PTAC meeting – 8 & 9 August 2007

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."

Note that this is not necessarily a complete record of the PTAC meeting; some material may be withheld for reasons such as protection of supplier commercial information that has been supplied in confidence.

Record of PTAC meeting held 9 & 10 May 2007

The Committee reviewed the record of the PTAC meeting held on 9 & 10 May 2007 and made the following minor amendments:

Pegylated interferon with ribavirin (Pegasys) – paragraph 8.3: replace “that these patients currently have” with “that patients with genotype 2 or 3 without bridging fibrosis or cirrhosis currently have”.

Solifenacin (Vesicare) – paragraph 12.3: replace “clinical trials - one, comparing solifenacin with placebo, one comparing solifenacin with placebo and tolterodine immediate release;” with “clinical trials: one comparing solifenacin with placebo; one comparing solifenacin with placebo and tolterodine immediate release;”.

Solifenacin (Vesicare) – paragraph 12.6: replace” The Committee considered that if solifenacin was listed in the Pharmaceutical Schedule, it would have to be as a second-line therapy behind oxybutynin. However, members noted that it is difficult to accurately define intolerance to oxybutynin, and that adverse effects are common to both agents.” with “The Committee considered that, if solifenacin were listed in the Pharmaceutical Schedule, it would have to be as a second-line therapy behind oxybutynin. However, members noted that it is difficult to define intolerance to oxybutynin, and that adverse effects are common to both agents.”

Varenicline (Champix) – paragraph 14.8: replace “there were no direct head-to-head studies” with “there were no head-to-head studies”.

Desogestrel for contraception

The Committee considered an application from Pharmaco for the listing of desogestrel (Cerazette), a progestogen-only contraceptive, on the Pharmaceutical Schedule. Members also noted a letter of support for this application from the Family Planning Association.

The Committee noted that there are two other oral progestogen-only preparations (POPs) listed in the Pharmaceutical Schedule, levonorgestrel and norethisterone. Members noted that these POPs primarily work by thickening the cervical mucus and therefore preventing sperm motility, but also by preventing ovulation in around half of all cases.

Members noted that POPs are primarily prescribed for lactating mothers, and in women considered to be at an elevated risk of venous thromboembolism. POPs are usually not used in preference to combined oral contraceptives (COCs) because they have a narrow window of compliance, cause irregular and unpredictable bleeding and can cause androgenic side-effects.

Members noted that the Committee had reviewed an application for the listing of desogestrel in 2000, and that at that stage the Committee was concerned about the safety of desogestrel. The Committee noted that there was no new evidence submitted

with this application, and that there were no studies presented that compared desogestrel with norethisterone, the most commonly prescribed POP in New Zealand. The Committee considered that updated safety data, particularly post-marketing surveillance data, would be useful.

Members noted one study (Eur J Contracept Reprod Health Care. 1998 Dec;3(4):169-78) that examined the use of desogestrel (n=989) compared with levonorgestrel (n=331), finding an improvement in the Pearl index in favour of desogestrel, although this advantage was not statistically significant.

Members noted that desogestrel has a lower rate of androgenic effects than other POPs, and because of this could be administered at a higher dose, which has the effect of increasing ovulation suppression. Members also noted that desogestrel has a greater window of compliance (12 hours versus 3 hours) than other POPs.

The Committee noted that the supplier had claimed that there would be a saving to the health sector from a reduction in the number of terminations. Members noted that while this is a possibility, there was no evidence provided to support this claim. Members noted that there is no evidence that a significant number of New Zealand women seeking terminations had been taking a progestogen-only contraceptive, and therefore could benefit from desogestrel.

The Committee noted that desogestrel has been available in a third-generation COC for many years, and that there had been a prescribing trend away from the use of third generation COCs due to elevated risks of venous thromboembolism (RR=2). Members noted that since 2000 there have been further reviews on the safety of desogestrel-containing COCs, which continue to highlight the risk of venous thromboembolism (RR=1.7 over second-generation COCs).

