

PTAC meeting held 6 & 7 November 2008

(minutes for web publishing)

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Note that this document is not necessarily a complete record of the PTAC meeting; only the Minute relating to PTAC discussions about an application that contain a recommendation in relation to an application are published.

PTAC 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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 - enable PHARMAC to carry on, without prejudice or disadvantage, negotiations, including commercial negotiations (section 9(2)(j)).
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Contents

1	Atomoxetine (Strattera) for Attention Deficit/Hyperactivity Disorder (ADHD): widening access to first-line treatment and to allow use in combination with a stimulant	3
2	Widening Access to Treatments for Multiple Sclerosis.....	5
3	Raltegravir (Isentress), anti-retroviral for HIV.....	9
4	Desogestrel (Cerazette) for contraception	10
5	Bortezomib (Velcade) for multiple myeloma.....	11
6	Sunitinib (Sutent) for Advanced Renal Cell Carcinoma.....	12
7	Finasteride for Haematuria Associated with otherwise Asymptomatic Benign Prostatic Hyperplasia	12
8	Dabigatran Etexilate for the Prevention of Venous Thromboembolic Events in Patients Undergoing Orthopaedic Surgery	13
9	Extended Release Nicotinic Acid in Combination with Laropiprant for the Treatment of Dyslipidaemia.	15
10	Low Molecular Weight Heparin - Access Criteria	16
11	Buprenorphine Transdermal Patch (Norspan) for the Treatment of Moderate-to-Severe Chronic Pain.....	18
12	Tenofovir Disoproxil Fumarate (Viread) for Hepatitis B.....	21
13	Triamcinolone Hexacetonide for Juvenile Idiopathic Arthritis	22

1 Atomoxetine (Strattera) for Attention Deficit/Hyperactivity Disorder (ADHD): widening access to first-line treatment and to allow use in combination with a stimulant

- 1.1 The Committee noted that funding of atomoxetine had recently been approved as a second-line treatment for attention deficit/hyperactivity disorder (ADHD) but that it could be used as a first-line agent when there is a significant risk of diversion with subsidised stimulant therapy. The Committee noted that one of the Special Authority criteria prevented use of atomoxetine in combination with a stimulant except for the purpose of transitioning from stimulant to atomoxetine therapy.
- 1.2 The Committee reviewed responses to the consultation on this funding decision, in which some responders requested changes to Special Authority criteria to allow use of atomoxetine as a first-line treatment for ADHD and to allow its use in combination with a stimulant. The Committee considered these two requests separately. The Committee noted that the supplier of atomoxetine, Eli Lilly, had provided some publications that were potentially relevant to the two requests, in response to a request from PHARMAC staff.

Atomoxetine as a first-line treatment for ADHD

- 1.3 The Committee considered that the evidence provided in support of the use of atomoxetine as a first-line treatment for ADHD was weak and of poor quality. The Committee noted that there were no studies specifically comparing atomoxetine with stimulant therapy (methylphenidate and/or dexamphetamine) in treatment-naïve (first-line) patients.
- 1.4 The Committee reviewed a number of studies in which atomoxetine was directly compared with various formulations of stimulant therapy. The Committee noted that the studies had various limitations, including high numbers of patients having had prior exposure to ADHD treatments, short study durations and small numbers of patients included in some studies.
- 1.5 Overall, the Committee considered that the weight of opinion suggests that atomoxetine provides similar clinical benefit to methylphenidate, although some study results suggested that methylphenidate might have some efficacy advantages over atomoxetine.
- 1.6 The Committee noted that the National Institute for Health and Clinical Excellence (NICE) updated ADHD clinical guidelines (September 2008) recommend methylphenidate as the first-line treatment for ADHD, with atomoxetine recommended as a second-line treatment or where there is risk of stimulant misuse or diversion. The Committee noted that similar recommendations were made in the Texas Children's Medication Algorithm publication (Pliszka et al. J Am Acad Child Adolesc Psychiatry 2006;45:642-657).
- 1.7 The Committee considered that atomoxetine would be of benefit for patients who do not tolerate or respond to stimulant therapy or in whom there is a risk of abuse or diversion of stimulant therapy, and noted that these patients would be eligible for atomoxetine

funding under the approved Special Authority criteria. The Committee noted that there were no specifically funded first-line treatment options for patients who did not wish to take methylphenidate or dexamphetamine preparations, although agents such as tricyclic antidepressants could be used. The Committee did not consider there to be an unmet clinical need.

- 1.8 The Committee considered that there was a financial risk associated with the use of atomoxetine as a first-line treatment.
- 1.9 The Committee **recommended** that the application to fund atomoxetine as a first-line treatment for ADHD be **declined**, on the basis of limited evidence, the financial risk and lack of unmet clinical need.
- 1.10 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; (vi) The budgetary impact (in terms of the pharmaceutical budget and the Government's overall health budget) of any changes to the Pharmaceutical Schedule.*

Atomoxetine as in combination with a stimulant for ADHD

- 1.11 The Committee considered that the evidence provided in support of the use of atomoxetine in combination with a stimulant for ADHD was weak and of poor quality.
- 1.12 The Committee noted that there was only one well-designed study but that this study had recruited only 25 of the required 80 participants. The Committee considered that the results of this study (Carlson et al. Child Adolesc Psychiatry Mental Health 2007;1:10) did not show any benefit from augmentation of atomoxetine treatment with methylphenidate. The Committee noted that the Texas Children's Medication Algorithm included the option of augmentation of atomoxetine with methylphenidate but acknowledged that there was no research evidence to support this.
- 1.13 The Committee noted that the best level of evidence appeared to be anecdotal or at the level of case reports.
- 1.14 The Committee **recommended** that the application to widen access to atomoxetine to allow its use in combination with a stimulant for ADHD be **declined**, on the basis of a lack of evidence.
- 1.15 The Decision Criteria particularly relevant to this recommendation are: *(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.*

