

## **Cancer Treatments Subcommittee of PTAC (CaTSoP) meeting**

**held 13 June 2008**

**(minutes for web publishing)**

CaTSoP minutes are published in accordance with the *Terms of Reference for the Pharmacology and Therapeutics Advisory Committee (PTAC) and PTAC Subcommittees 2008*:

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

CaTSoP 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.

Some material has been withheld to protect information which is subject to an obligation of confidence, where the making available of the information would be likely to prejudice the supply of similar information, or information from the same source, and it is in the public interest that such information should continue to be supplied (section 9(2)(ba)(i) of the Official Information Act 1982 (OIA)).

PTAC formally reviewed:

- (a) at its meeting on 4 July 2008, the CaTSoP minute in relation to trastuzumab and the relevant PTAC minute is available on the PHARMAC website; and
- (b) at its meeting on 19 & 20 February 2009, the remainder of these CaTSoP minutes.

The records of the PTAC meetings are available on the PHARMAC website.

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# 1 High dose imatinib (Glivec), dasatinib (Sprycel) and nilotinib (Tasigna) for imatinib refractory chronic myeloid leukaemia (CML)

- 1.1 The Subcommittee noted that the introduction of funded imatinib (Glivec) in 2002 for the treatment of CML has been associated with high rates of haematologic and cytogenetic response. Members noted that the standard dose of imatinib is 400 mg/day, but that some patients with accelerated or blast-phase CML were getting up to 600–800 mg/day on compassionate supply (noting these higher doses are not currently funded). However, members noted that some patients are unable to tolerate imatinib and some develop imatinib-resistant forms of CML. Members considered that the aim of CML treatment was to keep patients in the chronic phase, or even return accelerated phase patients back to chronic phase. Members considered that once patients had progressed to blast phase of disease there was little chance of treatment returning a patient to chronic phase and that such patients may be candidates for bone marrow transplantation.
- 1.2 The Subcommittee considered that currently patients intolerant to imatinib treatment would not remain on treatment; however, some refractory patients may continue treatment with imatinib depending on the clinical nature of disease progression. The Subcommittee considered that approximately 15% of the current pool of imatinib-treated CML patients would be eligible for alternative treatments if they were funded under criteria restricting access to patients with imatinib-refractory disease.
- 1.3 The Subcommittee considered that relative expenditure on current treatments for CML was very high (relative to expenditure on all other cancers) at approximately 20% of the entire hospital cancer treatments budget. Members considered that this expenditure would increase with introduction of new treatment options.

## *Dose escalation of imatinib*

- 1.4 The Subcommittee reviewed its previous minute from December 2007 and PTAC's minute from February 2007 regarding an application from Novartis to increase the maximum funded dose of imatinib from 400 mg to 600 mg per day in patients with chronic phase CML where clinically appropriate.
- 1.5 The Subcommittee re-iterated its previous **recommendation** from December 2007 that doses up to 600 mg/day imatinib should be funded, with high priority, for patients with chronic phase CML who do not respond to 400 mg/day treatment, with non-response defined as per the ELN classification system. However, the Subcommittee noted that its high priority recommendation was on the basis of there being no other funded option for these patients.

