Cancer Treatments Subcommittee of PTAC
Meeting held 3 October 2014

(minutes for web publishing)

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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 contains a recommendation are generally published.

The Cancer Treatment 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 14 &15 August 2014.

Record of the Cancer Treatments Subcommittee of PTAC meeting held at PHARMAC on 3 October 2014

1 Correspondence

1.1 *Bortezomib Special Authority*

1.1.1 The Subcommittee noted that PHARMAC received a significant number of Special Authority waiver requests for approval period extension for bortezomib. Members noted that the current Initial Approval period of 15 months was sufficient for the dosing anticipated at the time of funding, however, since that time other dosing schedules had become routinely used. Members noted that in most cases the total quantity of bortezomib used was within the original intent but that treatment was sometimes given before and after stem cell transplantation which often resulted in treatment delays.

1.1.2 The Subcommittee considered it was reasonable to extend the initial approval period to accommodate current treatment practices. However, members considered that the current Special Authority wording which limited treatment to 8 or 9 'treatment cycles' was ambiguous and it would be better to define a maximum cumulative dose to minimise financial risk as in the trastuzumab Special Authority.

1.1.3 The Subcommittee **recommended** PHARMAC report back to the next meeting with data on the range of actual doses claimed for bortezomib and options for Special Authority wording amendment.

1.2 *Subcutaneous Trastuzumab*

1.2.1 The Subcommittee noted that an application to fund subcutaneous trastuzumab for women with HER 2 positive breast cancer in the community was to be considered by PTAC at its November 2014 meeting.

1.2.2 The Subcommittee considered that subject to resource allocation and treatment protocols being amended it would, in principal, be feasible to deliver subcutaneous trastuzumab in the community noting that hypersensitivity reactions with trastuzumab were very uncommon and where they do occur they are associated with the very first dose of trastuzumab.

1.2.3 The Subcommittee noted that a central venous access device (CVAD) was not needed for all patients for current delivery of IV trastuzumab although they were sometimes in place for delivery of adjuvant chemotherapy in which case they would also be used to administer concurrent trastuzumab.

1.2.4 The Subcommittee considered that if subcutaneous trastuzumab was to be funded it should be made very clear upfront that treatment may move back to IV trastuzumab following introduction of biosimilars competition and associated price drops.

1.3 ***Pertuzumab Correspondence***

1.3.1 The Subcommittee considered correspondence from Roche Products (New Zealand) Limited in response to the 13-14 February 2014 PTAC meeting minute in relation to its application to fund pertuzumab for the first-line treatment of patients with HER2-positive metastatic breast cancer (mBC) in combination with trastuzumab and docetaxel.

1.3.2 The Subcommittee noted that PTAC also considered this correspondence at its 14-15 August 2014 meeting. Members noted that PTAC considered that no new evidence had been provided that would change its previous view and reiterated its February 2014 recommendations. The Subcommittee supported PTAC's view but noted that new longer term data had recently been presented at the European Society of Medical Oncology (ESMO) meeting; members looked forward to receiving this new evidence for consideration.

1.4 ***Ipilimumab Correspondence***

1.4.1 The Subcommittee considered correspondence from Bristol-Myers Squibb (NZ) Limited (BMS) in response to the 13-14 February 2014 PTAC meeting minute. Members noted that PTAC had recommended that the application for ipilimumab be referred to the Cancer Treatments Subcommittee for review once longer term data from the randomised study had been provided.

1.4.2 The Subcommittee noted that BMS indicated that longer term data from the randomised study (Hodi et al NEJM 2010) was not available.

1.4.3 The Subcommittee expressed disappointment that longer term data would not be forthcoming.

1.4.4 The Subcommittee reiterated its previous view that overall the evidence was relatively strong for ipilimumab providing a small increase in median overall survival but the evidence for any long term benefit was very weak. Members considered that the evidence at this time indicated that the autoimmune effects of ipilimumab were too hazardous to justify the small, and uncertain, benefit at the price being offered. Therefore, the subcommittee reiterated its previous **recommendation** that the application be declined.

