Cancer Treatments Subcommittee of PTAC
Meeting held 2 March 2012

(minutes for web publishing)

Cancer Treatments Subcommittee minutes are published in accordance with the *Terms of Reference for the Pharmacology and Therapeutics Advisory Committee (PTAC) and PTAC Subcommittees 2008*.

Note that this document is not necessarily a complete record of the Cancer Treatments Subcommittee meeting; only the relevant portions of the minutes relating to Cancer Treatments Subcommittee discussions about an Application or PHARMAC staff proposal that contain a recommendation are generally published.

The Cancer Treatments Subcommittee may:

(a) recommend that a pharmaceutical be listed by PHARMAC on the Pharmaceutical Schedule and the priority it gives to such a listing;
(b) defer a final recommendation, and give reasons for the deferral (such as the supply of further information) and what is required before further review; or
(c) recommend that PHARMAC decline to list a pharmaceutical on the Pharmaceutical Schedule.

These Subcommittee minutes were reviewed by PTAC at its meeting on 10 & 11 May 2012, the record of which will be available in June 2012.

Some material has been withheld, in accordance with the Official Information Act 1982 (OIA) in order to:

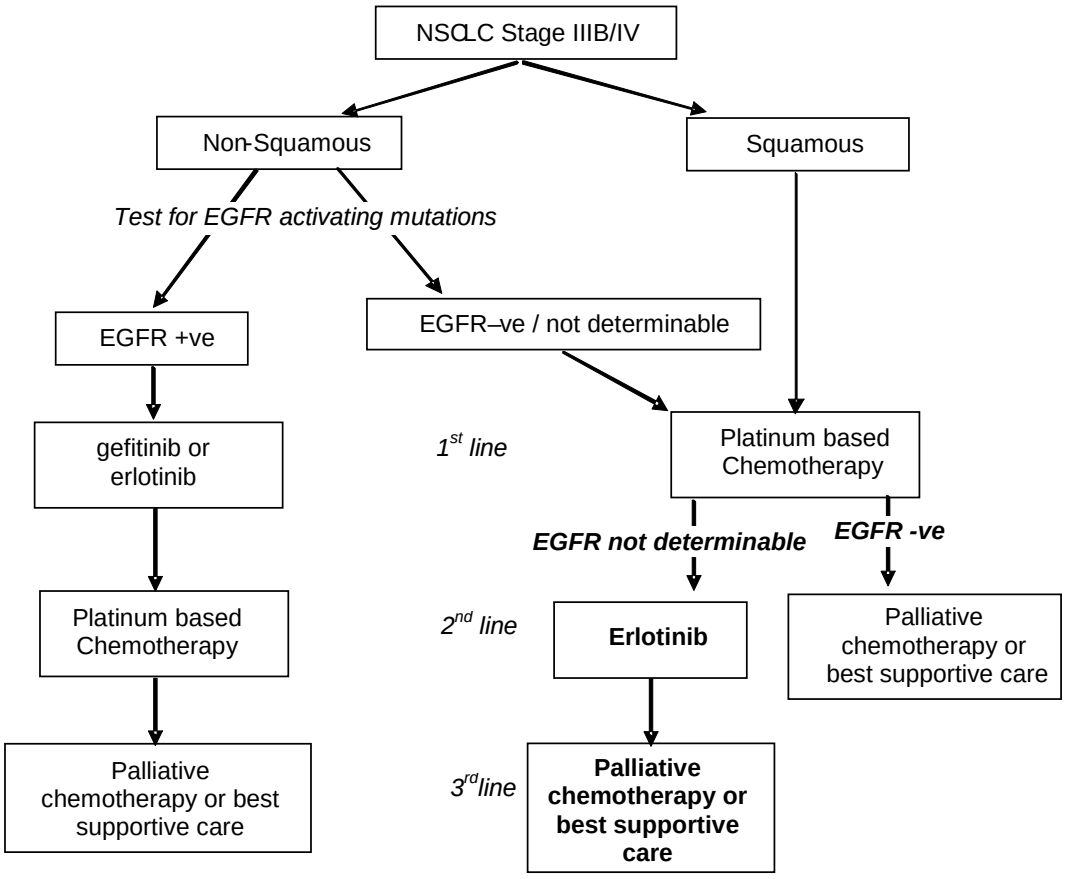
(a) protect the privacy of natural persons (section 9(2)(a) OIA)

