Osteoporosis Subcommittee of PTAC meeting held 25 August 2009

(minutes for web publishing)

Osteoporosis Subcommittee minutes are published in accordance with the *Terms of Reference for the Pharmacology and Therapeutics Advisory Committee (PTAC) and PTAC Subcommittees 2008*.

Note that this document is not necessarily a complete record of the Osteoporosis Subcommittee meeting; only the relevant portions of the minutes relating to Osteoporosis Subcommittee discussions about an application that contain a recommendation are published.

The Osteoporosis Subcommittee may:

(a) recommend that a pharmaceutical be listed by PHARMAC on the Pharmaceutical Schedule and the priority it gives to such a listing;
(b) defer a final recommendation, and give reasons for the deferral (such as the supply of further information) and what is required before further review; or
(c) recommend that PHARMAC decline to list a pharmaceutical on the Pharmaceutical Schedule.

Some material has been withheld, in accordance with the Official Information Act 1982 (OIA), in order to protect the privacy of natural persons (section 9(2)(a)).

Contents

1 Bone density scanning

1.1 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 a [withheld under s9(2)(a) of the OIA].

1.2 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.

1.3 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.

1.4 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.

1.5 Accordingly, the Subcommittee **recommended** that the Special Authority criteria for alendronate be 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) ≥ 2.5 standard deviations below the mean normal value in young adults (i.e. T-Score ≤ -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 ≤ -3.0 **(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 glucocorticosteriod therapy (≥ 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 ≥ 1.5 standard deviations below the mean normal value in young adults (i.e. T-Score ≤ -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 glucocorticosteriod therapy (≥ 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) ≥ 2.5 standard deviations below the mean normal value in young adults (i.e. T-Score ≤ -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 ≤ -3.0 **(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 ≤ -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.
~~c)~~ **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.

2 Alendronate Special Authority criteria

2.1 The Subcommittee noted that PHARMAC had recently consulted on widening access to alendronate to include patients with a 10-year risk of hip fracture $\geq$ 3%, according to a previous recommendation by the Subcommittee. The Subcommittee noted that PHARMAC had received feedback during consultation which suggested that the criterion was too loose and would be associated with significant financial risk, and clinical risk from inappropriate alendronate use, and that PHARMAC staff wished to seek the advice of the Subcommittee on this matter.

2.2 The Subcommittee considered that the financial and clinical risks could be reduced by specifying that the fracture risk should be calculated using published risk assessment algorithms (e.g. FRAX and Dubbo) which incorporate bone mineral density measurements, and **recommended** that this change to the proposed criterion be made.

2.3 The Subcommittee reiterated its previous view that there was a group of patients with a high risk of hip fracture (identified by FRAX and Dubbo) who would benefit from alendronate treatment but who are not captured by the current criteria (mainly due to there being no means of accurately identifying these patients when the criteria were first devised). The Subcommittee considered that it was difficult to accurately estimate how large this group of patients would be, although members felt that the financial risk would be relatively low if the recommended changes to the criterion were implemented.

2.4 Members considered that it would of interest to perform a cost effectiveness analysis of alendronate in this patient group, potentially by adapting international cost-utility analyses (e.g. Tosteson et al. Osteoporosis Int 2008;19(4):437-447 and Dawson-Hughes et al. Osteoporosis Int 2008;19(4):449-458) to the New Zealand setting.