## *Dasatinib*

- 1.6 The Subcommittee reviewed its previous minute from December 2007 and PTAC's minutes from August 2007 and February 2008 regarding an application from Bristol-Myers Squibb for the listing of dasatinib (Sprycel) for the treatment of patients with imatinib-resistant or imatinib-intolerant, accelerated or blast phase, CML. The Subcommittee also reviewed further information from Bristol-Myers Squibb regarding its application for the listing of dasatinib.
- 1.7 The Subcommittee noted that PTAC had considered that the December 2007 recommendation of CaTSoP to list dasatinib as a bridge to allogeneic stem cell transplant treatment for three to four months in patients with accelerated or blast phase CML resistant or intolerant to imatinib would be difficult to implement. Members agreed that such a recommendation would be difficult to implement, for example if such a patient was stabilised on dasatinib it is quite likely that it would be considered preferable to keep them on dasatinib while a response was maintained, rather than proceeding to a transplant. Members noted that in making its previous recommendation the Subcommittee had been aware of the very high cost of dasatinib and had thus aimed to target treatment to those with a good possibility of receiving a transplant. However, the Subcommittee considered that dasatinib would provide the same benefit to patients with accelerated or blast phase CML resistant or intolerant to imatinib regardless of whether or not a transplant donor was available.
- 1.8 The Subcommittee considered that the further information provided by the supplier, including longer-term data from the phase II studies CA180-005, CA180-006 and CA180-015 and data from a new phase III study (CA180-035), was of good quality and demonstrated durability of response to dasatinib in accelerated phase patients.
- 1.9 The Subcommittee **recommended** that dasatinib be listed on the Pharmaceutical Schedule for the treatment of patients with imatinib-resistant or imatinib-intolerant accelerated phase CML. The Subcommittee gave this recommendation a medium priority. The Subcommittee also considered that dasatinib may have a role in the treatment of patients with imatinib-resistant or imatinib-intolerant chronic phase CML; however, it noted that the supplier had not sought funding for dasatinib in this patient group.
- 1.10 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.*

## Nilotinib<sup>1</sup>

- 1.11 The Subcommittee also reviewed an application from Novartis New Zealand Limited for a listing of nilotinib (Tasigna) for the treatment of adult patients with imatinib-resistant or imatinib-intolerant, chronic or accelerated phase CML, and the relevant PTAC minute from May 2008.
- 1.12 The Committee noted that similar to dasatinib, nilotinib is an oral tyrosine kinase inhibitor, selective for BCR-ABL, derived from imatinib.
- 1.13 The Subcommittee considered that the quality of evidence provided was poor, comprising relatively early data from a single open-label non-randomised phase II study across various different disease cohorts. Members noted that there were no direct comparative studies of nilotinib versus other relevant comparators, i.e. dasatinib or high-dose imatinib.
- 1.14 The Subcommittee noted that that in this study nilotinib was dosed at 400 mg twice daily but the dose was able to be increased to 600 mg twice daily if a patient had not achieved a Haematological Response (HR) by three months, a Cytogenetic Response (CyR) by six months, or a Major Cytogenetic Response (MCyR) by 12 months. Members considered that in practice most patients would receive 400 mg twice daily and increasing the dose would provide little extra benefit.
- 1.15 The Subcommittee considered that the evidence provided demonstrated efficacy of nilotinib in patients with chronic and accelerated phase disease, albeit with relatively short-term follow-up.
- 1.16 The Subcommittee considered that the cost of nilotinib was high and that a key assumption of the supplier's, namely that patients currently resistant or intolerant to imatinib are all continuing with imatinib treatment, was incorrect, therefore the cost would be higher than the supplier's estimates. However, members considered that funding nilotinib may reduce the number, and associated costs, of bone marrow transplants.
- 1.17 The Subcommittee **recommended** that nilotinib be listed on the Pharmaceutical Schedule for imatinib-resistant or imatinib-intolerant, chronic or accelerated phase CML. The Subcommittee gave this recommendation a medium priority.
- 1.18 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*

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<sup>1</sup> At its February 2009 meeting, PTAC noted the recommendation by CaTSoP to list nilotinib on the Pharmaceutical Schedule; however PTAC considered that the data supporting nilotinib was very weak, therefore PTAC reiterated its previous recommendation to decline the application to list nilotinib on the Pharmaceutical Schedule.

*budgetary impact (in terms of the pharmaceutical budget and the Government's overall health budget) of any changes to the Pharmaceutical Schedule.*

### *General discussion*

- 1.19 The Subcommittee considered that imatinib remained the preferred first-line treatment for patients with CML. Members considered the relative place in therapy of the various treatment options recently evaluated for the second-line treatment of imatinib-resistant/intolerant patients – that is, high-dose imatinib versus dasatinib versus nilotinib.
- 1.20 The Subcommittee considered that although there were no direct comparative studies of nilotinib with dasatinib the two treatments were broadly similar, although there were better long-term data with dasatinib. Members considered that nilotinib and dasatinib had slightly different side-effect profiles; however, the differences were unlikely to be clinically significant.
- 1.21 The Subcommittee **recommended** that at minimum at least one of nilotinib, dasatinib or high-dose imatinib be listed on the Pharmaceutical Schedule for patients with imatinib-resistant or imatinib-intolerant, chronic or accelerated phase CML. Members considered that in the event that only one treatment were to be funded the relative priority of nilotinib and dasatinib was the same, with both being a higher priority for funding than high-dose imatinib. This was despite the fact that high-dose imatinib was previously given a high priority and dasatinib and nilotinib were each given a medium priority on this occasion.
- 1.22 Members considered that if dasatinib and nilotinib were both to be listed on the Pharmaceutical Schedule they should only be used as monotherapy and not in combination with each other or with imatinib (any dose).
- 1.23 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.*

