February 2006: PTAC minutes for web publishing

PTAC minutes are published in accordance with the following definitions from the PTAC Guidelines 2002:

““Minute” means that part of the record of a PTAC or Sub-committee meeting (including meetings by teleconference and recommendations made by other means of communication) that contains a recommendation to accept or decline an application for a new investment or a clinical proposal to widen access and related discussion.”

Reference pricing of topical corticosteroids

The Committee considered concerns from Schering (NZ) Limited regarding the classification of diflucortolone valerate 0.1% and betamethasone valerate 0.1% in the topical corticosteroids moderate strength therapeutic subgroup.

The Committee considered that there was no evidence suggesting that diflucortolone valerate 0.1% should not be in the same therapeutic subgroup as betamethasone valerate 0.1% and it considered that it is appropriate to have them in the same therapeutic subgroup.

The Committee considered that there is a demand to have a fatty base for some patients and that it is desirable to have a variety of bases available. However, Members also considered that a fatty base might be less well tolerated, and that it might be more allergenic.

The Committee **recommended** that no changes to the topical corticosteroid moderate strength subgroup occur. However, the Committee considered that it might be appropriate to include hydrocortisone butyrate 0.1% in the moderate strength subgroup.

ACE Inhibitors (cough/re-cough trial)

The Committee considered an application from PHARMAC staff to alter the Special Authority criteria for angiotensin II antagonists. The Committee noted that PHARMAC staff are seeking advice on the Special Authority requirement that a patient trial two ACE inhibitors, and develop intolerance due to cough to both, before being eligible for access to either of the angiotensin II antagonists, candesartan or losartan.

The Committee considered that the chronic cough associated with ACE inhibitors was a class effect. The Committee noted that there was little evidence to suggest that there was a difference in chronic cough side effect profile between any of the ACE inhibitors currently listed on the Pharmaceutical Schedule. Only a minority of patients could be successfully converted to a different ACE inhibitor without recurrent cough.

The Committee noted that evidence suggests that ACE inhibitor-associated chronic cough could linger for up to three months after cessation of treatment with the ACE inhibitor.

The Committee noted that it may be difficult to differentiate between viral bronchial hyper-reactivity and ACE inhibitor-associated chronic cough, but that the Special Authority Criteria should target the use of angiotensin II antagonists to patients truly intolerant of ACE inhibitors.

The Committee **recommended** that the criteria (as they relate to ACE inhibitors) should be changed as follows (changes in bold and strikethrough):

> "**Has been treated with, and cannot tolerate ~~two~~** an **ACE inhibitors~~,~~ due to persistent cough**, and on retrial, or trial of another ACE inhibitor, develops recurrent and persistent cough."

Erythropoietin for Oncology patients

The Committee considered a submission from a member of the public, forwarded through the Ministry of Health, requesting that they consider the use of erythropoietin in oncology to reduce tumour hypoxia and therefore improve patient's response to chemotherapy and/or radiation therapy.

The Committee considered that tumour oxygenation could increase the efficacy of radiation and/or chemotherapy. However, the Committee also noted that in anaemia, properties of the oxygen dissociation curve could compensate oxygen delivery; therefore, tumour necrosis may occur in severe hypoxia.

The Committee noted that trials examining the use of erythropoietin to increase survival were inconclusive and that clinical data on the role of erythropoietin as an adjuvant treatment are conflicting. Therefore, the Committee recommended that erythropoietin should not be used in this role.

The Committee also considered the use of erythropoietin in patients with cancers to prevent and treat anaemia associated with chemotherapy and/or radiation therapy.

The Committee noted that anaemia is a common problem among cancer patients and that the use of erythropoietin is increasing, especially in the United States.

The Committee noted that there is an increasing body of evidence which suggests that the use of erythropoietin in oncology patients may help to prevent and treat anaemia caused by chemotherapy and/or radiation therapy.

The Committee noted that a Cochrane review indicated that on average patients receiving erythropoietin reduced their transfusion requirement by only one unit of blood.

The Committee considered that the evidence supported a recommendation that erythropoietin be used to increase haemoglobin levels and therefore reduce the need for transfusions in patients with haemoglobin levels of 100 g/l or below.

Members expressed concern that erythropoietin may not be suitable for some forms of cancer, such as patients with breast and head and neck cancers due to the worse outcomes which may result from the growth stimulating properties of erythropoietin.

The Committee acknowledged that the requirement for, and cost of, blood transfusions is increasing. The Committee considered that managing anaemia in some patients who do not accept blood transfusions is a clinical challenge.

The committee considered that erythropoeitin could be considered as a alternative treatment option for non-cancer related anaemia.

The Committee considered that the use of erythropoietin instead of blood transfusions could be an issue that is more relevant to the Ministry of Health than to PHARMAC as PHARMAC does not manage the blood transfusion service.