1. Previous Meeting

1.1. The Subcommittee reviewed the minutes of its previous meeting held on 18 November 2011.

1.2. The Subcommittee noted that some patients with advanced non small cell lung cancer (NSCLC) would have indeterminable EGFr status, for example due to insufficient biopsy material. Members considered that such patients should continue to receive funded erlotinib as a second line treatment option. Therefore, the Subcommittee **recommended** that item 8.12 be amended as follows (changes in bold):

8.12 The subcommittee recommended the following testing and treatment algorithm for stage IIIB or IV NSCLC patients.



1.3. The Subcommittee noted a minor mistake in the proposed Special Authority criteria for sunitinib for gastrointestinal stromal tumours [item 11.10, item 7.10 in web

minutes] The Subcommittee **recommended** that “Initial Application – (RCC)” be amended to read “Initial Application – (GIST)”.

1.4. The remainder of the minute was accepted.

2. Matters Arising

2.1. *Correspondence regarding rituximab maintenance treatment*

2.1.1. The Subcommittee reviewed a letter from Roche Products NZ Ltd regarding its recommendations regarding the application for funding of rituximab (MabThera) on the Pharmaceutical Schedule for maintenance treatment in patients with relapsed/refractory follicular Non-Hodgkin's Lymphoma (NHL).

2.1.2. The Subcommittee reiterated its view that the key study (Van Oers) population was not representative of the majority of the NZ patient population; therefore, it would be inappropriate to extrapolate the benefits and risks seen in the study to the NZ population. Members noted that the recommendations for funding of rituximab maintenance by NICE in the UK and the SMC in Scotland, based on evidence from a different study (PRIMA), were for a different patient population (rituximab maintenance following primary treatment) than the funding being sought by Roche in its application to PHARMAC. The Subcommittee reiterated that it would welcome a submission from the supplier for funding of this population.

2.1.3. The Subcommittee did not consider that any of the points raised changed its view on the funding of rituximab maintenance treatment in patients with relapsed/refractory NHL. The Subcommittee reiterated its **recommendation** that the application be declined.

2.2. *Trastuzumab disease progression*

2.2.1. The Subcommittee noted a request for clarification regarding the intent and definition of “disease progression” in the trastuzumab funding criteria and whether this means any progression or only extracranial progression. The Subcommittee noted that that, because trastuzumab does not cross the blood-brain barrier, it is not expected to stop brain metastases from developing. Members noted that in some centres in NZ, if the brain is the only site of metastases, trastuzumab treatment is continued.

2.2.2. The Subcommittee noted that, although brain metastases are life limiting events, a small number of patients can survive 2-3 years with controlled brain metastases with trastuzumab treatment. Members considered that trastuzumab treatment should be continued in patients with controlled brain metastases but treatment should be discontinued on evidence of systemic disease progression outside the brain. Members considered that only a small number of patients would present with intracranial progression without evidence of systemic progression.

2.2.3. The Subcommittee did not consider any change to the current Special Authority criteria for trastuzumab was necessary.

2.3. *Correspondence regarding gefitinib and erlotinib*

2.3.1. The Subcommittee reviewed a letter from Roche Products NZ Ltd regarding PTAC's and the Subcommittee's November 2011 recommendations for the funding of gefitinib (Iressa) for the first line treatment of patients with NSCLC expressing EGFr activating mutations and amending the Special Authority criteria for erlotinib (Tarceva) or the second line treatment of patients with NSCLC.

