

26 January 2012

Proposal to fund lapatinib and pazopanib and amend funding criteria for trastuzumab

PHARMAC is seeking feedback on a proposal to:

- Fund lapatinib (Tykerb) as an alternative to trastuzumab (Herceptin) for the first line treatment of patients with HER 2 positive metastatic breast cancer; and
- Fund lapatinib for patients with HER 2 positive metastatic breast cancer who experience early intolerance to first line trastuzumab treatment; and
- Fund pazopanib (Votrient) for patients with advanced renal cell carcinoma

through a provisional agreement with GlaxoSmithKline New Zealand Limited.

In addition, PHARMAC also proposes to amend the funding criteria for trastuzumab (Herceptin) for patients with HER 2 positive metastatic breast cancer so that in addition to being funded as a first line treatment it would also be funded for patients who experience early intolerance to first line lapatinib treatment.

The proposal would result in new funded treatments for patients with advanced renal cell carcinoma and HER 2 positive metastatic breast cancer. Patients with HER 2 positive metastatic breast cancer would be able to receive funding for either lapatinib or trastuzumab as first line treatment. Patients who experience early intolerance on either lapatinib or trastuzumab would be able to receive funding for the alternative treatment as long as their disease had not progressed. Funding for trastuzumab for patients with HER 2 positive early breast cancer would remain unchanged.

Overall the funding of lapatinib and pazopanib as proposed is expected to be cost neutral to DHBs, taking into account expected changes in patient treatment pathways and DHB hospital resource requirements.

Further details of this proposal, including how to provide feedback and background information, can be found below and on the following pages. All changes would be implemented 1 April 2012 unless otherwise stated.

Feedback sought

PHARMAC welcomes feedback on this proposal. To provide feedback, please submit it in writing by **5 pm Thursday, 9 February 2012** to:

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All feedback received before the closing date will be considered by PHARMAC's Board (or Chief Executive acting under delegated authority) prior to making a decision on this proposal.

Details of the proposal

In relation to pazopanib (Votrient):

- Votrient 200 mg and 400 mg film-coated tablets would be listed in Section B and in Part II of Section H of the Pharmaceutical Schedule.
- The following prices and subsidies would apply (all prices are ex-manufacturer and exclude GST):

Brand	Presentation	Pack size	List price and subsidy
Votrient	200 mg Tablet	30	\$1,334.70
Votrient	400 mg Tablet	30	\$2,669.40

- A confidential rebate would apply to all subsidies for Votrient which would reduce its net price to the funder.
- Votrient would be funded subject to Special Authority criteria as follows:

Pazopanib – Special Authority – Retail Pharmacy

Special Authority for Subsidy

Initial application only from a relevant specialist or medical practitioner on the recommendation of a relevant specialist. Approvals valid for 3 months for applications meeting the following criteria:

All of the following:

- 1 The patient has metastatic renal cell carcinoma; and
- 2 Any of the following
 - 2.1 The patient is treatment naive; or
 - 2.2 The patient has only received prior cytokine treatment; or
 - 2.3 Both
 - 2.3.1 The patient has discontinued sunitinib within 3 months of starting treatment due to intolerance; and
 - 2.3.2 The cancer did not progress whilst on sunitinib; and
- 3 The patient has good performance status (WHO/ECOG grade 0-2); and
- 4 The disease is of predominant clear cell histology; and
- 5 The patient has intermediate or poor prognosis defined as :

Any of the following:

 - 5.1 Lactate dehydrogenase level > 1.5 times upper limit of normal; or
 - 5.2 Haemoglobin level < lower limit of normal; or
 - 5.3 Corrected serum calcium level > 10 mg/dL (2.5 mmol/L) ; or
 - 5.4 Interval of < 1 year from original diagnosis to the start of systemic therapy; or
 - 5.5 Karnofsky performance score of \leq 70; or
 - 5.6 \geq 2 sites of organ metastasis; and
- 6 Pazopanib to be used for a maximum of 12 weeks.

Renewal only from a relevant specialist or medical practitioner on the recommendation of a relevant specialist. Approvals valid for 3 months for applications meeting the following criteria:

Both:

- 1 No evidence of disease progression; and
- 2 The treatment remains appropriate and the patient is benefiting from treatment.

Notes:

Pazopanib treatment should be stopped if disease progresses.

Poor prognosis patients are defined as having at least 3 of criteria 5.1-5.6.

Intermediate prognosis patients are defined as having 1 or 2 of criteria 5.1-5.6

- Votrient would have subsidy and delisting protection until 30 June 2017.