The Committee considered that a cost-utility analysis would be required before erythropoietin could be considered for subsidisation in the prevention and treatment of anaemia associated with chemotherapy and/or radiation therapy.

The Committee **recommended** no change to the Pharmaceutical Schedule criteria.

Prednisolone acetate (Pred Forte)

In response to a request from, and the provision of further evidence by, an ophthalmologist, PTAC considered whether prednisolone acetate 1% should be fully subsidised on the Pharmaceutical Schedule and whether steroidal anti-inflammatory eye drops should be subgrouped according to potency, as previously recommended by the Ophthalmology subcommittee.

The Ophthalmology Subcommittee recommended dividing the steroidal anti-inflammatory eye drops sub-group according to potency as follows:

Therapeutic Sub-group / Chemical	Product
1. *Steroidal anti-infammatory*	
a. mild	
Fluorometholone	Flucon
Prednisolone acetate 0.12%	Pred Mild
b. medium	
Dexamethasone	Maxidex
c. strong	
Prednisolone acetate 1%	Pred Forte

The Committee noted that it had previously considered this issue but had found that there was not enough evidence to support any alteration to the sub-grouping. The Committee noted the additional evidence supplied suggesting that after topical administration prednisolone acetate 1% has better penetration through the cornea and achieves higher aqueous concentrations than dexamethasone 0.1%. The Committee noted, however, that there did not appear to be any experimental evidence to show that this resulted in a greater anti-inflammatory effect.

The Committee noted that there is a lack of published clinical data comparing prednisolone acetate 1% with dexamethasone 0.1%. However, it noted that the general opinion of local ophthalmologists is that, in clinical practice, prednisolone acetate 1% is more effective than dexamethasone 0.1% in controlling intraocular inflammation.

The Committee **recommended** that, based on the expert ophthalmological opinion, the steroidal anti-inflammatory eye drops be sub-grouped as recommended by the Ophthalmology subcommittee and that prednisolone acetate 1% be fully funded on the Pharmaceutical Schedule.

The Committee gave the recommendation a low priority.

The Decision Criteria relevant to this recommendation are: *(iv) the clinical benefits and risks or pharmaceuticals, and (vii) the direct cost to health service users.*

Lamivudine and abacavir (Kivexa)

The Committee reviewed an application from GlaxoSmithKline for the listing of a fixed-dose combination of abacavir with lamivudine (Kivexa) in Section B of the Pharmaceutical Schedule with the same Special Authority criteria as other antiretrovirals.

The Committee reviewed the data from one pivotal trial comparing fixed-dose combination abacavir/lamivudine (Kivexa) dosed once daily with the individual components abacavir and lamivudine dosed twice daily. The Committee also reviewed data from supporting trials comparing abacavir dosed once or twice daily combined with lamivudine and efavirenz.

The Committee considered that once-daily fixed-dose Kivexa was equivalent, in terms of efficacy as measured by HIV viral load suppression, to the individual components abacavir and lamivudine dosed once or twice daily. Members noted that there were no differences in adverse effects or emergence of viral resistance mutations when comparing Kivexa with the individual components, abacavir and lamivudine.

The Committee noted that adherence was greater in the Kivexa treatment groups. Members considered that the main advantage of Kivexa was the once-daily dosing with one tablet, making it the lowest pill burden of any dual NRTI regimen.

Members considered that there was a risk of possible rechallenge with Kivexa in patients who had previously experienced abacavir hypersensitivity, where the treating physician or patient may not realise that Kivexa contained abacavir. However, the Committee considered that the risk was small given that in New Zealand only named specialists could prescribe subsidised HIV medications.

The Committee considered that most patients currently on abacavir and lamivudine would switch to Kivexa and approximately 12% of other patients would start treatment with or switch to Kivexa as their backbone dual NRTI regimen.

The Committee noted that the proposed price for Kivexa represents a reduction on the sum of the prices of the individual components and would be cost saving to the Pharmaceutical Schedule. However, the Committee was concerned about the impact the listing might have on continuity of supply of the individual components abacavir and lamivudine.

The Committee **recommended** that combination abacavir with lamivudine (Kivexa) be listed on the Pharmaceutical Schedule, with high priority, with the same Special Authority criteria as other antiretrovirals. The Committee considered that PHARMAC should ensure that for the purpose of the anti-retroviral Special Authority, Kivexa is considered as two anti-retroviral medications.

The Decision Criterion relevant to this recommendation is: *(iii) the availability and suitability of existing medicines, therapeutic medical devices and related products and related things, as there are many other options for HIV therapy*.

Goserelin (Zoladex)

The Committee reviewed an application from AstraZeneca to widen the Special Authority criteria for goserelin to include the adjuvant treatment of locally-advanced prostate cancer following external beam radiotherapy (Stage T2b or T3 or T4, Node 0-1, M0).

