Endocrinology Subcommittee of PTAC
Meeting held 29 May 2012

(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 8 & 9 November 2012, the record of which will be available in January 2013.

Some material has been withheld, in accordance with the Official Information Act 1982 (OIA) in order to:

(i) enable PHARMAC to carry out, without prejudice or disadvantage, commercial activities (section 9(2)(i)); and/or
(ii) enable PHARMAC to carry on, without prejudice or disadvantage, negotiations, including commercial negotiations (section 9(2)(j));

1 Previous recommendations/action points

The Osteoporosis Subcommittee, March 2009

1.1 The Subcommittee noted that the Special Authority criteria for alendronate has been amended to include "≥3% 10-year risk of hip fracture" as an additional criterion.

1.2 The Subcommittee noted that zolendronic acid was listed on the Pharmaceutical Schedule in September 2010 and teriparatide and raloxifene were listed in July 2011.

1.3 The Subcommittee noted that PHARMAC had been in discussions with the supplier of strontium but had been unable to reach at an agreement at this stage.

The Hormone and Contraceptive Subcommittee May 2009

1.4 The Subcommittee noted that prednisolone oral solution had been included in the 2010/2011 tender but the tender had not yet been awarded.

1.5 The Subcommittee noted that the long acting reversible contraceptive, levonorgestrel subdermal 2 x 75 mg implant (Jadelle), was listed on the Pharmaceutical Schedule in August 2010 and propylthiouracil (PTU) was listed in May 2012, clomiphene citrate has been retained on the Pharmaceutical Schedule and the Special Authority for goserelin was removed in August 2009.

2 Therapeutic group review

Endocrinology preparations

2.1 The Subcommittee noted the review of funded endocrine pharmaceuticals provided by PHARMAC staff. The Subcommittee noted that expenditure in this group is relatively stable and is forecast to decrease slightly over the next four years.

2.2 The Subcommittee noted that the use of prednisolone oral liquid was high compared to Australia and continues to grow. The Subcommittee noted the current restriction on prednisolone oral liquid to children under 12 years of age and considered the majority of use was for the first line treatment of asthma in children and considered that there was no clinical reason not to remove the restriction. The Subcommittee considered that, despite a small incremental increase in usage recently for oropharyngeal lesion, removing the restriction was unlikely to lead to an increase in usage of the product to treat asthma. The Subcommittee **recommended** removing the restriction from the prednisolone oral liquid listing.

2.3 The Subcommittee noted there had been a significant price increase in the triamcinolone acetonide injections. The Subcommittee considered that while triamcinolone acetonide is preferred over some other injectable corticosteroids particularly for use in paediatrics, methylprednisolone acetate (Depo-Medrol) and betamethasone sodium phosphate with betamethasone acetate (Celestone Chronodose) could be suitable alternatives. The Subcommittee **recommended** the question of a suitable alternative be referred to the

Rheumatologists. The Subcommittee noted that triamcinolone hexacetonide was preferred in paediatrics for intra-articular injection (because of lower dose frequency given the need for general anaesthesia).

2.4 The Subcommittee considered the removal of specialist restrictions from dexamethasone tablets, methylprednisolone tablets and methylprednisolone sodium succinate injections. The Subcommittee noted concerns about the correct dosing (dose equivalence) being prescribed, in particular with the 100 mg methylprednisolone tablets, and considered that an educational article in BPAC would be useful. The Subcommittee considered that the Retail pharmacy - Specialist restriction on these products should be removed and that the "Only on a PSO restriction" should be removed from hydrocortisone inj 50 mg per ml, 2 ml (Solu-Cortef).

2.5 The Subcommittee considered the removal of the Retail pharmacy – Specialist restriction on testosterone cypionate, esters and undecanoate. They expressed concern that, if the restriction were removed, there may be a small number of prescribers that may prescribe testosterone for appearance medicine or muscle building. The Subcommittee **recommended** PHARMAC seek the advice of the Endocrinology Society before changing the restriction.

2.6 The Subcommittee noted the recommendation for the listing of testosterone undecanoate injection from PTAC's November 2007 meeting and were given a verbal summary of the discussion at PTAC's May 2012 meeting. The Subcommittee considered that compliance is significantly better with the 12 weekly testosterone undecanoate injection compared to the 2 to 4 weekly testosterone esters injection and that the smoothness of the testosterone levels achieved with the undecanoate form is an advantage. The Subcommittee noted that compliance was sometimes an issue with the testosterone esters injections and that there tended to be an increase in adverse events with an increase in the number of injections.

2.7 The Subcommittee **recommended** that testosterone undecanoate injection be listed on the Pharmaceutical Schedule providing a satisfactory commercial arrangement could be reached. Alternatively the Subcommittee considered that listing testosterone undecanoate injection second line to testosterone esters injection would be acceptable.

2.8 The Subcommittee noted that expenditure in the hormone replacement sub-group had decreased slightly [withheld under s 9(2)(i) and 9(2)(j) of the OIA] due to a price decrease for medroxyprogesterone acetate and that the number of prescriptions had remained steady over the past five years at around 140,000 per year. The Subcommittee noted that of the 44,500 patients currently being treated with hormone replacement therapy, approximately 50% are taking the fully funded medroxyprogesterone acetate and oestradiol valerate forms.

2.9 The Subcommittee noted that there were no fully funded oestrogen patches available on the Pharmaceutical Schedule but that full funding was available under Special Authority for a limited number of indications. The Subcommittee **recommended** that funding be widened to include obesity, hypertension, cardiovascular disorders, those at risk of stroke or clots, induction of puberty and premature menopause. The Subcommittee considered sole supply of an oestrogen patch would be appropriate providing it is a membrane patch.