In relation to lapatinib (Tykerb):

- Tykerb 250 mg tablets would be listed in Section B and in Part II of Section H of the Pharmaceutical Schedule.
- The following prices and subsidies would apply (all prices are ex-manufacturer and exclude GST):

Brand	Presentation	Pack size	List price and subsidy
Tykerb	250 mg Tablet	70	\$1,899.00
Tykerb	250 mg Tablet	84	\$2,278.08

- A confidential rebate would apply to all subsidies for Tykerb which would reduce its net price to the funder.
- Tykerb would be funded subject to Special Authority criteria as follows:

Lapatinib – Special Authority – Retail Pharmacy

Special Authority for Subsidy

Initial application — (metastatic breast cancer) 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:

Either

- 1 All of the following:
 - 1.1 The patient has metastatic breast cancer expressing HER-2 IHC 3+ or ISH+ (including FISH or other current technology); and
 - 1.2 The patient has not previously received trastuzumab treatment for HER 2 positive metastatic breast cancer; and
 - 1.3 Lapatinib not to be given in combination with trastuzumab; and
 - 1.4 Lapatinib to be discontinued at disease progression; or
- 2 All of the following:
 - 2.1 The patient has metastatic breast cancer expressing HER-2 IHC 3+ or ISH+ (including FISH or other current technology); and
 - 2.2 The patient started trastuzumab for metastatic breast cancer but discontinued trastuzumab within 3 months of starting treatment due to intolerance; and
 - 2.3 The cancer did not progress whilst on trastuzumab; and
 - 2.4 Lapatinib not to be given in combination with trastuzumab; and
 - 2.5 Lapatinib to be discontinued at disease progression.

Renewal — (metastatic breast cancer) 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 metastatic breast cancer expressing HER-2 IHC 3+ or ISH+ (including FISH or other current technology); and
- 2 The cancer has not progressed at any time point during the previous 12 months whilst on lapatinib; and
- 3 Lapatinib not to be given in combination with trastuzumab; and
- 4 Lapatinib to be discontinued at disease progression.

- Tykerb would have subsidy and delisting protection until 30 June 2017.

In relation to trastuzumab (Herceptin):

- The Special Authority criteria applying to all presentations of trastuzumab (Herceptin) in Section B of the Pharmaceutical Schedule would be amended as follows (changes in bold and strikethrough):

Trastuzumab – PCT only – Specialist – Special Authority

Special Authority for Subsidy

Initial application — (metastatic breast cancer) 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:

~~Both:~~ **Either**

- 1 All of the following:
 - 1.1 The patient has metastatic breast cancer expressing HER-2 IHC 3+ or ISH+ (including FISH or other current technology); and
 - 1.2 **The patient has not previously received lapatinib treatment for HER 2 positive metastatic breast cancer; and**
 - 1.3 **Trastuzumab not to be given in combination with lapatinib; and**
 - 1.4 Trastuzumab to be discontinued at disease progression; **or**
- 2 **All of the following:**
 - 2.1 **The patient has metastatic breast cancer expressing HER-2 IHC 3+ or ISH+ (including FISH or other current technology); and**
 - 2.2 **The patient started lapatinib treatment for metastatic breast cancer but discontinued lapatinib within 3 months of starting treatment due to intolerance; and**
 - 2.3 **The cancer did not progress whilst on lapatinib; and**
 - 2.4 **Trastuzumab not to be given in combination with lapatinib; and**
 - 2.5 **Trastuzumab to be discontinued at disease progression.**

Renewal — (metastatic breast cancer) 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:

~~Both:~~ **All of the following**

- 1 The patient has metastatic breast cancer expressing HER-2 IHC 3+ or ISH+ (including FISH or other current technology); and
- 2 The cancer has not progressed at any time point during the previous 12 months whilst on trastuzumab; **and**
- 3 **Trastuzumab not to be given in combination with lapatinib; and**
- 4 **Trastuzumab to be discontinued at disease progression.**

Initial application — (early breast cancer) only from a relevant specialist or medical practitioner on the recommendation of a relevant specialist. Approvals valid for 15 months for applications meeting the following criteria:

All of the following:

- 1 The patient has early breast cancer expressing HER 2 IHC 3+ or ISH + (including FISH or other current technology); and
- 2 Maximum cumulative dose of 106 mg/kg (12 months' treatment); and
- 3 Any of the following:
 - 3.1 9 weeks' concurrent treatment with adjuvant chemotherapy is planned; or
 - 3.2 12 months' concurrent treatment with adjuvant chemotherapy is planned; or
 - 3.3 12 months' sequential treatment following adjuvant chemotherapy is planned; or
 - 3.4 Other treatment regimen, in association with adjuvant chemotherapy, is planned.