1.5 ***Bevacizumab for Ovarian Cancer Correspondence***

1.5.1 The Subcommittee considered correspondence from Roche Products (New Zealand) Limited in response to the 13-14 February 2014 PTAC meeting minute in relation to its application to fund bevacizumab for patients with

treatment naïve advanced or metastatic epithelial ovarian, fallopian tube or primary peritoneal cancer.

1.5.2 The Subcommittee noted PTAC's recommendation to decline the application and to refer it to the Cancer Treatments Subcommittee to be reviewed once final data from the ICON7 trial had been published.

1.5.3 The Subcommittee noted that it would welcome the application upon full publication of the trial. Members considered that evidence for the primary population was not compelling and **recommended** that the application focus on the high risk subgroup.

1.5.4 The Subcommittee **recommended** that when it considers the application further information be provided about the subgroup analysis, in particular whether it was a pre-planned, or a post hoc retrospective analysis.

1.6 ***Plerixafor Correspondence***

1.6.1 The Subcommittee considered correspondence from Dr Andrew Butler, Haematologist, Canterbury Health Labs, in response to his queries regarding the Special Authority for plerixafor.

1.6.2 The Subcommittee noted that the Special Authority for plerixafor it proposed at its 21 March 2014 meeting needs further review. The Subcommittee considered that the listing of plerixafor would present a significant fiscal risk. The Subcommittee noted that there would be a temptation to use it early on in the mobilisation process and even patients who previously would not have been transplanted would be trialled on plerixafor. The Subcommittee considered that it would be difficult to draft restriction criteria to limit its use to those patients who would obtain the most benefit due to the subjectivity of the criteria.

1.6.3 The Subcommittee **recommended** PHARMAC research costs of stem cell collection, drugs and standard mobilisations before plerixafor is administered. The Subcommittee also **recommended** that PHARMAC complete a cost-utility analysis for its review.

2 Cetuximab and bevacizumab for mCRC confined to the liver

2.1 The Subcommittee noted correspondence and new evidence from Roche Products (New Zealand) Limited in relation to funding applications for bevacizumab (Avastin) for neoadjuvant treatment of metastatic colorectal cancer confined to the liver and Merck Serono in relation to cetuximab (Erbitux) for the treatment of KRAS wild-type metastatic colorectal cancer confined to the liver.

2.2 The Subcommittee noted that funding applications for these treatments had previously been considered by it and PTAC. Members also noted that the correspondence from Roche Products and Merck Serono had been reviewed by PTAC at its August 2014 meeting where it recommended that the application for cetuximab be declined and it restated its previous low priority funding recommendation for bevacizumab.

2.3 The Subcommittee noted that new published evidence from a study of cetuximab in patients with KRAS wild-type metastatic colorectal cancer confined to the liver (Primrose et al Lancet Oncology, 2014, 15, 601-11). Members noted that this study demonstrated that the addition of cetuximab to chemotherapy and surgery shortened progression-free survival. The Subcommittee considered that this study was of good quality and in contrast to the positive results shown in a previous study (Ye et al J Clinical Oncology 2013; 31:1931-38). Members considered that the new evidence created uncertainty about the benefit of cetuximab in metastatic colorectal cancer confined to the liver.

2.4 The Subcommittee noted that other RAS mutations had recently been identified that conferred resistance to cetuximab and considered further evidence was needed to clarify the patient group(s) that may benefit from cetuximab treatment. The Subcommittee **recommended** that the application for cetuximab be declined.

2.5 The Subcommittee noted that the cost effectiveness analysis for bevacizumab was very sensitive to resection rate assumptions. Members noted that the evidence for benefit of bevacizumab on resection rate were of limited quality and highly variable, ranging from 7% up to 32% depending on the study design and population being studied. Members considered that for the population being considered for funding, i.e. neoadjuvant treatment for all patients considered resectable, borderline resectable or those unresectable at baseline, it would be reasonable to model a 25% improvement in complete resection rate.

2.6 The Subcommittee considered funding for bevacizumab would be easier to implement than cetuximab since it could be used in all patients and did not require KRAS testing to be undertaken. Members further noted that bevacizumab could be administered in combination with oxaliplatin or irinotecan and considered treatment in these patients should be limited to a maximum cumulative dose of 30 mg/kg.