2 Widening Access to Treatments for Multiple Sclerosis

- 2.1 The Committee reviewed applications from the Multiple Sclerosis Society of New Zealand and from the Multiple Sclerosis Treatments Assessment Committee (MSTAC) to alter the criteria applying to funding of the multiple sclerosis (MS) treatments beta-interferon (interferon beta-1-alpha [Avonex] and interferon beta-1-beta [Betaferon]) and glatiramer acetate (Copaxone).
- 2.2 The Committee noted that the MSTAC are performing a difficult task very well and it is apparent that MSTAC, as well as patients and neurologists, are experiencing some frustrations with the current restrictions.
- 2.3 The Committee noted that the goal of long-term management of MS is to prevent or delay the appearance of permanent neurological disability. The Committee noted that the primary effect of the three MS treatments was to reduce relapse rates in patients with relapsing-remitting MS, and that there was evidence to suggest that this can delay disease progression. The Committee noted that it was generally accepted that progressive deterioration, usually measured by increases in Expanded Disability Status Scale (EDSS) scores, indicated that the medications were no longer effective.
- 2.4 The Committee noted that access to subsidies for MS treatments is administered by a panel of neurologists (MSTAC) according to defined entry and exit (stopping) criteria. The Committee considered that there were no alternative treatment options for patients who did not meet, or who no longer met, the access criteria for MS treatments.
- 2.5 The Committee noted that, collectively, the applicants proposed three key changes to the access criteria, as follows, which were considered separately:
- to allow treatment with a second class of MS medication after failure of treatment (as defined by current criteria) with the first class of treatment (referred to as “treatment switching”);
 - to amend the entry criteria to lower the threshold baseline annual rate of relapses to include patients with a lower frequency of relapses; and
 - to amending the exit criteria in one or more of the following ways:
 1. to allow longer disease progression times (by increasing the scale of deterioration manifest in increases in EDSS scores necessitating withdrawal from the programme);
 2. to have longer follow-up period to confirm persistent EDSS deterioration when still recovering from a relapse;
 3. to have more subjective criteria that are not based on EDSS measures of deterioration; and
 4. to remove the exit criteria entirely and replace them with a guideline.

MS Treatment Switching

- 2.6 The Committee considered that the strength of the evidence provided was weak and of poor quality. The three key studies provided were observational, with relatively small

patient numbers. However, the Committee considered that it was unlikely that randomised, controlled studies of treatment switching would be conducted in this patient group.

- 2.7 The first study (Caon et al. Eur J Neurol 2006;13:471–474) investigated response to glatiramer acetate in patients who switched from beta-interferon because of persistent disease activity (n=62) or unacceptable toxicity (n=23). The Committee noted that a subgroup analysis of patients who were switched because of lack of efficacy showed that the mean annualised relapse rate (ARR) was reduced from 1.32 on beta-interferon to 0.52 on glatiramer acetate ($P=0.0001$).
- 2.8 The second study (Carra et al. Eur J Neurol 2008;15:386–393) investigated outcomes in 114 patients who switched treatments following inadequate response to, or unacceptable side effects from, first-line treatment. Patients were followed for three years. Switching from beta-interferon to glatiramer acetate (n=52) resulted in a reduction in ARR from 0.63 to 0.14 and switching from glatiramer acetate to beta-interferon (n=16) resulted in a reduction in ARR from 0.52 to 0.17. Similar results were seen in the subgroup of patients who switched from first-line treatment because of lack of efficacy. The Committee noted that in the subgroup of patients who switched because of lack of efficacy, EDSS, which had been increasing during the three years prior to the switch, continued to increase in patients switching from glatiramer acetate to beta-interferon but not in patients switching from beta-interferon to glatiramer acetate.
- 2.9 The third study (Zwibel HL. Acta Neurol Scand 2006;113:378-386) investigated response to glatiramer acetate in treatment-naïve patients (n=558) and in patients who switched from beta-interferon because of inadequate response and/or side effects (n=247). The Committee considered that the reasons for stopping beta-interferon were not well defined. The Committee noted that the group of patients who had prior treatment with beta-interferon were older, had a longer duration of illness, a higher ARR, and higher Expanded Disability Status Scale (EDSS) scores than the treatment-naïve patients. Patients were followed for a mean of two years (patients with prior treatment with beta-interferon) or three years (treatment-naïve patients). The ARR declined by 75% in both patient groups ($P=0.1482$). Mean EDSS changed by less than 0.5 in both patient groups.
- 2.10 The Committee considered that the limited evidence suggested that patients who would most likely benefit from treatment switching were those with relapsing-remitting MS who stopped first-line treatment because of stable or increasing relapse rate over 12 months of treatment.
- 2.11 The Committee considered that treatment switching would not pose any new clinical risks and may result in reduction in ARR.
- 2.12 The Committee considered that reductions in ARR from treatment switching could potentially reduce or delay hospital admissions, specialist review and support services, although the Committee noted that there was no strong evidence to support this.
- 2.13 The Committee considered that the estimates of patient numbers (30%–50% of patients who stop treatment every year plus approximately 25% of patients who have already stopped treatment) appeared reasonable, but noted that because patients can stay on treatment for many years the costs could accumulate over time.

- 2.14 The Committee noted that the budget impact associated with permitting treatment switching would be significant and considered that it would be important to conduct a cost-utility analysis to help inform any funding decision.
- 2.15 The Committee **recommended** that the criteria for access to Multiple Sclerosis treatments be **amended** to permit treatment switching in patients with a stable or increasing relapse rate over 12 months of treatment (compared with the relapse rate prior to starting treatment), provided that no other exit criteria (either current exit criteria or exit criteria modified as recommended by the Committee, below) are met. The Committee assigned a medium priority rating to this recommendation, based on the budget impact, quality of the evidence and the lack of alternative treatment options.
- 2.16 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, (vi) The budgetary impact (in terms of the pharmaceutical budget and the Government's overall health budget) of any changes to the Pharmaceutical Schedule.*

Amending the entry criteria

- 2.17 The Committee considered that the strength of the evidence provided was weak and of poor quality, and noted that no studies were provided that specifically compared early treatment with later treatment.
- 2.18 The Committee noted that the supporting evidence consisted of expert opinion and analyses of select patient groups from three clinical studies (one unpublished), only two of which were supportive of early treatment improving longer-term outcomes (Coppola et al. Eur J Neurol 2006;13:1014-21 and posters by Goodin et al 2008). The Committee noted that there were a number of limitations with the clinical studies, including high dropout rates (30%–40%) which raised the possibility of bias. The Committee noted that expert opinion tended to favour earlier medical treatment of MS.
- 2.19 The Committee considered that the estimated patient numbers (10–20 extra patients per year) appeared reasonable.
- 2.20 The Committee **recommended** that the application to alter the entry criteria for access to Multiple Sclerosis treatments be **declined**, on the basis of lack of evidence. The Committee noted that it would be willing to review this recommendation on receipt of new evidence.
- 2.21 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; (vi) The budgetary impact (in terms of the pharmaceutical budget and the Government's overall health budget) of any changes to the Pharmaceutical Schedule*