The Committee noted that desogestrel is significantly more expensive than all other oral contraceptives, and considered that, if listed fully funded, it would likely result in a significant shift from other POPs and some shift from COCs.

The Committee **recommended** that desogestrel be listed in the Pharmaceutical Schedule and assigned a low priority to this recommendation.

The Decision Criteria relevant to this recommendation are: *(i) The health needs of all eligible people within New Zealand* as the rate of unplanned pregnancies continues to be very high in New Zealand; *(iii) The availability and suitability of existing medicines, therapeutic medical devices and related products and related things* as currently funded progestogen-only preparations have a narrow window of compliance and are therefore not always a suitable alternative to combination oral contraceptives*; and (v) The cost-effectiveness of meeting health needs by funding pharmaceuticals rather than using other publicly funded health and disability support services* as desogestrel would be significantly more expensive than all other funded oral contraception options.

Rituximab (MabThera) for indolent non-Hodgkin's lymphoma

The Committee reviewed a letter from Roche Products (NZ) Ltd in response to its February 2007 minute regarding the listing of rituximab (Mabthera) on the Pharmaceutical Schedule for use in combination with chemotherapy for patients with low-grade, symptomatic (stage III/IV), follicular non-Hodgkin's lymphoma (NHL). The Committee also reviewed identical letters from two groups of clinicians supporting this application.

The Committee reviewed updated survival data from study M39021 comparing cyclophosphamide, vincristine and prednisone (CVP) with R-CVP (CVP plus rituximab) (Marcus et al, American Society of Haematology (ASH) meeting, December 11 2006, abstract 481) and another Phase III trial comparing mitoxantrone, chlorambucil and prednisone (MCP) with MCP plus rituximab (Herold et al J Clin Oncol 25 (15) May 20 2007, pp 1-7).

The Committee noted that, in M39021, at median 53 months (4.4 years) follow-up, patients treated with R-CVP had a small but statistically significant improvement in overall survival compared with CVP treated patients (83% versus 77%, p=0.03). Similarly, members noted that in the Herold Study, 4-year overall survival rates were 87% for R-MCP compared with 74% for MCP (p=0.0096).

The Committee considered that these data demonstrate a survival advantage in favour of adding rituximab to chemotherapy in patients with low-grade, symptomatic (stage III/IV), follicular non-Hodgkin's lymphoma (NHL). The Committee recommended that these survival data be taken into account in any PHARMAC cost-utility analysis.

The Committee considered that the high drop-out rates seen in these studies were likely due to the open-label design of the studies and the higher rate of treatment failure in the control arms of the studies.

The Committee considered that, although there was no overall difference in infection rate, the incidence of grade 3 or 4 neutropenia was higher in rituximab-treated patients. The Committee considered that costs associated with the administration of GCSF in these patients would be limited due to dose reduction or dose delays being the standard management strategy in NZ for patients with grade 3 or 4 neutropenia. However, there would be additional costs associated with treatment of rituximab-related neutropenia; for example, standard infection work-up procedures and empirical treatment while results were awaited.

The Committee also reviewed data from various studies examining the use of rituximab (+/- chemotherapy) re-treatment in relapsed/refractory patients who had previously responded to rituximab (+/- chemotherapy), and the use of rituximab as maintenance treatment in patients responding to rituximab (+ chemotherapy) re-treatment.

The Committee noted that there appeared to be some benefit in using rituximab as re-treatment and/or maintenance therapy; however, before making any specific recommendations for its use in these settings, the Committee considered that a cost-utility analysis should be performed.

The Committee reiterated its previous **recommendation** that rituximab be listed on the Pharmaceutical Schedule for use in combination with chemotherapy for patients with low-grade, symptomatic (stage III/IV), follicular non-Hodgkin's lymphoma (NHL). The Committee gave this recommendation a low to medium priority.