## **2 Pegylated liposomal doxorubicin (Caelyx) for ovarian cancer**

- 2.1 The Subcommittee reviewed an application from Schering-Plough for the listing of pegylated liposomal doxorubicin hydrochloride (Caelyx, PLDH) on the

Pharmaceutical Schedule for the treatment of advanced epithelial ovarian cancer in women who have failed a first-line platinum-based chemotherapy regimen.

- 2.2 The Subcommittee noted that the application had been reviewed by PTAC at its November 2006 meeting and that PTAC considered that PLDH may have a place in therapy for platinum-sensitive patients; however, given its high cost and unfavourable toxicity profile in what is essentially a palliative setting PTAC had recommended that the application be declined. The Subcommittee noted that it had reviewed this PTAC minute at its December 2007 meeting and had raised some concerns. Members noted that given these concerns the PTAC chair had agreed that CaTSoP should be given the opportunity to review the supplier's application. Members expressed their appreciation of the opportunity to review this application.
- 2.3 The Subcommittee noted that ovarian cancer is the fifth most common cancer type in New Zealand women, with increased incidence in Maori compared with non-Maori.
- 2.4 The Subcommittee noted that currently first-line treatment for ovarian cancer is usually surgery followed by chemotherapy with a platinum agent (usually carboplatin) in combination with paclitaxel. Second-line treatment options have changed over recent years and that treatment would now include repeated carboplatin in combination with a taxane (in those for whom prior toxicity did not preclude taxane use) or carboplatin in combination with gemcitabine. Members noted that response to second-line treatment was dependent on platinum sensitivity (usually defined as relapse more than six months after first-line treatment with a platinum agent). Members noted that in New Zealand current third-line treatment options consisted of weekly (three weeks out of four) gemcitabine (for patients who had not previously received gemcitabine as part of second-line treatment) or oral etoposide. Members considered that neither of these third-line treatment options was optimal, with oral etoposide in particular being associated with wide intra-patient bioavailability, a narrow therapeutic index and complete alopecia. Members also considered that oral medication was a particularly difficult option in this population given the propensity for women in this situation to present with a degree of bowel obstruction. Members considered that maintaining quality of life in this patient population was important, and that as a result of these changes in practice there is an unmet need for these women.
- 2.5 The Subcommittee noted that PLDH is a pegylated liposomal formulation of doxorubicin hydrochloride. Members considered that the key evidence was from study 30-49 reported by Gorden et al (Gynaecologic Oncology 2004). This study was a Phase III open-label RCT of second-line treatment of ovarian cancer in 474 patients, most of whom had been previously treated with platinum agents and taxanes. Patients were randomised to receive PLDH 50 mg/m<sup>2</sup> every 28 days (n=239) or topotecan 1.5 mg/m<sup>2</sup> per day for five days every 21 days (n=235). The trial met its primary endpoint, but is a non-inferiority design. Members considered that the quality of the evidence was good but its application to the New Zealand setting was limited since the comparator, topotecan (Hycamtin, GSK), although registered in New Zealand, is not currently available.