Amending the exit criteria

- 2.22 The Committee considered that the strength of the evidence provided was weak, with no definitive evidence to support any of the proposed changes.
- 2.23 The Committee reviewed a study by Rio et al (Ann Neurol 2002;52:400-6) which investigated the sensitivity and predictive value of different criteria of treatment failure to identify patients who had permanent versus transient treatment failure. The study included 252 patients treated with beta-interferon with a follow-up of more than two years. The study concluded that the criterion of one EDSS point increase at six months following a relapse showed the best sensitivity (76.5%), with satisfactory specificity (89%).
- 2.24 The Committee noted that EDSS is the most common measure of disease progression used in clinical trials and considered that, at present, there was not a better scale with which to measure disease progression. The Committee noted that, for financial reasons, such a measure of disease progression was an important exit criterion if MS treatments were to remain targeted to patients most likely to benefit.
- 2.25 However, the Committee considered that there were some limitations associated with using a change in EDSS score of 1 as an exit criterion, given that the degree of functional impairment associated with an increase in one EDSS point varied considerably at different parts of the scale.
- 2.26 The Committee considered that it was not possible to extrapolate stopping rates from other countries, where there are different or no exit criteria, to the New Zealand situation. The Committee noted that while there may be some similarities, the treated population in New Zealand would be different from the international situation, partly due to differences in health systems and entry criteria.
- 2.27 The Committee **recommended** that the exit criteria for Multiple Sclerosis treatments be **amended** as outlined below (additions in bold, deletions in strikethrough). The Committee placed a medium priority on this recommendation, taking into account the unmet clinical need, financial risk and lack of good evidence. The Committee also **recommended** that the application to remove the exit criteria completely be **declined**, primarily for financial reasons. The Committee further **recommended** that the possibility of including secondary progressive MS as an exit criterion be considered, following a review of the relevant literature.
- 1) Confirmed progression of disability that is sustained for ~~three~~**six** months after a minimum of one year of treatment. Progression of disability is defined as ~~any of: either~~
 - (a) an increase of 2 EDSS points where starting EDSS was 2.0; or**
 - (b) an increase of 1.5 EDSS points where starting EDSS was 2.5 or 3.0; or**
 - (c) an increase of 1 EDSS point from the where starting EDSS was 3.5 or greater; or**
 - (d) an increase in EDSS score to 6.0 or more; or**
 - 2) stable or increasing relapse rate over 12 months of treatment (compared with the relapse rate on starting treatment); or
 - 3) pregnancy and/or lactation; or
 - 4) within the 12 month approval year, intolerance to interferon beta-1-alpha, and/or interferon beta-1-beta and/or glatiramer acetate; or
 - 5) non-compliance with treatment, including refusal to undergo annual assessment or refusal to allow the results of the assessment to be submitted to MSTAC; or

- 6) patients may, subject to conclusions drawn from published evidence available at the time, be excluded if they develop a high titre of neutralising anti-bodies to beta-interferon or glatiramer acetate.
- 2.28 The Decision Criteria particularly relevant to these recommendations 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, (vi) The budgetary impact (in terms of the pharmaceutical budget and the Government's overall health budget) of any changes to the Pharmaceutical Schedule.*

3 Raltegravir (Isentress), anti-retroviral for HIV

- 3.1 The Committee reviewed the application from Merck Sharp and Dohme (New Zealand) Limited for the listing of raltegravir (Isentress) on the Pharmaceutical Schedule for the treatment of HIV in combination with optimised background therapy (OBT). The application was for a listing of either second line treatment after initial treatment failure or as a treatment for multiple class resistant patients.
- 3.2 The Committee noted that there have been four clinical trials evaluating the efficacy of raltegravir in combination with OBT for the treatment of HIV. The Committee noted that two of the trials were phase three trials and two were phase two trials. The Committee considered that the clinical evidence provided on raltegravir was of good quality. Members noted however that the follow-up of patients in the clinical trials was limited to 48 weeks.
- 3.3 The Committee noted that raltegravir was a novel HIV medication; an inhibitor of HIV integrase strand transfer, which is normally required for HIV replication. Members noted that there was a low genetic barrier to resistance so raltegravir would need to be used in combination with other antiretroviral agents.
- 3.4 Members noted that the recommended dose of raltegravir for the treatment of HIV is 400mg twice daily, without regard to food. Members also noted that elimination is by metabolism via UGT1A1 and that inducers such as rifampicin can affect plasma concentration.
- 3.5 The Committee reviewed study 005, a dose-ranging placebo-controlled trial of raltegravir in combination with OBT. Members noted that the antiretroviral effect for raltegravir was better than placebo at all doses and similar in the sub studies. The Committee noted that at 24 weeks 71% of raltegravir versus 15.6% of placebo treated patients had HIV RNA below 400 copies per ml. The Committee noted that at 48 weeks virological failure was seen in 29% of patients receiving raltegravir in the double blind period.
- 3.6 The Committee reviewed the two Phase III BENCHMRK trials (BENCHMRK 1 and BENCHMRK 2), which were randomised placebo-controlled trials of raltegravir in combination with OBT. The Members noted that the published data showed complete

viral suppression at 48 weeks of 62.1% for raltegravir versus 32.9% in the placebo group (p<0.001).

