Endocrinology Subcommittee of PTAC
Meeting held 27 January 2016

(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 have yet to be ratified by PTAC and will be reviewed at its meeting on 5 & 6 May 2016.

Record of the Endocrinology Subcommittee of PTAC teleconference meeting on 27 January 2016

1. Potential Funding Arrangements for Leuprorelin and Goserelin

Recommendation

1.1. The Subcommittee **recommended** that PHARMAC issue a Request for Proposals (RFP) for the supply of a single gonadotropin-releasing hormone (GnRH) analogue, noting that it would be important to consider the suitability of the delivery mechanism for the range of indications, for both children and adults.

1.2. 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; (v) The cost-effectiveness of meeting health needs by funding pharmaceuticals rather than using other publicly funded health and disability support services; and (vi) The budgetary impact (in terms of the pharmaceutical budget and the Government's overall health budget) of any changes to the Pharmaceutical Schedule.*

Discussion

1.3. The Subcommittee noted a paper from PHARMAC staff regarding future funding arrangements for the gonadotrophin-releasing hormone (GnRH) analogues leuprorelin and goserelin.

1.4. The Subcommittee noted that PHARMAC staff were seeking feedback on:

1) the therapeutic equivalence of different brands of the same strengths of leuprorelin used to treat precocious puberty, endometriosis, uterine fibroids, and assisted reproduction, and;

2) the therapeutic equivalence of leuprorelin and goserelin to treat precocious puberty, endometriosis, uterine fibroids, and assisted reproduction.

1.5. The Subcommittee noted that GnRH analogues were also used in the treatment of breast and prostate cancer, which accounts for much of the $9.3 million expenditure of these analogues in both community and hospital settings. Members noted that the Cancer Treatments Subcommittee (CaTSoP) of PTAC had recently similarly reviewed potential funding arrangements for the two chemicals for the indications of breast cancer and prostate cancer.

1.6. The Subcommittee noted that there were no comparative studies of the two chemicals, leuprorelin acetate and goserelin acetate, in the treatment of precocious puberty. However, the Subcommittee considered that the two chemicals had a similar mode of action and could be expected to provide similar therapeutic effects in precocious puberty.

1.7. The Subcommittee considered that the majority of children received the 3-month presentation of leuprorelin for the treatment of precocious puberty, with the remainder using the 1-month presentation. The Subcommittee considered that a 6-month preparation was not clinically necessary for this indication.

1.8. [redacted]

[redacted]

1.9. The Subcommittee considered that there were other patient groups for whom the GnRH analogues were being prescribed including but not limited to, transgender youth, patients with menstrual related disorders and for preservation of fertility, prior to chemotherapy.

1.10. The Subcommittee noted a similar lack of comparative data between leuprorelin and goserelin for the treatment of endometriosis. However, the Subcommittee considered that given the two chemicals have the same mechanism of action they could be expected to provide the same or similar therapeutic effect for this indication. Members noted that available studies for this indication were for a period of 3 to 6 months; however, gynaecologists may use GnRH analogues to treat other indications such as pre-hysterectomy for up to 12 months. Members considered that access to the 1 and 3 month preparations of the GnRH analogues would be appropriate for the treatment of gynaecological indications and that it would not be clinically necessary for a 6-month preparation to be funded in these settings.

1.11. The Subcommittee noted that the only comparative study between leuprorelin and goserelin acetate they had been provided with was for the treatment uterine fibroids. The Subcommittee noted that this was the Lim et al study (Int J Gynecol Obstet 2008;101:178-183) comparing 4-weekly 3.6 mg goserlin acetate injection with 3.75 mg leuprorelin acetate in 68 patients pre-hysterectomy for uterine fibroids. The primary outcomes of the study were pre-operative haemoglobin, operative blood loss and operating time. The Subcommittee noted that the study authors concluded that there were no notable differences in the primary outcomes between the two groups.

1.12. The Subcommittee noted that the evidence for the use of GnRH analogues in assisted reproduction provided by PHARMAC staff was a Cochrane review that included only one study comparing GnRH agonists, (chiefly the analogues such as leuprorelin and goserelin) with GnRH antagonists. The Subcommittee considered that the review was not appropriate to draw conclusions from regarding the therapeutic equivalency of leuprorelin and goserelin in assisted reproduction. Members further considered that a number of GnRH antagonists were now being increasingly prescribed for assisted reproduction. Members considered that it may be of use to speak with a clinical expert in this field for further information about current GnRH prescribing habits.

1.13. The Subcommittee noted that there is a lack of data comparing different brands of leuprorelin for the indications of precocious puberty, endometriosis, uterine fibroids, and assisted reproduction. However, the Subcommittee considered that given that the mechanism of action is the same regardless of formulation, different brands of leuprorelin could be considered to provide the same or similar therapeutic effect across the same dosing frequencies (1-month, 3-month etc).

1.14. The Subcommittee noted that it would be preferable for the winning brand to provide evidence of efficacy for the endocrinology indications, noting that not all brands are registered for use in these indications. However, as noted above, members considered that all brands would likely provide the same or similar efficacy in these indications regardless of their registered indications. The Subcommittee considered that it would be reasonable to run a competitive process that would result in only one brand of funded leuprorelin for the indications of precocious puberty, endometriosis, uterine fibroids, and assisted reproduction.

1.15. The Subcommittee considered that the 1-month and 3-month preparations of a GnRH analogue were necessary to fund for the endocrinology indications discussed. Members further considered that the 6 month presentations were infrequently used to treat endocrinology indications at present and that not having access to this would be of little consequence in their practice.

1.16. The Subcommittee considered that patients being treated for precocious puberty may require additional monitoring if there was a brand or chemical switch. Members noted that

additional monitoring was usual clinical practice with dose changes when treating precocious puberty.

1.17. The Subcommittee considered that consideration needs to be given to the group of patients who experience problems with a change in drug formulation, whether real or perceived. Members considered that this was sometimes due to the difference in compound pharmacology. The Subcommittee considered that, as with brand switches for other pharmaceuticals, any change can potentially lead to a group of patients for whom formulation change is problematic. Members considered that, provided there was some mechanism available to seek funded access to an alternative treatment if necessary for patients within this subgroup, it would be reasonable to fund one chemical and one brand of GnRH analogue.

1.18. The Subcommittee considered that, on the basis that leuprorelin and goserelin can be expected to provide the same or similar therapeutic effect in the endocrinology indications, it would be clinically reasonable to apply reference pricing of leuprorelin to goserelin (or vice versa), or to run a competitive process that would result in only one of leuprorelin or goserelin being funded. [redacted]

1.19. The Subcommittee considered that, should a brand switch occur, the transition period would need to be a minimum of 6 months. The Subcommittee noted that any implementation activity around a brand change would need to include endocrinology nursing staff and paediatric community nurses as well as prescribers.