- 2.6 Members noted that in a subgroup analysis the survival benefit for PLDH was better than for topotecan in the platinum-sensitive patients (46% of the trial population): 108 weeks for PLDH vs. 70 weeks for topotecan ( $p=0.017$ , HR 1.432, 95% CI 1.066-1.923), but that there was no such survival difference in platinum-resistant patients. Members noted however that this should be interpreted with caution due to the lack of power and retrospective nature of the subgroup analysis.
- 2.7 The Subcommittee noted that a trial in the second-line setting comparing combination PLDH and carboplatin with carboplatin and paclitaxel was ongoing.
- 2.8 The Subcommittee noted that although PDLH was associated with some adverse effects, including severe skin reactions and stomatitis, most were manageable and, importantly, unlike oral etoposide or gemcitabine, the incidence of haematological and gastrointestinal toxicity was low and PLDH did not cause alopecia. The Subcommittee noted that alopecia and gastrointestinal toxicity were a significant issue for these patients. Members noted that a reduction in gastrointestinal toxicity was an important consideration in ovarian cancer patients who had undergone major abdominal surgery and that oral etoposide is not suitable for some patients with relapsed ovarian cancer because they may have extensive peritoneal disease/subacute bowel obstruction. The Subcommittee considered that the reduced frequency of dosing for PLDH compared with gemcitabine (once monthly versus two to three times monthly) would be beneficial to patients and to DHB hospitals. Members considered that quality of life considerations would drive the choice of PLDH over etoposide or gemcitabine in the majority of patients.
- 2.9 The Subcommittee noted the high cost of PLDH compared with other treatment options and in particular the high cost being proposed by the supplier compared with the current UK PLDH price.
- 2.10 The Subcommittee **recommended** that pegylated liposomal doxorubicin hydrochloride (Caelyx, PLDH) be listed on the Pharmaceutical Schedule for the third-line treatment of advanced epithelial ovarian cancer in women who have failed a first-line and second-line chemotherapy regimen (including platinum). Members noted that oncologists would likely want to use this drug in the setting of primary platinum resistance. However, the Subcommittee considered that the evidence for separating groups of patients was debatable (as discussed above) and oncologists already have funded access to three other therapies (etoposide, gemcitabine and tamoxifen) in this setting. Members considered that on the weight of the evidence and cost, that access should be restricted to platinum sensitive patients, that is patients who have relapsed more than six months after previous platinum treatment, as this is the primary area of unmet need. The Subcommittee gave this recommendation a medium priority.
- 2.11 The Subcommittee considered the decision criteria relevant to these recommendations are: *(i) the health needs of all eligible people within New Zealand; (ii) the particular health needs of Maori and Pacific peoples; (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.*

### **3 Trastuzumab for HER 2 positive early breast cancer<sup>2</sup>**

3.1 The Subcommittee considered further information from Roche Products NZ Limited for the use of 12 months' trastuzumab in HER2-positive early breast cancer. Members reviewed the following information provided by Roche:

- Abstract and slide presentation of the second interim analysis of the combined NCCTG N9831 and NSABP B-31 studies presented at ASCO 2007 (Perez E, et al. ASCO 2007. Abstract 512)
- Abstract and slide presentation from the PACS04 trial presented at the 2007 San Antonio Breast Cancer Symposia (Speilmann M, et al. SABCS 2007. Abstract 72)
- [ withheld under section 9(2)(ba)(i) of the OIA ]

3.2 The Subcommittee also considered summary graphs and tables provided by PHARMAC staff showing all the available disease free survival and overall survival data from relevant trastuzumab studies (HERA, NCCTG N9831, NSABP B-31, FinHer, BCIRG006 and PACS04) plotted against median follow-up time.

3.3 The Subcommittee noted that it had previously reviewed interim data reported from the combined NCCTG N9831 and NSABP B-31 studies (2 years median follow-up, Romond et al N Engl J Med. 2005 Oct 20; 353(16): 1673-84) and that the updated ASCO 2007 data demonstrated that efficacy had been maintained out to 2.9 years median follow-up.

3.4 The Subcommittee noted that it had not previously seen data from study PACS04, and this constituted new evidence. Members noted that this was a randomised, multicentre, phase III trial designed to evaluate the benefit of docetaxel/epirubicin versus anthracyclines (FEC100) in the adjuvant treatment of node-positive early breast cancer. HER2-positive patients were further randomised to receive, or not receive, 12 months trastuzumab commenced following chemotherapy treatment (i.e., sequential treatment). Members noted that of 528 HER2-positive patients, 260 were randomised to receive trastuzumab and 268 to observation. Members noted that after a median follow-up of 48 months (four years) there was no statistically significant difference in disease free survival or overall survival between the trastuzumab and observation treatment groups.