- 3.7 The Committee reviewed Protocol 004, a 48 week dose-ranging study of raltegravir compared with efavirenz, each administered in combination with tenofovir and lamivudine. Members noted that at week eight, more patients on raltegravir achieved viral load suppression below 50 copies per ml but by week 24 all treatment groups appeared similar with 85% to 95% of patients achieving this level of viral load suppression and maintaining it until week 48.
- 3.8 The Committee noted that the supplier had presented safety data of 322 patient years from clinical trials that showed adverse effects for raltegravir to be lower than that of comparator placebo arms. The Committee noted however that there is no long-term safety data available.
- 3.9 The Committee considered that there was an unmet clinical need for patients who develop multiple class resistance to currently available antiretroviral treatment. Members considered that raltegravir would be used before enfuvirtide in the treatment of multiple class resistant patients, but realised the importance of not adding raltegravir as a single additional agent to a failing antiretroviral regimen.
- 3.10 The Committee considered that further evidence was needed on the efficacy of raltegravir for first or second-line treatment of HIV.
- 3.11 The Committee **recommended** that raltegravir be **listed** on the Pharmaceutical Schedule with a medium priority for multiple class resistant patients. The Committee also requested that the Anti-infective subcommittee review raltegravir and its place in the treatment paradigm for HIV patients.
- 3.12 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;* (vi) *The budgetary impact (in terms of the pharmaceutical budget and the Government's overall health budget) of any changes to the Pharmaceutical Schedule*

4 Desogestrel (Cerazette) for contraception

- 4.1 The Committee reviewed the submission from Pharmaco for funding of desogestrel (Cerazette) in Section B of the Pharmaceutical Schedule for contraception.
- 4.2 The Committee noted its previous decision in November 2000 to not list desogestrel due to safety concerns. The Committee also noted its decision in August 2007 to **list** desogestrel with low priority and their request for Post Marketing Surveillance (PMS) data from the applicant.
- 4.3 The Committee considered that the evidence presented included no demonstrable PMS data, and hence there was no reason to change the listing priority.

5 Bortezomib (Velcade) for multiple myeloma

- 5.1 The Committee reviewed a submission from Janssen-Cilag for the listing of bortezomib (Velcade) for the treatment of multiple myeloma.
- 5.2 The Committee noted that bortezomib had previously been considered by PTAC and CaTSoP for third-line treatment of multiple myeloma, and had been declined. The Committee noted that CaTSoP's main concerns were bortezomib's toxicity and uncertainty relating to long term benefit. Members noted that this application was for the use of bortezomib as a second-line treatment. It was noted that since the previous application, the National Institute for Health and Clinical Excellence (NICE) in the UK and Pharmaceutical Benefits Advisory Committee (PBAC) in Australia had recommended that bortezomib may be used as second line treatment in patients with multiple myeloma. The drug is now funded for this indication in Australia, but certain conditions apply. Janssen-Cilag suggests using the same criteria for use and method of funding in New Zealand as that in Australia if it is recommended for funding.
- 5.3 The Committee noted that patient registers indicate that survival rates for multiple myeloma have improved in the last 20 years, and that this benefit is ascribed to the use of stem cell transplants and newer drug therapy.
- 5.4 Members noted that the supplier had proposed exit criteria at four weeks.
- 5.5 The Committee reviewed the recent publications of the APEX trial (N Engl J Med. 2005 Jun 16;352(24):2487-98 and Blood 2007 Nov 15;110(10):3557-60). The Committee noted that this was an open-label trial comparing the efficacy of bortezomib with dexamethasone. The Committee noted that the recent publications included longer-term follow-up of patients from the APEX trial.
- 5.6 The Committee noted that in the 2005 publication of the APEX trial, bortezomib demonstrated an improvement in median time to progression over dexamethasone (6.22 months vs. 3.49 months) in relapsed patients. The Committee noted that in the 2007 publication, a survival advantage of around six months was demonstrated with bortezomib (29.8 months vs. 23.7 months). In this latter trial, patients who had been randomised to dexamethasone were allowed to crossover to bortezomib whether they had progressive disease or not. The survival benefit was for the dexamethasone patients who had crossed over versus the original bortezomib group.
- 5.7 The Committee noted there are no head to head studies with thalidomide, which is the most commonly used second-line agent for multiple myeloma in New Zealand. Members noted that the clinical evidence to date indicates that bortezomib and thalidomide have different risk profiles, with both treatments associated with significant side-effects.
- 5.8 The Committee noted that the median age of patients in the APEX trial was 62 (47-73) years and that the average age of diagnosis of multiple myeloma in New Zealand is 70 years. The Committee considered that there is a paucity of good data for the use of bortezomib in patients aged over 70 years at this time.

- 5.9 The Committee considered that the magnitude of benefit with bortezomib was difficult to determine due to most trials allowing crossover of treatments. Furthermore there is evidence that patients who do not respond optimally to bortezomib might respond to added dexamethasone plus bortezomib (Jaganath et al. *Haematologica* 2006; 91: 929-34).
- 5.10 Members considered that the optimal placement of bortezomib in the treatment cascade for multiple myeloma is uncertain at this stage.
- 5.11 The Committee **deferred** its recommendation and requested that it reconsider this application following review by the Cancer Treatments Subcommittee and a PHARMAC cost-utility analysis.

6 Sunitinib (Sutent) for Advanced Renal Cell Carcinoma

- 6.1 The Committee reviewed an application from Pfizer for the listing of sunitinib (Sutent) for the treatment of advanced renal cell carcinoma. Members noted that this proposal had previously been considered by PTAC and CaTSoP and had been declined.
- 6.2 Members noted that the major evidence base for the use of sunitinib in renal cell carcinoma is the study by Motzer et al (*N Engl J Med.* 2007 Jan 11;356(2):115-24.), comparing sunitinib with interferon alpha.
- 6.3 The Committee noted that updated information presented by Figlin et al at the American Society of Clinical Oncology 2008 meeting indicated a survival advantage for sunitinib (26.4 months) over interferon (21.8 months). Members noted that this might under-represent the benefit of sunitinib as patients were allowed to switch treatment following disease progression.
- 6.4 The Committee noted that treatment with sunitinib was continued indefinitely until patients experienced either intolerable adverse events or progression of disease.
- 6.5 The Committee considered that although the new data indicated a survival advantage for sunitinib over interferon, it remains an essentially palliative treatment. The Committee considered that there was lack of correlation between progression-free survival and overall survival in the treatment of advanced renal cell carcinoma.
- 6.6 The Committee requested that it reconsider this application following review by the Cancer Treatments Subcommittee and a PHARMAC cost-utility analysis.