2.7 The Subcommittee **recommended** that bevacizumab should be listed in the Pharmaceutical Schedule subject to the following Special Authority criteria

> Bevacizumab – PCT only – Specialist – Special Authority
>
> Special Authority for Subsidy
> **Initial** Application only from a relevant specialist or medical practitioner on the recommendation of a relevant specialist. Approvals valid for 6 months for applications meeting the following criteria:
> All of the following:
> 1 the patient has metastatic colorectal cancer; and
> 2 metastases are confined to the liver only; and
> 3 neoadjuvant chemotherapy treatment prior to surgical resection of liver metastases is planned; and
> 4 bevacizumab to be used in addition to combination neoadjuvant chemotherapy to a maximum cumulative dose of 30 mg/kg.

2.8 Taking into account the relatively high cost of bevacizumab and the uncertainty of the evidence the Subcommittee gave this recommendation a low priority. The Subcommittee noted that priority would increase if cost was reduced.

2.9 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; 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 Dabrafenib for melanoma

3.1 The Subcommittee reviewed a funding application from GlaxoSmithKline NZ Ltd for the funding of dabrafenib (Tafinlar) for the treatment of BRAF V600 mutation-positive unresectable (Stage III) or metastatic (Stage IV) malignant melanoma.

3.2 The Subcommittee considered that New Zealand had a very high incidence of metastatic malignant melanoma and considered that there was a need for new treatments. The Subcommittee noted that two other treatments for metastatic malignant melanoma had been considered by it and/or PTAC in recent years, namely, ipilimumab (Yervoy) for previously treated unresectable (stage IIIC or stage IV) melanoma and vemurafenib (Zelboraf) BRAF V600 mutation positive unresectable (stage IIIC or stage IV) melanoma, both of which were recommended for decline.

3.3 Members noted that dabrafenib targeted cancer cells with activating mutations in the BRAF oncogene, similar to vemurafenib. Members considered that BRAF mutation testing was now routinely available across the country although at this time it was not funded by DHBs.

3.4 The Subcommittee noted that primary evidence for dabrafenib comprised a single Phase III, open-label, randomised study comparing oral dabrafenib with intravenous dacarbazine (DTIC) in previously untreated patients with BRAF V600E mutation positive advanced (stage III) or metastatic (stage IV) melanoma (BREAK-3 study, Hauschild et al Lancet. 2012;380(9839):358). Members considered that the study was of moderate strength and quality noting that the primary endpoint was investigator assessed progression free survival which was subject to some risk of bias.

3.5 The Subcommittee noted that BREAK-3 enrolled 250 randomly assigned patients (3:1) to receive dabrafenib (150 mg twice daily, orally) (n=187) or dacarbazine (1000 mg/m2 intravenously every 3 weeks) (n=63) with treatment continued until disease progression, death, study treatment discontinuation, or withdrawal. Members noted that 50% of the patients enrolled were treatment naïve and 28 of 63 patients (44%) of patients in the dacarbazine group crossed over to receive dabrafenib after disease progression.

3.6 The Subcommittee noted that median progression-free survival as assessed by the investigator, the primary endpoint of the study was 5.1 months for the dabrafenib group compared with 2.7 months for the dacarbazine group (HR 0.30 (95% CI 0.18–0.51;p<0.0001)). Members noted that median progression-free survival as assessed by an independent review committee (IRC) was 6.7 months for dabrafenib versus 2.9 months for dacarbazine (HR 0.35; 95% CI 0.20–0.61). Members noted that the Medsafe approved datasheet for dabrafenib indicated

median progression free survival of 6.9 months for dabrafenib compared with. 2.7 months for dacarbazine. Members could not identify the source data for these results and considered that the datasheet may have an error.

3.7 The Subcommittee noted that overall response rate (compete response or partial response), as assessed by the investigator, was 72% for dabrafenib compared with 24% for dacarbazine; members considered this rate was high for dacarbazine compared with an expected normal ORR of around 15%. Members noted that overall response rate dropped to 50% for dabrafenib and 6% for dacarbazine when independently assessed and confirmed. Members noted duration of response was approximately 8 months in both treatment groups.

