Osteoporosis Subcommittee of PTAC meeting

held 31 March 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 meeting; only the Minutes relating to Osteoporosis discussions about an application that contain a recommendation in relation to an application 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.

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1 Zoledronic Acid

1.1 The Subcommittee noted that PHARMAC had received applications from Novartis for the funding of zoledronic acid for the treatment of Paget's disease and as a second-line treatment for osteoporosis. The Subcommittee noted that these applications were reviewed by PTAC in July 2008 and that Novartis had subsequently provided a commercial proposal for zoledronic acid as a first-line bisphosphonate treatment for osteoporosis (i.e. as an alternative to alendronate).

Zoledronic acid for Paget's disease

1.2 The Subcommittee considered that zoledronic acid was the preferred treatment for Paget's disease, and agreed with PTAC's recommendation to list zoledronic acid for this indication with a high priority.

1.3 The Subcommittee considered that all patients with Paget's disease would switch from alendronate to zoledronic acid if it was funded.

1.4 The Subcommittee reviewed the Special Authority criteria proposed by the supplier (Novartis) and proposed the following changes (deletion in strikethrough, additions in bold):

> Initial application **(Paget's disease)** ~~only from a relevant specialist~~ **from any relevant practitioner**. Approvals valid for a single infusion for applications meeting the following criteria. Both:
> 1 Paget's disease; and
> 2 Any of the following:
> 2.1 Bone or articular pain; or
> 2.2 Bone deformity; or
> 2.3 Bone, articular or neurological complications; or
> 2.4 Asymptomatic disease, but risk of complications~~ due to site (base of skull, spine, long bones of lower limbs)~~; or
> 2.5 Preparation for orthopaedic surgery.
> Renewal only from a relevant specialist. Approvals valid for a single infusion where the treatment remains appropriate and the patient is benefiting from treatment.

Zoledronic acid for first-line bisphosphonate treatment of osteoporosis

1.5 The Subcommittee considered that there was an unmet clinical need in patients for whom currently funded treatments were unsuitable or ineffective due to compliance difficulties or intolerance.

1.6 The Subcommittee noted that there were few head-to-head trials comparing the efficacy of zoledronic acid with alendronate. Members noted the practical difficulties associated with conducting such trials given the differences in dosing and administration regimens.

1.7 Subcommittee members considered that, based on their understanding of the literature in support of each agent as first-line bisphosphonate treatment for osteoporosis (which was not reviewed at the meeting), zoledronic acid appeared to provide similar or superior efficacy to alendronate.

1.8 The Subcommittee considered that the side effect profile of zoledronic acid appeared favourable, noting that there was less gastrointestinal side effects with zoledronic acid compared with alendronate. The Subcommittee noted that there was less longer-term data with zoledronic acid compared with alendronate, but that there was good 3-year data. The Subcommittee noted that 6-year and 9-year follow-up data would be available in due course.

1.9 The Subcommittee noted that lack of compliance with alendronate therapy was a major problem, and that in members' experience up to half of patients who are initiated on alendronate have stopped taking it a year later. Members noted that this was particularly a problem for patients with dementia who do not have their medication delivery supervised. The Subcommittee noted that patients with dementia were at particularly high risk of falls and fractures.

1.10 The Subcommittee considered that if zoledronic acid was funded as a first-line option it could be used in place of alendronate in up to 60%–70% of cases, although members noted that the likely usage was difficult to accurately estimate and could be lower than this. The Subcommittee considered that most (~90%) patients who discontinued alendronate because of intolerable side effects or lack of efficacy due to non adherence would be likely to try zoledronic acid. The Subcommittee considered that discontinuation of alendronate due to lack of efficacy unrelated to non compliance would be rare. The Subcommittee also considered that some patients (approximately 10%) may prefer tablets over an infusion, especially those patients who have a fear of needles.

1.11 The Subcommittee noted that zoledronic acid was associated with infusion reactions in some patients, but this was usually minimised by administration of ibuprofen or paracetamol after the infusion.

1.12 The Subcommittee considered that zoledronic acid should be viewed as a community medicine and not just a hospital pharmaceutical, noting that the majority of General Practice surgeries would be capable of delivering the intravenous infusion, and that rural GPs would be more likely to be equipped to provide such a service. However, members noted that many surgeries may choose not to provide this service due to resourcing or financial constraints. The Subcommittee considered that delivery of zoledronic acid would take up about 30 minutes of nursing time, which would rarely require prescriber input.

1.13 Members considered that there is currently significant inequity of access to treatment with zoledronic acid throughout the country, with some DHB hospitals choosing not to fund zoledronic acid. However, members were concerned that the provision of zoledronic acid by General Practitioners may also create access difficulties due to the additional cost to the patient of the General Practitioner visit. The Subcommittee considered that it was likely an additional fee would be associated with the consultation and infusion, which could be a barrier to treatment for those on low incomes.

1.14 The Subcommittee considered that if zoledronic acid was listed as a first-line option it should be funded subject to the same Special Authority restrictions as alendronate.

1.15 The Subcommittee **recommended** that zoledronic acid be funded as a first-line bisposphonate treatment for osteoporosis if it was cost-neutral versus alendronate. The Decision Criteria particularly relevant to this recommendation are: (i) The health needs of all eligible people within New Zealand; (iii) The availability and suitability of existing medicines, therapeutic medical devices and related products and related things; (iv) The clinical benefits and risks of pharmaceuticals; and (v) The cost-effectiveness of meeting health needs by funding pharmaceuticals rather than using other publicly funded health and disability support services.

Zoledronic acid as a second-line treatment for osteoporosis following oral bisphosphonates

1.16 The Subcommittee considered that it would not be unreasonable to limit funding of zoledronic acid to patients who were intolerant to oral bisphosphonate therapy if there was a substantial price differential, and agreed with PTAC's recommendation to list zoledronic acid for this indication with a medium-high priority (in the context of all pharmaceuticals currently under consideration for funding).

1.17 The Subcommittee reviewed the Special Authority criteria proposed by the supplier (Novartis) and proposed the following changes (deletion in strikethrough, additions in bold):

Initial application (~~Postmenopausal~~ Osteoporosis) ~~only from a relevant specialist or vocationally registered general practitioner~~. **from any relevant practitioner.** Approvals valid without further renewal unless notified for applications meeting the following criteria:

1 Patient intolerant to oral bisphosphonate therapy (alendronate or etidronate); and

2 Any of the following:

- 2.1 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); or
- 2.2 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
- 2.3 History of two significant osteoporotic fractures demonstrated radiologically; or
- 2.4 Documented T-Score ≤ -3.0.

1.18 The Subcommittee considered that if zoledronic acid was funded under the above proposed criteria, approximately 40% of patients would move off alendronate or etidronate onto zoledronic acid. The Subcommittee noted that this figure was higher than the ~10% of patients who would be clinically intolerant to oral bisphosphonates; however, due to the difficulties in taking oral

bisphosphonate therapy (particularly alendronate), it was likely that more patients would claim intolerance or would refuse to take alendronate and would be classed as intolerant to therapy with alendronate.