendronate Special Authority restrictions. The Subcommittee noted that this request had arisen from a query from a supplier of [ withheld under s9(2)(a) of the OIA ].
- 3.2 The Subcommittee considered that ultrasound was not an acceptable means to derive T-scores in order to meet the requirements for subsidised alendronate treatment, for the following reasons:
  - Ultrasound does not directly measure bone density;
  - The relationship between ultrasound measurements and the relevant variables (i.e. fracture risk and response to alendronate) is not well established and has not been validated in large clinical trials;
  - Ultrasound measurements are associated with considerable variability, including equipment-related, operator-related and temperature-related variability, and standardisation of measurements is problematic in a real-world setting;
  - Age-related changes in heel ultrasound measurements do not correlate well with age-related hip and spine bone density changes; and
  - Ultrasound bone density measurements are not used in standard fracture risk algorithms.
- 3.3 The Subcommittee noted that results of a meta-analysis (Nayak et al. Ann Intern Med 2006;144:832-841) suggest that results of quantitative ultrasound do not correlate well with dual-energy x-ray absorptiometry (DXA)-determined osteoporotic measures.
- 3.4 The Subcommittee considered that there were similar problems with the use of quantitative computed tomography (QCT) with respect to its use to derive T-scores to satisfy alendronate funding requirements.

The Subcommittee's minutes were noted and accepted by PTAC at its November 2009 meeting.