3.8 The Subcommittee noted that overall survival data in the Hauschild et al 2012 publication were not mature with 21 (11%) having died in the dabrafenib group and 9 (14%) in the dacarbazine group. Members noted data provided in the application that indicated that at 12 months 70% of patients in the dabrafenib group and 63% of patients in the dacarbazine group were still alive. Members also noted an update on overall survival recently presented by Hauschild et al, at the European Society of Medical Oncology (ESMO) conference 2014 (abstract 5785) that indicated after median follow-up of 16.9 months Median Overall Survival in the dabrafenib arm was 20.0 months compared with 15.6 months in the dacarbazine arm. Members considered it was not possible to determine with any certainty the extent of improvement in Overall Survival conferred by dabrafenib as the data were confounded by crossover. Members considered that the supplier had overestimated overall survival gain for dabrafenib and PHARMAC should undertake sensitivity analyses in its cost effective analysis.

3.9 Overall the Subcommittee considered that dabrafenib provided a small, 2.4 month, increase in progression free survival compared with dacarbazine. Members considered that the magnitude of benefit for dabrafenib was small and comparable to vemurafenib. The Subcommittee considered that the magnitude of benefit for both treatments was disappointing and the price being requested was very high for such benefit. Members noted that studies combining dabrafenib with trametinib, a new MEK1/2 inhibitor, were ongoing and looked forward to receiving an application in that setting once trametinib was approved by Medsafe.

3.10 The Subcommittee **recommended** that dabrafenib be funded for the treatment of BRAF V600 mutation-positive unresectable or metastatic melanoma with low priority. Members recommended access be limited to the population enrolled in the BREAK-3 study with active CNS disease. The Subcommittee noted that the priority of funding would increase if its cost was reduced.

3.11 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; (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.*

4 Aminolevulinic acid for glioma

4.1 The Subcommittee considered an application from a clinician, for the funding of 5-aminolevulinic acid (5-ALA, Gliolan) for visualisation of malignant tissue during surgery for malignant glioma. The Subcommittee considered that the application was very good quality.

4.2 The Subcommittee noted that 5-ALA did not have a therapeutic effect itself and that there were no similar products listed on the Pharmaceutical Schedule. The Subcommittee noted that 5-ALA was a prodrug of heme (prosthetic group of haemoglobin, myoglobin, and the cytochromes) that results in accumulation of porphyrins within malignant glioma tissue which in response to blue light strongly fluoresces and can be visualised with a specific filter attachment on a standard neurosurgical microscope. Members noted that normal brain tissue reflects the violet-blue light and appears blue, whereas solid tumour tissue reflects as red and infiltrating tumour cells appear pink. The Subcommittee noted that 5-ALA was not yet registered with Medsafe.

4.3 The Subcommittee noted that approximately 260 patients are diagnosed with primary brain cancer each year in New Zealand with peak incidence occurring between 45-75 years old. Members noted that approximately 70% were diagnosed with glioblastoma multiforme (GBM), the rest anaplastic astrocytoma. Members noted that GBMs were not curable and treatment is aimed at reducing symptoms and prolonging disease free progression and extending survival. Members noted that current treatment comprised debulking surgery, where possible, combined with adjuvant radiation and temozolomide. Members noted that complete resection of GBM was relatively rare and that around 10-20% of patients simply had a biopsy, especially older patients.

4.4 The Subcommittee noted that good prognostic factors for GBM patients included younger age (<50 years), completeness of resection, O6-methylguanine-DNA methyltransferase (MGMT) promoter methylation and treatment with chemotherapy and radiation therapy.

