Endocrinology Subcommittee of PTAC
Meeting held 17 June 2014

(minutes for web publishing)

Endocrinology 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 Endocrinology Subcommittee meeting; only the relevant portions of the minutes relating to Endocrinology Subcommittee discussions about an Application or PHARMAC staff proposal that contain a recommendation are generally published.

The Endocrinology 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.

These Subcommittee minutes were reviewed by PTAC at its meeting on 6 & 7 November 2014 and are now available on the PHARMAC website.

1 Matters arising

Cinacalcet

1.1 The Subcommittee noted correspondence from The New Zealand Society of Endocrinology who, following a PTAC meeting in May 2012, were asked to submit evidence for consideration that supports prescribing cinacalcet for Primary Hyperparathyroidism (PHPT). The Subcommittee noted that the opinion from the New Zealand Society of Endocrinology was that cinacalcet could be available for patients with PHPT who have significant/symptomatic hypercalcemia (>3mmol/L) and can't be treated surgically, and for a trial of palliation for patients with parathyroid carcinoma. The Subcommittee noted that the opinion from the New Zealand Society of Endocrinology was that there would be very few patients who would meet these criteria nationally and did not consider that there were any other indications where treatment with cinacalcet was necessary.

1.2 The Subcommittee noted the fairly recent EVOLVE trials in 2012 and 2013 using cinacalcet for the treatment of secondary hyperparathyroidism did not offer hard data outcomes. The Subcommittee considered that there should be a treatment option available for patients where surgery is not an option.

1.3 The Subcommittee considered that a Special Authority could be developed for Endocrinologists and Renal Physicians to prescribe cinacalcet for severe unremitting secondary hyperparathyroidism with the following criteria:

i. Patient has severe unremitting secondary hyperparathyroidism not successfully treated surgically **or**
ii. Patient has calciphylaxsis **or**
iii. Patient has severe bone pain not amenable to pain relief **and**
iv. Patient's serum calcium level is ≥ 3 mmols

1.4 The Subcommittee **recommended** that cinacalcet is funded in the HML, restricted to endocrinologists and renal physicians using the above criteria.

2 Therapeutic group review update

Corticosteroids and Related Agents for Systemic Use

Prednisolone Sodium Phosphate

2.1 The Subcommittee noted that the Special Authority (SA) restriction had not yet been removed from the prednisolone sodium phosphate oral listing. The Subcommittee considered that there would not be a financial risk due to increased patient numbers with the removal of the restriction

2.2 The Subcommittee considered that the 30 ml prednisolone sodium phosphate presentation was the appropriate size to fund versus the 100 ml presentation.

2.3 The Subcommittee **recommended** that the Special Authority restriction is removed for prednisolone sodium phosphate but that the impact of removing the Special Authority restriction is monitored.

Hormone Replacement Therapy (HRT)

Progesterone

2.4 The Subcommittee noted that progesterone capsules are now fully funded under Special Authority for subsidy for the prevention of pre-term labour. The Subcommittee considered that micronised progesterone remains the safest and optimal form of progesterone to prescribe as HRT.

2.5 The Subcommittee noted that there are relatively newly published randomized control trials with regards to HRT, using micronised progesterone as the progestogen. The Subcommittee further considered that in the trials there is a consistent finding of more beneficial effects from either progesterone or dydrogesterone as the progestogen in HRT medicines.

2.6 The Subcommittee **recommended** that the application to list progesterone for hormone replacement therapy be taken back to PTAC with the newly published trials for reconsideration.

Trophic Hormones

LAR Octreotide Acetate

2.7 The Subcommittee noted that there are a few smaller studies supporting the use of LAR octreotide acetate to treat patients with acromegaly in preparation for pituitary surgery. The Subcommittee noted that the pre-treatment was indicated mainly for large tumours, with the greatest effect after the first two treatments.

2.8 The Subcommittee **recommended** the Special Authority is changed for LAR octreotide acetate to include the indication of patients with acromegaly who have large pituitary tumours, to use pre-operatively in preparation for pituitary surgery.