The Committee further **recommended** that the application be referred to the Cancer Treatments Subcommittee (CaTSoP) for advice regarding appropriate combination chemotherapy regimens and whether or not relapsed patients should be able to access a second course of rituximab and maintenance treatment.

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, 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.

Exenatide (Byetta) for type 2 diabetes mellitus

The Committee considered an application from Eli Lilly to list exenatide (Byetta) on the Pharmaceutical Schedule. The Committee noted that exenatide was an injectable incretin mimetic used in the treatment of patients with type 2 diabetes

The Committee noted that the application proposed that exenatide would be listed on the Pharmaceutical Schedule subject to the following Special Authority criteria:

> Initial applications only from a relevant specialist. (Endocrinologists, Diabetologists and General Physicians only) Approvals valid for 6 months for patient with type 2 diabetes under the following treatment regimens:
>
> In Combination with Sulphonylurea
>
> For use in combination with a sulphonylurea for patients who after diet and lifestyle changes and a six-month trial of sulphonylurea, titrated to maximum effective dosage, have poor glycaemic control (defined as HbA1c > 7.5% measured within the last month of the six-month period). AND
>
> Metformin is contraindicated or not tolerated after a minimum of a four-week trial period. OR
>
> In Combination with Metformin
>
> For use in combination with metformin for patients who after diet and lifestyle changes and a six-month trial of metformin, titrated to maximum effective dosage, have poor glycaemic control (defined as HbA1c > 7.5% measured within the last month of the six month period). AND
>
> Sulphonylurea is contraindicated or not tolerated, or the patient's body mass index (BMI) exceeds 33 kg/m^2.
>
> In Combination with Metformin and a Sulphonylurea
>
> For use in combination with metformin and sulphonylurea for patients who after diet and lifestyle changes and a six-month trial of the maximum tolerated dose of metformin and sulphonylurea have poor glycaemic control (defined as HbA1c > 7.5% measured within the last month of the six month period).

Note - Not to be used in combination with Insulin

The Committee considered that the application was of good strength and quality. However, it considered that the cost-utility analysis provided was of limited relevance to the current treatments available in New Zealand and the proposed Special Authority criteria.

The Committee noted that exenatide represented a unique mode of action relative to other treatments available.

The Committee noted the key trials comparing exenatide with other oral treatments currently used in the treatment of patients with type 2 diabetes: three randomised, triple-blind, 3-arm parallel-group trials comparing exenatide 5 or 10 µg with placebo twice daily for 30 weeks in combination with either metformin (≥ 1,500 mg/day) (Defronzo RA et al. 2005), a sulphonylurea (Buse JB et al. 2004) or metformin and a sulphonylurea. (Kendall DM et al. 2005).

The Committee noted that in the key trials, treatment with exenatide was associated with a decrease in HbA1c of approximately 0.8% and a reduction in body weight of approximately 2 kg. The Committee questioned whether the magnitude of weight reduction would be clinically meaningful. However, the Committee noted the ongoing weight reductions and somewhat favourable cardiovascular risks in the open-label extension.

The Committee noted that treatment with exenatide was associated with a high rate of nausea and questioned whether nausea was a contributor to the weight loss reported in the treatment groups.

The Committee noted that the trial population recruited in the key trials included patients with HbA1c from 7.1% to 11.0%. Members questioned whether an HbA1c percentage measure of 7.1% constituted “out of control” diabetes mellitus.

The Committee considered two open-label, randomised, non-inferiority trials that compared exenatide 10 µg twice daily with insulin glargine once daily (Heine RJ et al. 2005) and biphasic insulin aspart twice daily (Nauck MA et al. 2007)

The Committee noted that treatment with exenatide resulted in similar reductions in HbA1c compared with insulin glargine (both -1.1%) and biphasic insulin aspart (-1.04% vs. -0.89%). The Committee noted that in both studies, patients treated with exenatide showed significant reductions in mean body weight of approximately 2.4kg, whilst those on insulin had a weight increase.