Renewal — (early breast cancer)* 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:

~~Both~~ **All of the following:**

- 1 The patient has metastatic breast cancer expressing HER-2 IHC 3+ or ISH+ (including FISH or other current technology); and
- 2 ~~Either:~~
 - ~~2.1 Both:~~
 - ~~2.1.1. The patient received prior adjuvant trastuzumab treatment for early breast cancer; and~~
- 3 **Either:**
 - 2.1 ~~Both:~~ **All of the following:**
 - 2.1.1 **The patient has not previously received lapatinib treatment for metastatic breast cancer; and**
 - 2.1.2 **Trastuzumab not to be given in combination with lapatinib; and**
 - 2.1.3 Trastuzumab to be discontinued at disease progression; or
 - 2.2 **All of the following:**
 - 2.2.1 **The patient started lapatinib treatment for metastatic breast cancer but discontinued lapatinib within 3 months of starting treatment due to intolerance; and**
 - 2.2.2 **The cancer did not progress whilst on lapatinib; and**
 - 2.2.3 **Trastuzumab not to be given in combination with lapatinib; and**
 - 2.2.4 **Trastuzumab to be discontinued at disease progression; or**
 - 2.3 **All of the following:**
 - 2.3.1 The cancer has not progressed at any time point during the previous 12 months whilst on trastuzumab; **and**
 - 2.3.2 **Trastuzumab not to be given in combination with lapatinib; and**
 - 2.3.3 **Trastuzumab to be discontinued at disease progression**

Note: *For patients with relapsed HER-2 positive disease who have previously received adjuvant trastuzumab for early breast cancer.

Background

Pazopanib (Votrient)

In November 2010 PHARMAC funded the oral tyrosine kinase inhibitor (TKI) sunitinib (Sutent, Pfizer) subject to Special Authority criteria for patients poor and intermediate prognosis advanced or metastatic renal cell carcinoma (RCC). Pazopanib is also a new oral tyrosine kinase inhibitor similar to sunitinib. Clinical evidence demonstrates that treatment with pazopanib significantly improves median progression free survival (PFS) by 5 months compared with placebo in patients with advanced RCC.

There is no direct evidence comparing pazopanib with other TKIs or interferon in patients with advanced RCC. There is no evidence to support the use of pazopanib after sunitinib treatment failure, or vice versa, but they have different side effect profiles; therefore, may be useful alternatives in patients who experience early treatment limiting toxicity to either treatment.

PTAC and its Cancer Treatments Subcommittee (CaTSoP) have reviewed the funding of pazopanib. CaTSoP considered that because sunitinib was already funded there was no evidence that pazopanib would address any unmet medical need in the treatment of patients with advanced RCC. However, members considered that competition in the TKI market through the introduction of a second molecule may be useful given the high cost of these treatments and would give clinicians and patients more choice.

Published PTAC and CaTSoP minutes relating to pazopanib can be found on PHARMAC's website.

Lapatinib (Tykerb) and trastuzumab (Herceptin)

Breast cancer is the most common cancer found in women; it is also the most common cause of cancer-related deaths in women. Human epidermal growth factor receptor 2 protein (ErbB-2/HER2/neu) is a protein found on the surface of certain cancer cells. HER 2 is a receptor for the growth factor human epidermal growth factor. When human epidermal growth factor attaches itself to HER 2 receptors on breast cancer cells, it stimulates the cells to divide and grow.

Māori and Pacifica women have a higher prevalence of breast cancer in general, and of HER 2 positive breast cancer compared with NZ European women. Māori and Pacifica women present with more advanced breast cancers – even more so with HER 2 disease – when compared with other women, and Māori and Pacifica women have higher rates of breast cancer deaths.

Standard treatment for women with HER-2 positive metastatic breast cancer in New Zealand is currently trastuzumab (Herceptin), given as an infusion either as monotherapy or in conjunction with other treatments such as a taxane or hormonal treatment.

Lapatinib is an oral dual tyrosine kinase inhibitor which interrupts the HER 2 growth receptor pathway. Overall, evidence demonstrates that the addition of lapatinib to standard first line metastatic treatments (letrozole or paclitaxel) results in statistically significant improvement in progression free survival with numerical improvement in overall survival.

PTAC and its Cancer Treatments Subcommittee (CaTSoP) have reviewed the funding of lapatinib on a number of occasions. PTAC recommended that lapatinib should be funded as

an alternative to trastuzumab for the first line treatment of patients presenting with HER 2 positive metastatic breast cancer. However, PTAC recommended that the funding of lapatinib as a second line treatment following disease progression on trastuzumab be declined.

CaTSOP recommended that lapatinib should be funded as an alternative to trastuzumab for the first line treatment of patients presenting with HER 2 positive metastatic breast cancer and that funding should be structured such that patients receive only one funded HER2 targeted treatment course, either trastuzumab or lapatinib, unless toxicity issues prevented first choice treatment being completed. CaTSOP agreed with PTAC's recommendation to decline funding of lapatinib as a second line treatment.

There are no head-to-head studies comparing lapatinib to trastuzumab in the HER2 positive metastatic breast cancer setting. Lapatinib with trastuzumab both target HER 2, but they have different routes of administration and different side effect profiles; therefore, clinicians and patients may have a preference for one over the other. Unlike trastuzumab, which must be administered in hospital by IV infusion, lapatinib is an oral treatment; therefore, if patients choose to be treated with lapatinib rather than trastuzumab they would not need to go to a DHB hospital to receive their treatment. Lapatinib treatment would be more convenient for patients and would free up DHB hospital chemotherapy infusion resources.

Published PTAC and CaTSOP minutes relating to lapatinib and trastuzumab can be found on PHARMAC's website.