4.5 The Committee reviewed key evidence from an interim analysis of a randomised Phase III study comparing 5-ALA and fluorescence-guided resection with conventional microsurgery (Stummer et al. Lancet Oncol 2006; 7:392-401). Members noted that the study enrolled 322 patients aged 23-73 with suspected malignant glioma contrast enhancing tumour amenable to complete resection and patients were randomised 1:1 to receive either 20mg/kg of 5-ALA given orally 24 hours prior to surgery and fluorescence-guided resection (n=161), or conventional microsurgery with white light (n=161). Members noted that 270 patients were included in the interim analysis which resulted in the study being terminated

4.6 The Subcommittee noted that contrast-enhancing tumour was completely resected in 90 (65%) of 139 patients in the 5-ALA groups compared to 47 (36%) of patients in the conventional treatment group. Members further noted that 5-ALA improved progression free survival (PFS) at 6 months (41.0% vs 21.1%, difference of 19.9% with 95% CI of 9.1-30.7, p=0.0003) and reduced the risk of death or progression (hazard ratio 0.73, 95% CI 0.57-0.94, p=0.01). Members noted that there was no

difference in the frequency or severity of adverse events within 7 days of surgery and at 6 weeks post-surgery.

4.7 Members considered these result impressive and noted that the resection rate for the control group was better than current practice in NZ therefore considered that gains would likely be greater in practice than seen in the study. Members further noted that in the study, which was conducted in 2006, patients only received adjuvant radiation therapy which was standard at that time, members considered that with current standard adjuvant therapy comprising of temozolomide and radiation therapy gains would likely be greater.

4.8 The Subcommittee also reviewed evidence from a number of other supportive studies. Overall, the Subcommittee considered that there was good evidence that the use of 5-ALA and fluorescence-guided resection improved resection rates and extent of tumour resection in patients with GBM which led to improved progression free survival and overall survival rates.

4.9 The Subcommittee noted that 5-ALA required a neurosurgical microscope fitted with a specific filter attachment. Members considered that most neurosurgical units in NZ either already had this filter or would likely introduce it in the near future during standard equipment upgrades. Members noted that capital equipment such as neurosurgical microscopes are routinely replaced every 5-10 years.

4.10 The Subcommittee considered that if funded 5-ALA would likely be used in approximately 40% of all GBM cases per year (approximately 90 patients each year). Members considered that the funding of 5-ALA would likely increase the duration of neurosurgical procedures and theatre time as surgeons would likely be more motivated to attempt complete resection. Members considered that surgeon willingness to undertake aggressive surgery was a powerful positive prognostic variable, however, this needed to be balanced with increased risk of complications, longer recovery time and increased risk of post-surgical morbidity. Members considered that there was limited evidence that 5-ALA improved quality of life post-surgery.

4.11 The Subcommittee **recommended** that 5-aminolevulinic acid hydrochloride (5-ALA, Gliolan) should be funded in DHB Hospitals for visualisation of malignant tissue during surgery for malignant glioma with a high priority subject to Medsafe approval. Members recommended that funding be restricted to the same patient group enrolled in the Stummer et al 2006 trial.

4.12 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; (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.*

5 Rituximab for retreatment of CLL/SLL

5.1 The Subcommittee considered an application from a clinician requesting that rituximab retreatment be funded for patients with chemosensitive relapsed chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL), which has responded for at least 24 months to prior combination fludarabine, cyclophosphamide, rituximab (FCR) treatment.

5.2 The Subcommittee noted that in 2010/11 it had previously considered an application from Roche Products (NZ) Ltd for the funding of rituximab for treatment naive and relapsed refractory CLL. Members noted that at that time the Subcommittee considered there was no evidence to support the use of rituximab retreatment in this setting. Members further noted that this current clinician application had been reviewed by PTAC at its August 2014 meeting where it also recommended that the application be declined because of insufficient evidence.

5.3 The Subcommittee noted that the applicant provided evidence from two studies in support of the application, - REACH study (Robak et al. J Clin Oncol. 2010 Apr 1;28(10):1756-65) and Wierda et al study (J Clin Oncol. 2005 Jun 20;23(18):4070-8.). Members noted that this evidence had been previously reviewed by CaTSoP and PTAC in 2010. Members considered that neither study were directly relevant to the application since REACH enrolled rituximab treatment naïve patients and whilst a small proportion of the patients enrolled in the Wierda study had previously received rituximab, no subgroup analysis was performed, so it was not possible to determine the benefit and risks of rituximab retreatment in these patients.