The Committee considered that the evidence provided was of good quality and provided sufficient long-term data. The Committee noted that, for patients with locally-advanced prostate adenocarcinoma, the evidence indicated that the disease-free survival rate for patients in the goserelin treatment group was 37% versus 23% in the control group, at 10 years, which was statistically significant. Data also indicated long-term increases in overall survival, although this evidence was not always significant and in the case of the 10-year trial, was not robust.

The Committee noted that prolonged GnRH analogue therapy is associated with bone loss through androgen deprivation, and increases the risk of osteoporosis.

The Committee considered papers that examined the cost-effectiveness of adjuvant goserelin treatment in advanced prostate cancer that were based on the cost-effectiveness to the French and Canadian Health Systems. The Committee noted that the papers evaluated cost-effectiveness on the assumption of three years of adjuvant treatment with goserelin, and that adjuvant treatment may continue indefinitely. The Committee considered that the evaluation of costs per year of life saved should be interpreted in relation to the New Zealand health system, and that PHARMAC may need to undertake its own cost-utility analysis to determine the value of gonadotropin releasing hormone (GnRH) analogues in the treatment of locally-advanced prostate cancer.

The Committee considered that the benefits of goserelin in locally-advanced prostate cancer may be a class effect that could be applied to other GnRH analogues.

The Committee noted that neoadjuvant and adjuvant GnRH analogue treatment of locally-advanced prostate cancer would often be used in combination with anti-androgens to achieve maximum androgen blockade. Anti-androgens would also be used at the start of GnRH analogue treatment to prevent disease flare.

The Committee noted that GnRH analogue treatment of prostate cancer is currently restricted, by Special Authority, to “advanced prostate cancer”. The Committee noted that prostate cancer is subject to many classifications of disease, including Tumour Node Metastases (TNM score), Gleason score, WHO histological grade, and PSA level. As a consequence, the current Special Authority criteria are open to interpretation, and the Committee noted that patients with “locally-advanced” and “advanced” disease may well be accessing GnRH analogues under the current Special Authority criteria. Therefore the Committee considered that the current Special Authority criteria provided access to patients with locally-advanced disease as defined in the application as Stage T2b or T3 or T4, Node 0-1 M0 (using TNM score).

The Committee **recommended** that goserelin should be subsidised for use in locally-advanced prostate cancer, and gave this recommendation a high priority. However, the Committee considered that as GnRH analogues may already have subsidised access for use in locally advanced disease, the Special Authority Criteria may not need to be changed.

The Committee considered that a prescribing note specifying use of GnRH analogues in adjuvant treatment of locally advanced prostate cancer and/or palliative treatment of advanced prostate cancer may be useful to clarify the situation. The Committee noted that if the Special Authority Criteria for GnRH Analogues were to be altered, specialist advice would be needed regarding the suitable change in wording.

Trastuzumab (Herceptin)

These minutes have previously been published on the PHARMAC website at the following address: http://www.pharmac.govt.nz/latest_PTAC_minutes.asp

Aromatase Inhibitors

Anastrozole

The Committee considered a submission from AstraZeneca relating to the use of anastrozole in early breast cancer. The Committee noted that it had considered an application previously, and that this submission provided updated information for PTAC's consideration.

The Committee noted that anastrozole is currently available for post-menopausal women with hormone-receptor positive breast cancer, either in the treatment of advanced disease, or in early disease where tamoxifen is not tolerated. The Committee noted that the proposal is for anastrozole to be used after two years of treatment with tamoxifen.

The Committee noted that it had previously considered the papers in support of anastrozole separately, but that now they were presented as a meta-analysis. The Committee noted that these were randomised, open-label studies.

The Committee noted that there was no overall survival benefit, but that there was an increase in disease-free survival over tamoxifen in the ATAC trial (Lancet. 2005 Jan 1-7; 365(9453): 60-2). Members noted that overall survival was significant in the meta-analysis provided by AstraZeneca.

The Committee noted that adverse events differed across treatment arms, with a higher frequency of thromboembolic events in the tamoxifen arm, and a higher fracture risk with anastrozole.

The Committee considered that anastrozole, letrozole and exemestane appear to have the same or similar therapeutic effect, and that they are equal to or slightly better than tamoxifen. Members noted that the magnitude of benefit is relatively small.

The Committee considered that anastrozole may have a place in treatment after two years of tamoxifen, but that there was insufficient benefit to recommend the use of anastrozole before tamoxifen.

The Committee **recommended** that access to anastrozole could be widened for patients with early breast cancer after two years of tamoxifen, and gave a moderate priority to this recommendation. The Committee **recommended** referring this proposal to the Cancer Treatments Subcommittee.

The Decision Criteria 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;* (vi) *The budgetary impact (in terms of the pharmaceutical budget and the Government's overall health budget) of any changes to the Pharmaceutical Schedule;* (vii) *The direct cost to health service users; and* (viii) *The Government's priorities for health funding, as set out in any objectives notified by the Crown to PHARMAC, or in PHARMAC's Funding Agreement, or elsewhere.*