The Committee noted that exenatide was associated with a similar rate of hypoglycaemic events when compared to insulin glargine, but was associated with a lower rate of hypoglycaemia when compared to biphasic insulin aspart.

The Committee questioned the appropriate place in therapy of exenatide. The Committee considered that, as it delivered a fixed dose, it offered an improvement over multiple daily injections of insulin. However, the Committee noted that as exenatide

required twice-daily injections, there was limited value over once-daily insulin preparations such as insulin glargine.

The Committee noted that the average daily cost of exenatide was significantly higher than other treatments currently listed on the Pharmaceutical Schedule. The Committee considered that the incremental benefits, as seen in the clinical trial data, were unlikely to justify the additional cost of exenatide.

The Committee considered that longer-term data were required to demonstrate a satisfactory safety profile and prolonged and consistent therapeutic benefit.

The Committee **recommended** that the application to list exenatide on the Pharmaceutical Schedule be declined at this time.

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; (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.

Ranibizumab (Lucentis) for neo-vascular (wet) age-related macular degeneration (AMD)

The Committee reviewed an application from Novartis New Zealand Limited for the listing of ranibizumab (Lucentis) on the Pharmaceutical Schedule for the treatment of neo-vascular (wet) age-related macular degeneration (AMD).

The Committee noted that wet AMD is quite prevalent and that current and potential treatments include verteporfin (Visudyne) photodynamic therapy, pegatinib sodium (Macugen), bevacizumab (Avastin) and ranibizumab (Lucentis). The Committee noted the cost of these treatments.

The Committee noted the results of the MARINA (Rosenfeld et al, 2006 and Boyer et al, 2007), ANCHOR (Brown et al, 2006), PIER (Yue et al, 2006), and FOCUS (Heier et al, 2006) clinical trials. The Committee noted that in all of these trials the visual outcomes of the patients treated with ranibizumab were significantly better than the comparators (sham injections or verteporfin) as measured by the proportions of patients who gained ≥ 15 letters or lost < 15 letters, and by the mean change in visual acuity. The Committee also noted that the number of serious side effects reported in these trials (including endophthalmitis and serious uveitis) was low.

The Committee considered that the studies were of good quality; however, it noted that there was variability in the dosing regimes employed, and the proposed maintenance dosing regime was flexible and based on the open-label, non-randomised PRONTO trial

(Fung et al, 2007). The Committee also noted that the follow-up data was limited to two years.

The Committee considered that there was no one patient population that appeared to benefit from ranibizumab more than any other. It also considered that while wet AMD could be classified into a number of subgroups, this was difficult, as about 30% of cases would be reclassified if a second opinion was sought.

The Committee noted the other treatments for wet AMD and considered that the outcome of head-to-head trials of ranibizumab with bevacizumab would be of interest.

The Committee considered that the proposed cost of ranibizumab was very high and therefore it could not be recommended for listing on the Pharmaceutical Schedule, as the budgetary impact would be significant.

The Committee considered that this was an area of health need; however, it considered that treatment for wet AMD with ranibizumab would only occur in hospital outpatient clinics or in the private setting. The Committee considered that the use of ranibizumab in outpatient clinics could be funded by District Health Boards.

The Committee **recommended** that ranibizumab be declined for listing on the Pharmaceutical Schedule due to the budgetary impact and considered that the place of AMD treatments, especially high cost treatments, is within DHB ophthalmology service budgets.

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; (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.

Rosuvastatin (Crestor) for hypercholesterolaemia and dyslipidaemia

The Committee reviewed a submission from AstraZeneca regarding the safety of the 40 mg dose of rosuvastatin.

The Committee noted that it had considered the listing of rosuvastatin twice previously and that in August 2004 it had considered that there were safety concerns, including an increased risk of myositis and proteinuria, with the 40 mg and 80 mg doses.

The Committee noted the claim in the submission that rosuvastatin treatment at 40 mg daily is safe and that there is no reason to restrict its use as an appropriate therapeutic choice.