2.10 The Subcommittee considered that combination patches are preferable for women with an intact uterus and for the estimated one in eight who have problems with tablets (side effects, remembering to take them etc). The Subcommittee **recommended** that the Society of Obstetricians and Gynaecology should submit an application for the listing of sequential and continuous combination patches. The tablet forms Kliovance (oestradiol and norethisterone) and Angeliq (drosperidone with oestradiol) could be considered as alternatives.

2.11 The Subcommittee noted that the only natural progesterone on the Pharmaceutical Schedule, Duphaston (dydrogesterone) had been discontinued by the supplier and **recommended** that, if possible, another natural progesterone be listed. It is important to note that increases in breast cancer risk have been reported with both medroxyprogesterone acetate and norethisterone. This risk appears to be absent or substantially less common with micronised progesterone and for safety reasons, micronized progesterone is the preferred option now.

2.12 The Subcommittee discussed the availability of the levonorgestrel intrauterine system, Mirena, and considered that the Special Authority should be widened to women in the age group 45 – 55 as an alternative treatment to hysterectomy.

2.13 The Subcommittee noted that propylthiouracil (PTU) was listed on the Pharmaceutical Schedule in May 2012 in response to the number of applications being received through the Named Patient Pharmaceutical Assessment pathway (NPPA). The Subcommittee noted that, following the notification of approval of the listing, PHARMAC had received correspondence outlining the FDA black box warning regarding the use of PTU in patients less than 18 years old and requesting that this be reflected in the Special authority criteria. The Subcommittee **recommended** adding the following criteria to the Special Authority:

> Either:
> The patient is over 18; or
> The patient is under 18 and pregnant.

2.14 The Subcommittee noted that liothyronine tablets continue to be supplied through NPPA and considered that remained an appropriate pathway due to the fact that the product is not registered and is considerably more expensive than levothyroxine. The Subcommittee considered automatic approval should be given to patients who have thyroid cancer; patients with an underlying problem with their metabolism of levothyroxine should also be considered; and, rarely, patients who are resistant to T4.

2.15 [withheld under s 9(2)(i) and 9(2)(j) of the OIA].

2.16 The Subcommittee noted correspondence from Dr Mike Croxson requesting the Subcommittee consider the use of cabergoline in the treatment of acromegaly. The Subcommittee noted that cabergoline is currently listed on the Pharmaceutical Schedule with a restriction of two tablets per prescription which can be waived if the application is made by an obstetrician, endocrinologist or gynaecologist for the treatment of pathological hyperprolactinemia. The Subcommittee noted that many acromegaly patients have increased prolactin levels and therefore could qualify under the current Special Authority criteria.

2.17 The Subcommittee considered the Meta-Analysis by Sandret et al (J Clin Endocrinol Metab 96: 1327-1335,2011) which suggested that cabergoline single-agent therapy normalises IGF-1 levels in one third of patients with acromegaly and that when a somatostatin analogue fails to control acromegaly, cabergoline adjunction normalises IGF-1 in about 50% of the cases. The Subcommittee noted that Sandret et al gave a strong recommendation for the use of cabergoline in the treatment of acromegaly on what the Subcommittee considered low quality evidence however, the Subcommittee considered that the Special Authority should be amended to include the treatment of acromegaly as there was no doubt that it worked in a third of patients depending on how high their IGF-1 levels were.

2.18 The Subcommittee considered whether there was any advantage in adding cabergoline to treatment with somatropin analogues. It was estimated that there are approximately 240 acromegaly patients in New Zealand of whom half have been cured by surgery. A further 40% of patients will be treated with somatropin analogues, leaving approximately 20 to 30 patients plus a further 2 to 3 new patients per year who may benefit from being treated with cabergoline.

2.19 The Subcommittee **recommended**, with a medium priority, changing the cabergoline Special Authority for waiver of the two tablet rule to read (changes in strike out and bold):

> Initial application only from an ~~obstetrician, endocrinologist, or gynaecologist~~ **relevant prescriber**. Approvals valid for two years without further renewal unless notified where the patient has pathological hyperprolactinemia **or acromegaly*.**
>
> **Note: Indications marked with * are Unapproved Indications.**

2.20 The Subcommittee noted the significant increase in expenditure and the number of prescriptions for clomiphene citrate following the removal of the Special Authority in June 2012 which had restricted use to the treatment of female patients only. The Subcommittee considered that clomiphene should only be used with strict monitoring and **recommended** that PHARMAC analyse the data to see why there had been such a significant increase in usage.

2.21 The Subcommittee noted the low use of danazol, gestrinone and metyrapone and the restrictions that applied to these products in Australia and that there are no restrictions on the use of danazol in the UK. The Subcommittee noted that these products are listed on the Pharmaceutical Schedule with a Retail pharmacy – Specialist restriction and recommended the Retail pharmacy – Special restriction be removed with a high priority.

2.22 The Subcommittee noted the expenditure and number of prescriptions for pharmaceuticals currently listed in the Drugs Affecting Bone Metabolism therapeutic subgroup and that funding applications for denosumab, risendronate and strontium are outstanding.

2.23 The Subcommittee noted that there is a gap in this therapeutic area in that currently listed products are not recommended for use in patients with a glomular filtration rate (GFR) of <35 mL/min. The Subcommittee noted that denosumab does not have that restriction is showing superiority in oncology settings with a recent approval by the FDA

for the treatment of prostate and breast cancer. The Subcommittee also noted that the Special Authority for zolendronic acid should be widened to allow for the treatment of children with inherited bone fragility disorders for example osteogenesis imperfecta. The Subcommittee estimated that there would be 30 children per annum who benefit from this treatment.