7 Finasteride for Haematuria Associated with otherwise Asymptomatic Benign Prostatic Hyperplasia

- 7.1 The Committee noted that finasteride was recently funded for symptomatic Benign Prostatic Hyperplasia (BPH) under special authority criteria as a second line agent after alpha-blockers, where these agents do not adequately control symptoms or are contra-indicated.
- 7.2 The Committee reviewed responses to the consultation on this funding decision, in which responders requested changes to Special Authority criteria to allow use of finasteride for the treatment of haematuria in non-symptomatic BPH. Members noted urological referral for painless haematuria is commonplace and if subsequent investigation is normal it is presumed to be of prostatic origin in older men.
- 7.3 The Committee considered the Bandolier review of finasteride treatment. This review consisted of three randomised controlled trials of finasteride with associated haematuria, and four observational studies. Members noted that across all RCT's there was a 15% vs 66% recurrence of haematuria for those taking finasteride compared to no treatment. Members noted that there was a consistency of results for all RCT's and observational studies showing efficacy of finasteride.
- 7.4 The Committee noted that cyproterone is currently used off-license for this indication but considered that the side-effects would deter many prescribers.
- 7.5 The Committee considered that with the exclusion of other causes, haematuria can be considered a symptom of BPH and **no change** was needed to the special authority criteria. The Committee also noted that haematuria was not a listed indication for finasteride. The Committee asked PHARMAC staff to inform the urological society of this view.

8 Dabigatran Etexilate for the Prevention of Venous Thromboembolic Events in Patients Undergoing Orthopaedic Surgery

- 8.1 The Committee reviewed an application from Boehringer Ingelheim for the listing of dabigatran etexilate (Pradaxa) on the Pharmaceutical Schedule for the prevention of venous thromboembolic events in patients undergoing orthopaedic surgery.
- 8.2 The Committee noted that without prophylaxis the incidence of venographically demonstrated venous thromboembolism is 40% to 60% after joint replacement surgery to the lower limb. However the Committee considered that a large number of these events are asymptomatic and do not impact on either morbidity or mortality. The Committee noted that information submitted by the supplier indicated mortality rates resulting from pulmonary embolism ranged between 0.1% and 7.5% after lower limb joint replacement surgery. The Committee considered that there is a historical aspect to these high rates and that recent data (2006/2007) from the Scottish Arthroplasty Registry indicated lower overall morbidity and mortality in a country where aspirin and mechanical prophylaxis predominated over low molecular weight heparin (LMWH) prophylaxis. Complete Scottish data for 2006/2007 showed symptomatic venous thromboembolism within 90 days and all cause mortality within 90 days occurring in 1.3% and 0.7% of patients

undergoing a total hip replacement and 1.3% and 0.5% of patients undergoing a total knee replacement.

- 8.3 The Committee noted the RE-MOBILIZE, RE-MODEL, and RE-NOVATE Phase III clinical trials which compared the efficacy and safety of dabigatran to enoxaparin in the prevention of venous thromboembolism following hip and knee orthopaedic surgery. The Committee noted that the studies showed that the efficacy, adverse effect profile including hepatotoxicity, and the risk of bleeding of dabigatran was non-inferior to that of enoxaparin.
- 8.4 The Committee considered that the studies were of good quality, but noted that there were a number of exclusion criteria which could affect the studies' generalisability to clinical practice, and the studies were not powered adequately for safety outcomes. The Committee also noted that the primary endpoint was the incidence of total VTE and all-cause mortality however there is some debate as to whether total VTE is an appropriate endpoint.
- 8.5 The Committee noted that current venous thromboembolism prophylaxis practice varies between New Zealand hospitals in both duration and the type of pharmaceutical agent used. The Committee noted that low molecular weight heparin, warfarin and aspirin are used to varying degrees in clinical practice. The Committee noted that concern regarding bleeding and infection rates partially accounted for the reluctance of some centres to use low molecular weight heparins. Therefore the Committee considered that there was a question as to whether dabigatran, if made available, would be used by surgeons for the same reasons.
- 8.6 The Committee considered that the most appropriate comparator to dabigatran was low molecular weight heparin as this was the comparator used in the clinical trials; however, aspirin or warfarin are often used in clinical practice in New Zealand. The Committee considered that dabigatran and low molecular weight heparin had the same or similar clinical effect and that they could be reference priced for thromboprophylaxis following elective orthopaedic surgery.
- 8.7 The Committee noted that dabigatran was a tablet and considered that it would therefore be preferred to enoxaparin which was an injection and could result in significant local bruising. The Committee considered that the current market would grow if dabigatran became available and also wondered if it might be used for unregistered indications.
- 8.8 The Committee considered that dabigatran would be especially useful in elderly patients but noted that there was no antidote to dabigatran and that this could be an issue if there is a major bleeding complication.
- 8.9 The Committee noted that dabigatran was cheaper than the MIMS price of enoxaparin.
- 8.10 The Committee **recommended** that dabigatran be **declined** for a listing in Section B of the Pharmaceutical Schedule but that it be **listed** on the Discretionary Community Supply (DCS) list with a low priority following knee and hip orthopaedic surgery for a duration of up to 10 days and 35 days respectively.
- 8.11 The Committee **recommended** that PHARMAC staff write to orthopaedic surgeons to determine what current practice is, and what place in therapy, if any, they considered

dabigatran would occupy. The Committee also **recommended** that PHARMAC monitors further safety signals.

The Decision Criteria particularly relevant to this recommendation are: *(iii) The availability and suitability of existing medicines, therapeutic medical devices and related products and related things; and (v) The cost-effectiveness of meeting health needs by funding pharmaceuticals rather than using other publicly funded health and disability support services.*

9 Extended Release Nicotinic Acid in Combination with Laropiprant for the Treatment of Dyslipidaemia.

- 9.1 The Committee reviewed an application from Merck Sharp & Dohme for the listing of extended release (ER) nicotinic acid with laropiprant (Tredaptive) on the Pharmaceutical Schedule for the treatment of dyslipidaemia.
- 9.2 The Committee noted that dyslipidaemia treatment has improved considerably with the advent of statins. However, the Committee also noted that some patients cannot tolerate statins and alternatives are required for these patients.
- 9.3 The Committee noted that the currently listed immediate release (IR) nicotinic acid is limited by the dosing schedule and its side-effects which include flushing.
- 9.4 The Committee noted that the supplier claimed that ER nicotinic acid plus laropiprant has the same clinical effects as nicotinic acid with reduced flushing. The Committee noted that the supplier considered that the reduced flushing side-effect increases compliance.
- 9.5 The Committee noted that the supplier provided four large phase III trials, P020, P022, P023 and P054, which appeared to be well conducted, however none of them were published in peer reviewed journals. The Committee noted that none of these trials were over a long period and therefore there was no long term safety or outcome data available. The Committee also noted that there are no trials investigating the effect of laropiprant alone available.
- 9.6 The Committee was concerned about the quality of the application from the sponsor. The Committee considered that good critical appraisal of the phase three trials was not possible as only selective information from the various trials was provided in the summary.
- 9.7 The Committee noted that discontinuation rates of ER nicotinic acid due to flushing in randomised control trials were significantly lower than the discontinuation rates presented in the submission. The Committee also noted that there is reasonable clinical outcome data supporting the use of IR nicotinic acid in lowering cholesterol but that hard clinical outcome data supporting ER nicotinic acid is limited.
- 9.8 The Committee noted that ER nicotinic acid plus laropiprant has been approved for marketing in the European Union but not in the United States of America. The