The Committee considered the information supplied by AstraZeneca and the use of the 40 mg tablet in other countries including Australia, the United States of America and the United Kingdom.

The Committee noted that no long-term safety or clinical outcome data were presented.

The Committee noted that there was a modest gain, in terms of reduction in cholesterol, when increasing the dose from 20 mg to 40 mg daily, but there is likely to be at least a doubling in the potential rate of side-effects. However, the Committee considered that 40 mg rosuvastatin may be appropriate in a small number of patients, although its use should be carefully considered.

The Committee considered that rosuvastatin 40 mg could be listed in the Pharmaceutical Schedule but noted that:

- The PBAC (Australia) advised that the 40 mg dose should be prescribed with caution;
- The NPS RADAR (Rational Assessment of Drugs and Research) December 2006 summary for rosuvastatin states that "the 40 mg dose should only be considered for patients who are still at high cardiovascular risk after their response to 20 mg daily is assessed and in whom regular follow-up is planned. Do not exceed the 40 mg dose in any patient and do not use this dose in patients of Asian descent";
- The United States datasheet states that "The 40 mg dose of Crestor is reserved only for those patients who have not achieved an LDL-C goal utilization on the 20 mg dose once daily (see WARNINGS. Myopathy/Rhabdomyolysis)"; and that,
- The February 2005 MeReC Briefing (Issue 28) providing an "Update on statins" states that the 40 mg dose should only be necessary in a minority of patients with severe hypercholesterolemia at high CV risk.

The Committee considered that the 40 mg dose should not be exceeded in any patient and that the 40 mg dose should not be used in patients of Asian descent.

The Committee noted that in Australia, the USA and the UK, the 5 mg dose is also registered. The Committee noted that the usual daily dose internationally is 5 mg to 20 mg, with the appropriate starting dose being 5 mg, especially in patients of Asian descent, patients with severe renal impairment or patients on cyclosporin.

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The Committee considered that rosuvastatin should not be listed on the Pharmaceutical Schedule without listing the 5 mg tablet and the current New Zealand datasheet being updated.

The Committee considered that while rosuvastatin 40 mg could be listed on the Pharmaceutical Schedule, due to safety concerns it **recommended** that:

1. Any listing include an annotation in the Pharmaceutical Schedule and on any relevant forms, including on the Special Authority form, that indicates that the rosuvastatin 40 mg dose may be associated with increased risk of proteinuria and increased potential for myositis/rhabdomyolysis and should be used with caution.

2. While the lower doses of rosuvastatin could be listed without Special Authority, the 40 mg dose should always be restricted by Special Authority

The Committee considered the use of ezetimibe in combination with rosuvastatin. The Committee noted the result of the EXPLORER study (Am J Cardiol 2007; 99: 673-680). The Committee considered that safety issues with the combination of rosuvastatin and ezetimibe do not seem likely but that the current safety and long-term benefit data are inadequate.

The Committee **recommended** that rosuvastatin 40 mg be listed on the Pharmaceutical Schedule with a low to medium priority, as a small number of patients may benefit from its use.

The Committee considered the dosing equivalence between rosuvastatin and atorvastatin. The Committee noted the lack of head-to-head trials comparing the clinical efficacy of different doses of different statins, the lack of standard deviations presented for the results of the trials comparing the LDL-lowering of different statins, and the lack of statistical analysis at a dose level with these trials.

The Committee noted that the NPS radar and PBAC assessments considered that the ratio of equi-effective doses between rosuvastatin and atorvastatin was 1:3. The Committee also considered the results of the STELLAR trial (2003) which suggested that rosuvastatin 10 mg was equivalent to atorvastatin 40 mg, rosuvastatin 20 mg was equivalent to atorvastatin 80 mg, and rosuvastatin 40 mg was equivalent to atorvastatin 80 mg. The Committee noted the small additional absolute reduction in cholesterol levels that rosuvastatin 40 mg provides over rosuvastatin 20 mg and atorvastatin 80 mg.