5.4 The Subcommittee also reviewed a Cochrane group meta-analysis of (Bauer et al, Cochrane Database of Systematic Reviews 2012, Issue 11), National Comprehensive Cancer Network guidelines (National Comprehensive Cancer Network, 2014), European Society for Medical Oncology guidelines (Eichhorst et al, 2011); and National Cancer Institute–sponsored Working Group (NCI-WG) on chronic lymphocytic leukaemia guidelines (Hallek et al 2008) provided in support of the application. The Subcommittee noted that the guidelines recommended rituximab retreatment despite there being no direct evidence to support these recommendations; members further noted that the Cochrane analysis didn't address this question.

5.5 The Subcommittee acknowledged that there was no evidence to support rituximab retreatment in CLL/SLL and considered that it was very unlikely that any further evidence would be generated in the future. However, members noted that rituximab retreatment was currently funded for other closely-related indolent B cell malignancies, where evidence was equally limited.

5.6 The Subcommittee noted that in their experience rituximab retreatment did offer benefit to lymphoma patients whose disease had a durable response (minimum 2-3 years) to prior rituximab treatment. Members considered that it was entirely logical to expect similar outcomes in patients with CLL/SLL even though there was no direct evidence to support this conclusion. Members also considered that rituximab retreatment may improve some of the auto-immune complications associated with CLL.

5.7 The Subcommittee noted that new treatments for CLL were in development and considered that these would likely be more expensive than rituximab.

5.8 The Subcommittee acknowledged that with each subsequent line of therapy the cost effectiveness of treatments would diminish, therefore members considered that it would be appropriate to limit rituximab treatment to first relapse only. Members considered that up to 50 patients per year would be treated in this setting.

5.9 The Subcommittee **recommended** that the Special Authority criteria for rituximab for CLL should be widened to include funding for retreatment as follows (changes in bold)

Initial application — (Chronic lymphocytic leukaemia) only from a relevant specialist or medical practitioner on the recommendation of a relevant specialist. Approvals valid for 12 months for applications meeting the following criteria:
All of the following:

1. The patient has progressive Binet stage A, B or C chronic lymphocytic leukaemia (CLL) requiring treatment; and
2. The patient is rituximab treatment naïve; and
3. Either:
    - 3.1 The patient is chemotherapy treatment naïve; or
    - 3.2 Both:
        - 3.2.1 The patient's disease has relapsed following no more than three prior lines of chemotherapy treatment; and
        - 3.2.2. The patient has had a treatment-free interval of 12 months or more if previously treated with fludarabine and cyclophosphamide chemotherapy; and
4. The patient has good performance status; and
5. The patient has good renal function (creatinine clearance ≥ 30 ml/min); and
6. The patient does not have chromosome 17p deletion CLL; and
7. Rituximab to be administered in combination with fludarabine and cyclophosphamide for a maximum of 6 treatment cycles;
8. It is planned that the patient receives full dose fludarabine and cyclophosphamide (orally or dose equivalent intravenous administration).

Renewal application – (Chronic Lymphocytic Leukaemia) only from a relevant specialist or medical practitioner on the recommendation of a relevant specialist. Approvals valid for 12 months for applications meeting the following criteria:
All of the following:

1. **The patients disease has relapsed following no more than one prior line of treatment with rituximab for CLL; and**
2. **The patient has had a rituximab treatment–free interval of 36 months or more; and**
3. **The patient does not have chromosome 17p deletion CLL; and**
4. **It is planned that the patient receives full dose fludarabine and cyclophosphamide (orally or dose equivalent intravenous administration); and**

5. **Rituximab to be administered in combination with fludarabine and cyclophosphamide for a maximum of 6 treatment cycles.**

Notes: 'Chronic lymphocytic leukaemia' includes small lymphocytic lymphoma. A line of chemotherapy treatment is considered to comprise a standard therapeutic chemotherapy regimen and supportive treatments. 'Good performance status' means ECOG score of 0-1; however, in patients temporarily debilitated by their CLL disease symptoms a higher ECOG (2 or 3) is acceptable where treatment with rituximab is expected to improve symptoms and improve ECOG score to <2.

5.10 The Subcommittee gave this recommendation a Medium priority. The Subcommittee noted that priority would increase if cost was reduced.

5.11 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; (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.*