Committee noted that the US Food and Drug Administration (FDA) raised concerns including the lack of hard outcome data and whether the magnitude of the reduction in flushing led to a meaningful improvement in compliance and adverse effects. The Committee noted that the FDA considered that the results of the HPS2-THRIVE outcome study should be considered.

- 9.9 The Committee noted that a number of techniques are used to reduce flushing including the use of aspirin, using an ER formulation, taking nicotinic acid with meals, and avoidance of alcohol and hot baths. The Committee also noted that a natural tolerance to flushing can develop although some patients may stop therapy before this occurred.
- 9.10 The Committee noted that no head to head trial of ER nicotinic acid plus laropiprant versus IR nicotinic acid plus aspirin were available.
- 9.11 The Committee noted that a long-term trial is being conducted to look at hard cardiovascular outcomes with ER nicotinic acid.
- 9.12 The Committee **recommended** that the application for ER nicotinic acid plus laropiprant be **declined** due to a lack of long-term efficacy and safety data.
- 9.13 The Committee considered that the application could be reconsidered following the publication of long-term outcome data and that in any reapplication PHARMAC staff should consult with lipid experts as to the place in therapy of ER nicotinic acid.
- 9.14 The Decision Criteria particularly relevant to this recommendation are: *(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, (vi) The budgetary impact (in terms of the pharmaceutical budget and the Government's overall health budget) of any changes to the Pharmaceutical Schedule.*

10 Low Molecular Weight Heparin - Access Criteria

- 10.1 The Committee considered a submission from PHARMAC staff regarding the funding of Low Molecular Weight Heparin (LMWH) and the possibility of listing it in Section B of the Pharmaceutical Schedule.
- 10.2 The Committee noted that LMWH is currently funded via Discretionary Community Supply (DCS) and is available for a range of conditions.
- 10.3 The Committee noted the Draft Minutes of the 28 August Cardiovascular Subcommittee, which also considered PHARMAC's submission regarding LMWH, and the November 2003 PTAC minutes and the August 2003 LMWH Working Group minutes. The Committee also noted that in November 2003 PTAC recommended that LMWH is not listed in the Pharmaceutical Schedule as some general practitioners may not have sufficient experience and access to equipment such as ultrasound to use LMWH appropriately.

10.4 The Committee considered that there were no safety concerns with listing LMWH on the Pharmaceutical Schedule on Special Authority for relevant prescribers and that it would improve accessibility. However, the Committee considered electronic Special Authority access would be required and that this was not being used by all clinicians; that educational support for prescribers would be required to ensure appropriate use and follow-up; that good patient education is essential and that currently this is being provided by hospital pharmacies; and that there was some uncertainty as to who would administer the injections in the Community.

10.5 The Committee reviewed the current LMWH DCS criteria and made the following comments (comments/changes are in bold and strike-through):

For the treatment of venous thromboembolism (VTE) for a maximum of 14 days or until a stabilised therapeutic INR is established.

For a maximum treatment period from the time of diagnosis to 8 weeks post partum for a confirmed thromboembolic event during pregnancy.

For prophylaxis of thromboembolism for patients considered high risk after consultation with a specialist from diagnosis of pregnancy to 8 weeks post partum. – **There is no problem with using LMWH or warfarin when breastfeeding.**

For a maximum treatment period from diagnosis of pregnancy to 8 weeks post partum for women normally maintained on long-term oral anticoagulation who are at very high risk of thromboembolism. **These patients would be under consultant care and therefore GP's could prescribe as assistance would be available.**

For the treatment for a maximum of 7 days pre and post operatively for patients on oral anticoagulants requiring surgical intervention in a ~~public~~ hospital or until an appropriate therapeutic INR level is reached. **These patients would be under consultant care and therefore GP's could prescribe as assistance would be available.**

For a maximum of 14 days prophylaxis treatment in high-risk patients post pelvic, colo-rectal and major orthopaedic surgery. – **The ACC guidelines recommend a minimum of 10 days and a maximum of 35 days.**

For a maximum of 7 days treatment for patients with an acute coronary syndrome (ACS) awaiting further hospital intervention.

For a maximum of 14 days treatment post cardioversion in non anticoagulated patients with atrial fibrillation or until appropriate therapeutic INR level is reached.

For treatment of malignancy – associated venous thromboembolism. – **This is not included in the Cancer basket. ~~Up to 6 months~~**

10.6 The Committee considered that the above criteria could be simplified by placing the criteria under the following headings:

Venous thromboembolism (VTE)

Pregnancy

Surgery

Cardiovascular

Oncology

10.7 The Committee noted that there are a number of patients applying for LMWH via Exceptional Circumstances for a wide variety of indications. The Committee also noted that there is a perceived opinion amongst clinicians that LMWH is safer than warfarin and that the monitoring of warfarin treatment is more involved than that of LMWH. The Committee therefore considered that if LMWH was listed on the Pharmaceutical Schedule then the market would increase.

- 10.8 The Committee noted that the LMWH currently available were enoxaparin, dalteparin and tinzaparin. The Committee noted that these products have differences in their in-vivo properties, molecular weights, anticoagulant activity, indications and dosing. The Committee noted that there are few comparative trials; that there is no conclusive evidence to suggest that LMWH's differ in their safety and efficacy; and that clinical guidelines do not distinguish between them. However, the Committee noted the clinical consensus that enoxaparin is preferred for treating acute coronary syndrome.
- 10.9 The Committee noted three funding options provided by PHARMAC staff. The Committee considered that there would be no clinical issues with having only one LMWH in the hospital, DCS, and community setting as long as it was enoxaparin. The Committee also considered that there would be no clinical issues with having all three available in the hospital and DCS setting and only one available in the community setting as long as it was enoxaparin or dalteparin.
- 10.10 The Committee noted that there is small tinaparin usage and considered that PHARMAC staff should consult renal physicians and those hospitals using tinzaparin to determine reasons for its use.