Drugs Affecting Bone Metabolism

Strontium ranelate

2.9 The Subcommittee noted that the European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC) issued a recommendation in January 2014 that strontium ranelate should no longer be used to treat osteoporosis due to an unfavourable risk: benefit profile. In particular, the PRAC highlighted the cardiovascular risks (including heart attacks and blood clots) as well as serious skin reactions, disturbances in consciousness, seizures, liver inflammation and reduced number of blood cells. The benefits of strontium ranelate were described by the PRAC as modest.

2.10 The Subcommittee **recommended** that the funding application for strontium ranelate be declined. The Subcommittee considered that the cardiovascular risks outweighed the modest clinical benefit and considered that PHARMAC should no longer be considering strontium ranelate for funding.

2.11 Members noted that in addition to the cardiovascular risks it was difficult to assess the effect of strontium ranelate on bone density because it replaces calcium in the bone matrix which interferes with bone density measurements.

Ibandronate

2.12 The Subcommittee considered that, broadly speaking, ibandronate provided a similar clinical benefit to other potent bisphosphonates (alendronate, risedronate and zoledronic acid), although members considered that the evidence base was stronger for the other treatments. Members noted the 2012 update of a 2007 report from the Agency for Healthcare Research and Quality (AHRQ) in the US, which reviewed the safety and efficacy of osteoporosis treatments.

2.13 The Subcommittee considered that it could be useful to have access to a once-monthly treatment, although members considered that this was unlikely to increase compliance or have any impact on clinical outcomes.

2.14 The Subcommittee considered that there was no current unmet clinical need that could be met by funding ibandronate.

2.15 The Subcommittee **recommended** that ibandronate be funded only if it was no more expensive than the least expensive funded oral bisphosphonate.

Denosumab

2.16 The Subcommittee noted that in May 2012 PTAC considered a funding application for denosumab (Prolia) as a second-line treatment of osteoporosis in postmenopausal women following bisphosphonate treatment failure or where bisphosphonates are contraindicated. PTAC recommended that the application be declined pending further information about the long-term safety of treatment with denosumab.

2.17 The Subcommittee noted that the safety and efficacy data for denosumab now extended to six to seven years, also noting that this was longer than the available data when zoledronic acid and alendronate were funded.

2.18 The Subcommittee noted that some key patient groups of interest for denosumab treatment were:

- young women with amenorrhoea, eating disorders and other bone disorders;
- patients who are intolerant to bisphosphonates;
- patients in whom bisphosphonates are not recommended (e.g. patients with renal impairment); and
- patients who have completed a course of teriparatide (as an alternative to recommencing bisphosphonate treatment).

2.19 The Subcommittee noted that the main emerging safety risks were infections and cancer risk; however, members considered that these risks appeared low.

2.20 The Subcommittee noted that one potential disadvantage of denosumab was the lack of ongoing benefit once treatment is stopped, compared with zoledronic acid which provides several years of protection after treatment is stopped.

2.21 The Subcommittee considered that there was some evidence to suggest that denosumab increased the efficacy of bisphosphonates by approximately 10% when used in combination.

2.22 The Subcommittee requested that PTAC re-review denosumab in light of the availability of longer-term data.

Zoledronic acid

2.23 The Subcommittee noted that one of the funded indications for zoledronic acid inj 0.05 mg per ml, 100 ml vial (Aclasta) on the HML was osteogenesis imperfecta.

2.24 The Subcommittee considered that there was a very small number of patients with other rare inherited bone fragility disorders such as osteoporosis pseudoglioma syndrome, McCune-Albright syndrome and some metabolic bone disorders (e.g. the mucolipidoses), who could benefit from zoledronic acid but who are potentially missing out on treatment because of the way the restriction is worded.

2.25 The Subcommittee **recommended** that the HML restrictions for this indication be amended as follows (deletions in strikethrough, additions in bold):

> ~~Osteogenesis imperfecta~~ **Inherited bone fragility disorders**
> Patient has been diagnosed with **an inherited bone fragility disorder (e.g.** ~~clinical or genetic~~ osteogenesis imperfecta**)**

Vitamin D

2.26 The Subcommittee considered that there was an unmet clinical need for a funded orally available vitamin D preparation suitable for children, i.e. vitamin D oral liquid. The Subcommittee requested that PHARMAC staff investigate the possibility of listing an oral liquid formulation.