2.3.2. The Subcommittee noted that Roche had submitted an application to PHARMAC for its treatment, erlotinib, to be funded as a first line treatment of patients with NSCLC expressing EGFr activating mutations. However, members noted that erlotinib was not approved by MedSafe for use in this setting and considered it appropriate that review of the application be deferred until approval was granted.

2.3.3. The Subcommittee considered that, whilst there may be some differences in the pharmacokinetics, pharmacodynamics and populations studied, erlotinib and gefitinib had similar modes of action and were clinically not substantially different from each other.

2.3.4. The Subcommittee did not consider that any changes to its **recommendations** regarding gefitinib or erlotinib were necessary.

2.4. *Correspondence regarding tyrosine kinase inhibitors for metastatic thyroid cancers*

2.4.1. The Subcommittee reviewed a letter from [withheld under section 9(2)(a) of the OIA] requesting review of the funding of tyrosine kinase inhibitors (sorafenib, sunitinib and/or pazopanib) for metastatic thyroid cancer.

2.4.2. The Subcommittee considered that, given their high cost, it would be appropriate for PHARMAC to consider a Pharmaceutical Schedule funding application for these treatments for patients with metastatic thyroid cancer. The Subcommittee **recommended** that PHARMAC staff request a funding application from the New Zealand Association of Cancer Specialists.

3. Therapeutic group review including CaEC review

3.1. The Subcommittee reviewed expenditure and usage of cancer pharmaceuticals including funding applications considered under the Cancer Exceptional Circumstances (CaEC) scheme.

3.2. *Gemcitabine and oxaliplatin for germ cell tumours*

3.2.1. The Subcommittee noted that since November 2009, PHARMAC had received 2 CaEC applications for gemcitabine and 2 CaEC applications for gemcitabine plus oxaliplatin for the treatment of patients with relapsed advanced germ cell tumours, all of which had been approved.

3.2.2. The Subcommittee reviewed the evidence provided by applicants in support of their CaEC applications.

3.2.3. The Subcommittee considered that standard first line therapy for patients with advanced germ cell tumours comprising BEP (bleomycin, etoposide and cisplatin) and was successful in most patients; however, approximately 10% of patients treated with BEP would relapse and would likely be treated with an ifosfamide regimen. The majority of these patients would relapse again and it was considered that the funding of gemcitabine and oxaliplatin as third line treatment would be potentially beneficial for these patients. Members considered that the total number of patients accessing gemcitabine and oxaliplatin would be small, around 5-10% of all advanced germ cell cancer patients.

3.2.4. The Subcommittee **recommended** that gemcitabine and oxaliplatin should be funded for patients with BEP chemotherapy refractory advanced germ cell tumour and members gave this recommendation a high priority.

3.3. *Mitotane for adrenocortical carcinoma*

3.3.1. The Subcommittee noted that since 2007 PHARMAC had received 12 CaEC applications for mitotane for the treatment of adrenocortical carcinoma, all of which had been approved. Members considered that mitotane is the standard treatment in this indication and was mistakenly omitted from the original cancer basket.

3.3.2. The Subcommittee **recommended** that mitotane should be listed on the Pharmaceutical Schedule for patients with adrenocortical carcinoma.

3.4. *Oxaliplatin for small bowel cancer*

3.4.1. The Subcommittee noted that since February 2009, PHARMAC had received 6 CaEC applications for oxaliplatin for the treatment of small bowel carcinoma, all of which had been approved. Members reviewed evidence provided by applicants in support of their CaEC applications.

3.4.2. The Subcommittee noted that the outcomes of oxaliplatin treatment for small bowel cancer appeared comparable to those seen in colorectal cancer studies, with median overall survival in the region of 20 months.

3.4.3. The Subcommittee **recommended** that oxaliplatin should be funded for patients with small bowel cancer under the same criteria as current funding for colorectal cancer.. Members gave this recommendation a high priority.