11 Buprenorphine Transdermal Patch (Norspan) for the Treatment of Moderate-to-Severe Chronic Pain

- 11.1 The Committee reviewed an application from Mundipharma New Zealand Limited for the listing of buprenorphine transdermal patches on the Pharmaceutical Schedule for the treatment of moderate-to-severe chronic pain.
- 11.2 The Committee considered that the supplier's application was difficult to follow. The Committee considered that the supplier's claim that the prevalence of chronic pain in New Zealand is 18.5% seemed very high, and queried whether this was the lifetime prevalence rather than the point prevalence as indicated in the application.
- 11.3 The Committee noted that buprenorphine transdermal patches were designed to provide continuous delivery of buprenorphine for seven days.
- 11.4 The Committee considered that the strength and quality of the evidence provided was moderate. The Committee noted that the supplier had provided six clinical study reports in support of its application, only one of which has been published in a peer reviewed journal. The Committee expressed its concern as to why the remaining trials had not been published, given that they were all conducted several years ago, although the Committee noted that the supplier told PHARMAC staff that it had submitted a number of the remaining trials for publication. The Committee noted the large proportion of dropouts due to adverse reactions and lack of efficacy, and the difficulties in maintaining blinding in these types of studies.
- 11.5 The Committee considered that the study results supported the efficacy of buprenorphine transdermal patches compared with placebo in patients with chronic back pain and osteoarthritis. The Committee noted that the efficacy of buprenorphine transdermal

patches appeared similar to buprenorphine sublingual tablets in patients with osteoarthritis. The Committee considered that the study results suggested that buprenorphine transdermal patches provided similar efficacy to oxycodone/paracetamol and hydrocodone/paracetamol at doses used in the studies. The Committee noted that hydrocodone is not registered or funded in New Zealand.

- 11.6 The Committee considered that buprenorphine transdermal patches provided no particular safety advantages over other opiates. The Committee noted that approximately 15% of patients experienced skin reactions to the patch in the clinical trials.
- 11.7 The Committee considered that a 24-hour dose of a 5 mg buprenorphine transdermal patch would be roughly equivalent to 36 mg oral morphine, 18 mg oral oxycodone, 360 mg codeine, 180 mg tramadol, and 360 mg dihydrocodeine tartrate, based on the assumption that a 24-hour dose of the 5 mg patch is equivalent to 0.6 mg of sublingual buprenorphine.
- 11.8 The Committee considered that treatments likely to be used in combination with buprenorphine transdermal patches would be similar to those used with other opiates, being antiemetics, laxatives, paracetamol, anti-inflammatories and treatments for breakthrough pain.
- 11.9 The Committee noted that buprenorphine is a partial opioid receptor agonist and, as such, there is potential for buprenorphine to reduce the effect of other opiates. The Committee noted that because of this the data sheet contains a warning advising against prescribing buprenorphine transdermal patches for known or suspected narcotic dependent patients.
- 11.10 The Committee considered that there were currently no problems with access to alternative treatments. The Committee noted that widening of access to fentanyl transdermal patches, via funding of a new brand of patch, had recently been approved, and that PHARMAC staff were intending to recommend progressing a listing of tramadol via the annual tender process.
- 11.11 The Committee considered that the weekly patch could provide convenience, and potentially compliance, advantages over oral opiate formulations in some patients, particularly elderly patients who have a significant pill burden. The Committee considered that patients who have difficulty swallowing would also benefit from a weekly patch. The Committee considered that the patch could result in skin tearing/reactions in elderly patients with papery skin, given that it would need to stick firmly enough to remain stuck to the skin for a week.
- 11.12 The Committee noted that buprenorphine transdermal patches have a relatively slow onset of action and, due to its mechanism of action, it could take a relatively long time for any side effects to diminish once the patch was removed. The Committee also noted that it would be difficult to adjust the dose rapidly. In addition, buprenorphine was not currently available in oral or injectable forms for rapid titration related to breakthrough pain.
- 11.13 The Committee considered that buprenorphine transdermal patches would most benefit patients who received inadequate pain relief from other opiates, or in patients in whom

non-steroidal anti-inflammatory agents were not tolerated or contraindicated. The Committee considered that there was currently no significant unmet health need in these patients.

- 11.14 The Committee considered that if buprenorphine transdermal patches were funded there would be no clinical reason for any access restrictions, aside from those applying to controlled drugs, and that any such restrictions would be for financial reasons.
- 11.15 The Committee considered that if buprenorphine transdermal patches were funded they would be used instead of dihydrocodeine tartrate, codeine and tramadol in approximately 5% to 10% of patients, and could reduce the use of fentanyl patches (when access is widened) and tramadol (if funded). The Committee considered that buprenorphine transdermal patches could also be used instead of oxycodone and morphine, particularly in the elderly.
- 11.16 The Committee considered that funding of buprenorphine transdermal patches would be unlikely to result in any significant changes in health-sector expenditure other than for direct pharmaceutical costs.
- 11.17 The Committee noted that the supplier claimed that buprenorphine transdermal patches have low abuse potential compared with pure agonist analgesics, and that the patches have reduced potential for abuse than buprenorphine sublingual tablets because the patches are a comparatively low dose. However, the Committee noted that buprenorphine sublingual tablets were extensively abused in New Zealand before their withdrawal and considered that there remained potential for abuse of the buprenorphine transdermal patches.
- 11.18 The Committee considered that it would be difficult to target treatment to patients who would most benefit (particularly the elderly and patients who have difficulty swallowing), and that there is a high risk of widespread misuse. It was noted that a wide range of analgesic formulations is already funded, including suppositories, oral liquid, tablets/capsules and injections.
- 11.19 The Committee noted that the supplier claimed that buprenorphine transdermal patches would not be used to treat opiate dependence, and noted that this was not a registered indication for buprenorphine transdermal patches. The Committee considered that it was possible that buprenorphine transdermal patches would be used off-label for this indication.
- 11.20 The Committee **recommended** that the application for funding of buprenorphine transdermal patch be declined, taking into account the lack of longer-term studies and post-marketing data, the relative lack of studies versus funded comparator treatments and the lack of unmet clinical need.
- 11.21 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; (vi) The budgetary impact (in terms of the pharmaceutical budget and the Government's overall health budget) of any changes to the Pharmaceutical Schedule.*