For the purposes of reference pricing, the Committee considered that on average, a 1:3 ratio of rosuvastatin and atorvastatin was appropriate. However, the Committee noted that this implies a linear relationship, whereas the dose response curve is non-linear, with a lower-end to middle dose ratio of approximately 1:4, and a top-end dose ratio of approximately 1:2. Therefore, the Committee considered that rosuvastatin and atorvastatin had the same or similar effect as follows:

Rosuvastatin	Atorvastatin
10 mg	40 mg

20 mg	80 mg
40 mg	80 mg

The Committee considered, however, that there may be a small number of patients who gain a small benefit from the 40 mg dose of rosuvastatin.

Bicalutamide for advanced prostate cancer

The Committee reviewed an application from Rex Medical Ltd for the listing of bicalutamide (Bicalutamide-Rex) on the Pharmaceutical Schedule for the treatment of advanced prostate cancer, in combination with GnRH (LHRH) agonist therapy or surgical castration.

The Committee noted that this application was from a generic supplier (Rex-Medical). Members noted that a funding application for the proprietary brand bicalutamide (Cosudex, Astra Zeneca) was submitted for review at PTAC's November 2001 meeting; however, it was not reviewed by PTAC at that time as it had not been approved by Medsafe for the funding indication requested. Members noted that although AstraZeneca was invited to resubmit its application it had yet to do so. The Committee noted that Bicalutamide-Rex was bioequivalent to Cosudex.

Prostate cancer is the most commonly diagnosed cancer in New Zealand men and the third most common cause of male cancer deaths. The majority of prostate cancers are early or locally advanced and can be controlled for many years using surgery, medical (GnRH/LHRH analogues) or surgical castration, radiotherapy to the prostate and surrounding area, or a combination of treatments. Approximately 20-25% of prostate cancers are advanced/metastatic at diagnosis and the prognosis for this group is poor. Currently, advanced prostate cancers are treated with non-steroidal anti-androgens in combination with medical (combined androgen blockade, CAB) or surgical castration.

The Committee noted that bicalutamide is a non-steroidal anti-androgen, which acts by competitively blocking the binding of testosterone to receptors on prostate cancer cells. The Committee further noted that Bicalutamide-Rex is indicated for the treatment of advanced prostate cancer in combination with GnRH (LHRH) agonist therapy or surgical castration. The Committee noted that the other anti-androgens, including flutamide tablets (Flutamin) and cyproterone acetate tablets and injection (Siterone, Androcur Depot) are currently fully funded on the Pharmaceutical Schedule.

The Committee noted that systematic reviews/meta-analyses of clinical trials demonstrated that the addition of non-steroidal anti-androgens to castration resulted in a small (approximately 3%) improvement in overall survival, but was associated with increased adverse events and reduced quality of life.

The Committee considered that currently in New Zealand advanced prostate cancers would likely be treated with flutamide in combination with medical or surgical castration.

The Committee reviewed data from a key multicentre, randomised, double-blind, non-inferiority phase 3 clinical trial comparing bicalutamide (50mg once daily) with flutamide (250mg three times daily) combined with GnRH/LHRH analogues in 813 patients with advanced prostate cancer (Schellhammer, Urology, 1997 50(3): 330-336). Data out to 160 weeks indicated that time to progression and overall survival favoured bicalutamide, although the results were not statistically significant. However, the incidence of diarrhoea was significantly lower for bicalutamide compared with flutamide (12% versus 26%, p=<0.001) and the median duration of treatment was higher for the bicalutamide group compared to the flutamide group (72 weeks vs 59 weeks), likely due to its better tolerability profile.

The Committee considered that the data supported the assertion that bicalutamide was not inferior to flutamide in advanced prostate cancer and that it was associated with a better tolerability profile and lower pill burden. The Committee further noted [

] increased duration of treatment compared with flutamide due to the better tolerability of bicalutamide.