3.4.4. The Subcommittee noted that small bowel carcinoma is relatively rare (<2% of all GI cancers) and considered that, if funded as recommended, fewer than 20 new patients would access funded treatment.

3.4.5. The Subcommittee re-iterated its August 2011 recommendation that the Special Authority restriction applying to oxaliplatin should not be removed at this time. Members considered that removal of the Special Authority restriction applying to oxaliplatin would result in significant increased use particularly in gastric cancers.

4. Vemurafenib for metastatic melanoma positive for BRAF V600 mutation

4.1. The Subcommittee considered an application from Roche Products NZ Ltd for the funding of vemurafenib (Zelboraf) for patients with unresectable stage IIIC or stage IV melanoma positive for BRAF V600 mutation.

4.2. The Subcommittee noted that the application had been considered by PTAC at its February 2012 meeting, where it recommended that the application be declined.

4.3. The Subcommittee considered that New Zealand has a very high incidence of melanoma and it is a significant health concern. The Subcommittee noted that vemurafenib is the one of the first in a new class of targetted drugs for the treatment of cancer. Members noted that vemurafenib targets cancer cells with activating mutations in the BRAF oncogene and that several other BRAF targeted drugs were in development for cancer. Members considered that the cost of vemurafenib was very high and that high costs would also likely be an issue with other BRAF inhibitors.

4.4. The Subcommittee considered that there was currently no standardisation of BRAF mutation testing in New Zealand. Members noted that, whilst there was a Roche test kit available, several other, cheaper, in-house testing options were also available. Members considered that it was not necessary, nor appropriate, for Roche to control BRAF testing in New Zealand.

4.5. The Subcommittee considered that the key evidence for vemurafenib comprised one open label phase 3 randomised clinical trial (BRIM-3 Chapman PB et al. N Engl J Med 2011; 364: 2507–16) and one recently published open label phase II study (Sosman JA et al. N Engl J Med 2012;366:707-14). Members noted that BRIM-3 enrolled patients with previously untreated, metastatic melanoma (Stage IIIC or IV) with BRAF mutations, whereas the Sosman study enrolled patients with previously treated, metastatic melanoma.

4.6. The Subcommittee considered interim data from BRIM-3 demonstrated that treatment with vemurafenib significantly improved median progression free survival (PFS) compared with DTIC (5.3 months vs. 1.6 months). Members also noted that response rates were also significantly improved in patients treated with vemurafenib compared with DTIC (48% vs. 5%).

4.7. The Subcommittee considered that, although the evidence was encouraging, it appeared that the durability of the response to vemurafenib in the BRIM-3 study was short, at around 8 months. Members noted that follow-up from the BRIM-3 study was short and considered that overall survival and longer term data would be confounded by cross over to vemurafenib of patients randomised to the DTIC control arm.

4.8. The Subcommittee noted that follow-up in the Sosman study was longer than the BRIM-3 study at 12.9 months. Members noted that in this single arm study, response to vemurafenib was 53%, with median PFS of 6.8 months and median overall survival of 15.9 months. Members considered that such responses were better than historically seen with DTIC treatment.

4.9. Overall, the Subcommittee considered that, although vemurafenib provided a modest, but important, early efficacy advantage over standard treatment for metastatic melanoma, this benefit did not appear to be durable. Members also considered that, although short term toxicities appeared manageable, the longer term toxicities of vemurafenib were unknown at this time. The Subcommittee also considered that the cost of vemurafenib was extraordinarily high and disproportionate to the benefits offered.

4.10. The Subcommittee **recommended** that vemurafenib should be funded for patients with unresectable stage IIIC or stage IV melanoma positive for BRAF V600 mutation. Because of the high cost of vemurafenib and the short term evidence, members gave this recommendation a low priority. Members noted that if the price of vemurafenib were to significantly decrease, its priority rating may improve.

4.11. 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.*