12 Tenofovir Disoproxil Fumarate (Viread) for Hepatitis B

- 12.1 The Committee reviewed an application from Gilead Sciences New Zealand for the listing of tenofovir (Viread) on the Pharmaceutical Schedule for the treatment of chronic hepatitis B (CHB).
- 12.2 The Committee considered that the evidence in the application was of moderate strength and quality. Members noted that data for tenofovir in hepatitis B was limited to 48 weeks and that there was a lack of long-term follow-up with regard to safety, efficacy and resistance. The Committee noted that there were no studies comparing tenofovir with entecavir for the treatment of hepatitis B.
- 12.3 The Committee noted that the supplier provided data from four unpublished study reports. Members noted that the frequency of adverse effects was similar between tenofovir and adefovir.
- 12.4 The Committee reviewed data from study 0102, a phase 3 randomised double blind evaluation of tenofovir 300 mg daily versus adefovir 10 mg daily in patients with hepatitis B early antigen-negative CHB. Members noted that significantly more patients receiving tenofovir achieved HBV DNA below 400 copies per ml than with adefovir, 93.2% versus 63.2% ($p < 0.001$) respectively. Members noted that similar histological responses were seen with both medications.
- 12.5 The Committee reviewed the data from study 0103 a phase 3 randomised double blind evaluation of tenofovir 300 mg daily versus adefovir 10 mg daily in patients with hepatitis B early antigen-positive CHB. Members noted that 68.8% of tenofovir patients achieved undetectable viral load compared with 8.9% of adefovir patients at week 48 ($p < 0.001$). Members noted that at 48 weeks 13.6% of tenofovir patients had ongoing viral replication compared to 72.2% of adefovir patients.
- 12.6 The Committee reviewed the data from study 0106, a phase 2 randomised, double blind study comparing tenofovir monotherapy versus tenofovir and emtricitabine in patients showing ongoing viral replication while on adefovir. Members noted that 76% of patients on tenofovir monotherapy and 69% of patients on tenofovir and emtricitabine achieved complete suppression of viral load.
- 12.7 The Committee reviewed the data from protocol 0109, an open label study evaluating tenofovir 300 mg daily in patients with CHB and persistent viral replication after long term therapy with adefovir 10 mg daily. Members noted that at week 12 there was a mean change from baseline of $-2.15 \log_{10}$ copies per ml.
- 12.8 The Committee noted that meta-analysis from 13 trials showed that tenofovir had the highest probability of achieving undetectable HBV DNA levels after one year in HBeAg positive patients. Members noted there was no significant difference in the e antigen conversion rate observed.

- 12.9 The Committee noted that there are currently two treatments listed on the Pharmaceutical Schedule under Special Authority criteria for the treatment of chronic hepatitis B: lamivudine (Zeffix) as first-line treatment and adefovir dipivoxil (Hepsera) as a second-line treatment for lamivudine-resistant patients (as monotherapy or in combination with lamivudine).
- 12.10 The Committee considered that the viral resistance rates associated with lamivudine was a significant concern. It was noted that international guidelines no longer recommend that lamivudine be used for the first-line treatment of hepatitis B. Members noted that viral resistance is often seen in the presence of ongoing viral replication. Members noted that there are no long-term data available on the resistance rates for tenofovir, but that current data indicate that tenofovir is likely to be associated with significantly lower resistance rates compared with adefovir.
- 12.11 Members noted that more potent treatments are less likely to encourage development of resistance. It was noted however that no combination of treatment has yet been demonstrated to be better than monotherapy with the more potent drugs.
- 12.12 The Committee considered that there was an unmet clinical need for patients that develop viral resistance to currently available treatments.
- 12.13 The Committee **recommended** that the application to list tenofovir on the Pharmaceutical Schedule be **deferred** pending review by the Anti-infective Subcommittee of PTAC and the Hepatitis Advisory Group. Members also noted that they had received applications for entecavir and pegylated interferon and requested a Subcommittee review of the treatment paradigm for Hepatitis B.

13 Triamcinolone Hexacetonide for Juvenile Idiopathic Arthritis

- 13.1 The Committee reviewed an application from [redacted] withheld under section 9(2)(a) of the OIA], for the listing of triamcinolone hexacetonide (TH) on the Pharmaceutical Schedule for intra-articular therapy in juvenile idiopathic arthritis (JIA).
- 13.2 The Committee noted that triamcinolone acetonide (TA) is currently listed in the Pharmaceutical Schedule unrestricted, and therefore is available for treatment of this group of patients. Members noted that TH is not registered for use in New Zealand although TH has previously been listed on the Pharmaceutical Schedule.
- 13.3 The Committee noted that the clinical evidence indicates that TH is likely to provide a greater and longer suppression of intra-articular inflammation compared with TA.
- 13.4 The Committee reviewed evidence from three clinical studies, supplied by [withheld under section 9(2)(a) of the OIA]. The first study was a prospective study presenting results for 85 children randomly treated with TH or TA (Zulian et al 2003). A double-blind trial of 37 children randomly assigned to intra-articular injections with TH or TA was also reviewed by the Committee (Zulian et al 2004). The Committee also considered a retrospective chart review of 51 children who had received an intra-articular injection with either TH or TA (Eberhard BA et al 2004). All the studies showed higher rate of response and lower

rate of relapse after injections with TH. A total of six patients developed skin atrophy at the injection site.

- 13.5 The Committee considered that the clinical evidence for TH was of moderate to poor quality. It was noted that patients administered TH in the clinical trials were also administered a number of other pharmaceuticals, therefore it was difficult to evaluate the efficacy of TH. The Committee considered that there was insufficient evidence to indicate that TH was significantly more effective compared with TA.
- 13.6 The Committee considered that patients with JIA who require intra-articular injections with TH would need to receive the injections under sedation, therefore it is unlikely that treatment would be administered by a General Practitioner. The Committee therefore considered methods other than the community pharmaceutical schedule, such as in hospital treatment could be accessed to fund this treatment. The Committee therefore **recommended** that the application to list triamcinolone hexacetonide on the Pharmaceutical Schedule be **declined**.
- 13.7 The Decision Criteria particularly relevant to this recommendation are: *(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;*