The Committee noted that studies had reported on the use of 150 mg bicalutamide as monotherapy in locally advanced or advanced prostate cancer or as adjuvant therapy in localised or locally advanced prostate cancer. The Committee considered that if bicalutamide was listed on the Pharmaceutical Schedule there would likely be off-label use in these settings. However, data in these settings failed to demonstrate a survival advantage and reported increased adverse events; therefore, at this time the Committee did not recommend bicalutamide for use in these settings.

Members noted that flutamide was currently listed on the Pharmaceutical Schedule without Special Authority, therefore, listing bicalutamide in the same way would likely lead to usage outside the proposed indication of advanced prostate cancer.

The Committee **recommended** that because it was associated with similar efficacy [
] and better tolerated than flutamide in the advanced prostate cancer setting, bicalutamide should be listed on the Pharmaceutical Schedule with a high priority for this indication.

The Committee further recommended that the application be referred to the Cancer Treatments Subcommittee (CaTSoP) for advice regarding appropriate targeting criteria for advanced prostate cancer and advice regarding issues relating to usage in off-label indications.

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, and (iv) the clinical benefits and risks of pharmaceuticals.

Adalimumab delivery system – Humira Pen

The Committee considered an application from Abbott Laboratories to list an automated adalimumab injection delivery device (Humira Pen) on the Pharmaceutical Schedule.

The Committee noted that it was not proposed that the Humira Pen would replace the current pre-filled adalimumab syringe, and that it was proposed that the Humira Pen would be listed at the same price as the pre-filled adalimumab syringe.

The Committee noted a small study that compared patient-reported experience when using the Humira Pen and the pre-filled adalimumab syringe (Kivitz, A et al. 2006). The Committee noted that the Humira pen was generally very well tolerated and did not present any additional clinical risk compared with the pre-filled adalimumab syringe.

The Committee considered that the Humira Pen presented a benefit to patients as it would make administration of adalimumab easier, and could reduce the number of patients who are unable to self-inject. Members estimated that approximately 30% of patients required the assistance of another person to administer adalimumab using the current pre-filled adalimumab syringe.

The Committee noted that the Humira Pen would be beneficial to patients who had fear of injections, as the needle tip was not visible.

The Committee **recommended** that the Humira Pen be listed on the Pharmaceutical Schedule along side the pre-filled adalimumab syringe with a high priority.

Pemetrexed disodium (Alimta) for locally advanced or metastatic non-small cell lung cancer

The Committee reviewed a letter from Eli Lilly in response to its February 2007 minute regarding the listing of pemetrexed disodium (Alimta) on the Pharmaceutical Schedule for the treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) after prior platinum-based chemotherapy (second-line).

The Committee noted that the supplier considered that it was inappropriate for the Committee to compare differences in total hospitalisation rates between pemetrexed and docetaxel-treated patients in study JMEI (J Clin Oncol. 2004 May 1;22(9):1589-97) since these differences were principally driven by differences in drug administration, social reasons, protocol procedures or non-drug related adverse events.

In particular, the Committee noted that, in the trial, there were more admission days for 'social reasons' with pemetrexed compared with docetaxel (380 vs 163), mainly due to there being more patients who were hospitalised for an extended period at trial sites in Russia.

The Committee noted that, for the purposes of economic analysis, the supplier considered that it is only appropriate to compare hospitalisations due to drug-related adverse events, and that under such comparison the number and duration of hospitalisations was lower in pemetrexed-treated patients.

The Committee considered that justification of differences in hospitalisation rates due to factors such as social reasons simply highlighted its concern that the study was of poor

quality and raised doubts amongst members about the generalisability of the study results and the validity of other study endpoints.

The Committee reiterated its August 2006 and February 2007 **recommendation** that the application be declined on the basis that the evidence showed no additional efficacy benefit of pemetrexed compared with docetaxel, which is currently funded for second-line treatment of NSCLC.

The Committee **recommended** that its minute be provided to the Cancer Treatments Subcommittee of PTAC for comment.

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, and, (iv) the clinical benefits and risks of pharmaceuticals.