3.5 The Subcommittee noted that some parties had criticised the validity of data from the PACS04 study because approximately 10% of trastuzumab randomised

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<sup>2</sup> PTAC considered this portion of the CaTSoP minute at its meeting on 4 July 2008, the relevant PTAC minute pertaining to trastuzumab is available on the PHARMAC website

patients did not start treatment and approximately 18% of patients did not complete the full 12 months of treatment. Members considered that these criticisms were invalid because the same situation applied to other trastuzumab studies, for example in the Romond study (combined NCCTG N9831 and NSABP B-31) approximately 10% of patients failed to commence treatment and an additional 20% of patients did not complete more than nine months of trastuzumab therapy. Members considered that despite the PACS04 study being smaller than some of the other 12 month trastuzumab studies the data were of good quality.

- 3.6 [ withheld under section 9(2)(ba)(i) of the OIA ]
- 3.7 The Subcommittee considered that the main body of evidence for trastuzumab in HER2-positive early breast cancer comprised four studies examining concurrent treatment (NCCTG N9831, NSABP B-31, BCIRG006 and FinHer) and three studies examining sequential treatment (HERA, NCCTG N9831 and PACS04). Members considered that evidence from the all concurrent studies was consistent with trastuzumab producing a relative risk reduction in disease recurrence of around 50% and around 33% in overall survival. The Subcommittee considered that results of the FinHer study supported a similar overall survival benefit; however, members noted that this benefit did not reach statistical significance, likely due to the small size of the FinHer study.
- 3.8 The Subcommittee noted that although data from the HERA study for sequential trastuzumab treatment were similar to the concurrent studies, both PACS04 and NCCTG N9831 (sequential arm) demonstrated non-statistically significant improvements in disease free survival for sequential trastuzumab treatment.
- 3.9 The Subcommittee considered that trastuzumab treatment was associated with an increased risk of cardiotoxicity. Members considered that evidence to date indicated that the early cardiotoxicity was generally manageable and reversible; however, less information was available regarding late-stage cardiac toxicity. Members commented that the assessment tools for cardiotoxicity used in the trials were crude, for example a patient has generally lost a considerable degree of heart function before it can be detected on an ECHO cardiogram and normal echocardiograms frequently occur in patients in heart failure (Ewer J, Lenihan D. Left ventricular ejection fraction and cardiotoxicity: is our ear really to the ground (Editorial). *J Clin Oncol* 2008;26:1201-1203). Therefore, members considered that although diagnostic testing appeared to show reversibility of trastuzumab-associated cardiotoxicity, patients' hearts may not have returned to normal. Members noted that the longer-term risks of trastuzumab associated cardiotoxicity were still unknown.
- 3.10 The Subcommittee considered that the weight of evidence indicated that concurrent treatment with trastuzumab was probably more efficacious than sequential treatment, although, with the exception of nine weeks treatment, concurrent treatment was associated with increased cardiotoxicity.

- 3.11 The Subcommittee considered that more clinical research was needed to determine the optimal duration of trastuzumab treatment, and reiterated its support for the SOLD study which is designed to compare 12 months' concurrent trastuzumab with nine weeks' concurrent trastuzumab.
- 3.12 The Subcommittee noted that the benefits of trastuzumab treatment in the HERA study had decreased over time, whereas the benefits in the combined data from NCCTG N9831 and NSABP B-31 were maintained. Members considered that it was too early to say if the early benefits seen for trastuzumab were durable long-term. The Subcommittee considered that further follow-up data from all studies were necessary to determine the durability of efficacy for trastuzumab treatment; however, members noted that longer-term data may be confounded by cross-over in some of the studies.
- 3.13 The Subcommittee noted that there was no additional information of relevance presented at the recent American Society of Clinical Oncology meeting (ASCO 2008).
- 3.14 The Subcommittee considered that the weight of evidence currently supported 12 months concurrent treatment; however, the cost of trastuzumab was very high and, therefore **recommended** that the current nine weeks funding of trastuzumab for HER2-positive early breast cancer remained reasonable.
- 3.15 The Subcommittee considered 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; (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; and (viii) The Government's priorities for health funding.*

#### **4 Oral vinorelbine (Navelbine) for Non Small Cell Lung Cancer (NSCLC)**

- 4.1 The Subcommittee reviewed an application from Pierre Fabre Medicament Australia Pty Limited for the listing of vinorelbine soft capsule (Navelbine Oral) on the Pharmaceutical Schedule for use as a single agent or in combination for the treatment of patients with non-small cell lung cancer (NSCLC). Members noted that the application had been reviewed by PTAC at its February 2008 meeting.
- 4.2 The Subcommittee noted that lung cancer is a major problem and is the leading cause of cancer death in New Zealand and worldwide, and that lung cancer incidence and mortality are 2–3 times higher in Maori males and 3–4 times higher in Maori females, compared with non-Maori.

- 4.3 The Subcommittee considered that a platinum-based doublet, such as intravenous (IV) cisplatin plus IV vinorelbine, was standard in the management of operable and inoperable NSCLC. Therefore, members considered that, if it were funded, oral vinorelbine would be used in both the adjuvant and advanced settings. In these settings IV vinorelbine is given on days 1, 8 and sometimes 15 at a dose of 25-30 mg/m<sup>2</sup>.
- 4.4 The Subcommittee noted that bioequivalence studies have shown that oral vinorelbine administered at 60 mg/m<sup>2</sup> and 80 mg/m<sup>2</sup> is equivalent to 25 mg/m<sup>2</sup> and 30 mg/m<sup>2</sup> of IV vinorelbine respectively.
- 4.5 The Subcommittee reviewed key data from two Phase II studies (study CA 205, Jassem et al *Annals of Oncology* 2001;12(10);1375-81 and Hirsh et al *American Journal of Clinical Oncology* 2007 30 (3);245-251) comparing oral vinorelbine with intravenous vinorelbine in patients with previously untreated advanced NSCLC. Members considered that the data demonstrated that oral vinorelbine was associated with increased gastrointestinal side-effects compared with the intravenous form, including vomiting and diarrhoea. Members noted that in the CA 205 study oral vinorelbine was comparable in terms of efficacy to intravenous vinorelbine; however, in the Hirsch study oral vinorelbine was inferior to intravenous vinorelbine. Members noted that the supplier considered that the worse outcome for oral vinorelbine in the Hirsch study was due to the study enrolling patients with lower performance status, however, members considered that it was exactly these type of patients who would be offered oral vinorelbine if it were funded in New Zealand.
- 4.6 The Subcommittee noted that evidence from other studies provided examined the use of oral vinorelbine in combination with other chemotherapy agents; members noted that no comparative data were provided in the adjuvant NSCLC setting.
- 4.7 The Subcommittee considered that an oral formulation may have some advantages over an intravenous formulation in terms of reduced number of intravenous procedures and hospital visits, replacing the day 8 and 15 doses of IV vinorelbine. However members also considered that there may be compliance issues with replacing intravenous treatment in older frail patients or Maori populations. Members considered that the availability of an oral form of vinorelbine would grow the market considerably, especially if the oral form was given as a single agent instead of intravenous vinorelbine in combination with other intravenous chemotherapy such as cisplatin. The Subcommittee considered that use of oral vinorelbine may reduce some paclitaxel and gemcitabine usage but it was unclear to what extent.
- 4.8 The Subcommittee considered that, overall, oral vinorelbine did not provide any significant outcome improvement and was associated with increased adverse effects compared with intravenous vinorelbine; however, it may offer some practical advantage over intravenous vinorelbine.
- 4.9 The Committee **recommended** that oral vinorelbine only be listed in the Pharmaceutical Schedule for the treatment of NSCLC if cost-neutral to the health sector. Members considered that assessment of cost should include likely growth in the vinorelbine market, costs relating to the management of the gastrointestinal

side-effects of the treatment (e.g. 5HT3 antagonists) and cost offsets, such as reduced intravenous service costs.

- 4.10 The Subcommittee considered 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; (v) The cost-effectiveness of meeting health needs by funding pharmaceuticals rather than using other publicly funded health and disability support services; and (viii) The Government's priorities for health funding.*