1 March 2012

Approval of proposal to fund pazopanib, lapatinib and amend the Special Authority criteria applying to trastuzumab

PHARMAC is pleased to announce approval of the proposal to fund pazopanib (Votrient) and lapatinib (Tykerb) and amend the Special Authority criteria applying to trastuzumab (Herceptin). This was the subject of a consultation letter dated 26 January 2012.

In summary, the effect of the decision is that from 1 April 2012 new treatments for patients with advanced renal cell carcinoma and HER 2 positive metastatic breast cancer will be funded.

Patients with HER 2 positive metastatic breast cancer will receive funding for either lapatinib or trastuzumab as first line treatment and those who experience early intolerance to their first choice treatment will 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 remains unchanged.

Details of the decision

In relation to pazopanib (Votrient):

- Votrient 200 mg and 400 mg film-coated tablets will be listed in Section B and in Part II of Section H of the Pharmaceutical Schedule from 1 April 2012 at the following prices and subsidies (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 will apply to all subsidies for Votrient which will reduce its net price to the Funder.

- Votrient will 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

Level 9, 40 Mercer Street, PO Box 10-254, Wellington 6143, New Zealand
Phone: 64 4 460 4990 - Fax: 64 4 460 4995 - www.pharmac.govt.nz

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 ≤ 70; or
5.6 ≥ 2 sites of organ metastasis; and
6 Pazopanib to be used for a maximum of 3 months.

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 will have subsidy and delisting protection until 30 June 2017.

In relation to lapatinib (Tykerb):

- Tykerb 250 mg tablets will be listed in Section B and in Part II of Section H of the Pharmaceutical Schedule from 1 April 2012 at the following prices and subsidies (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 will apply to all subsidies for Tykerb which will reduce its net price to the funder.

- Tykerb will be funded subject to Special Authority criteria as follows:

Lapatinib ditosylate – 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 will 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 will be amended from 1 April 2012 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:**

2.2.1 The patient has not previously received lapatinib treatment for metastatic breast cancer; and

2.2.2 Trastuzumab not to be given in combination with lapatinib; and

2.2.3 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.

Feedback received

We appreciate all of the feedback that we received and acknowledge the time people took to respond. All consultation responses received by 9 February 2012 were considered in their entirety in making a decision on the proposal. In general, most responders supported the proposal. A minor change was made to the pazopanib Special Authority criteria in response to consultation. Key issues raised and PHARMAC comments on these issues are discussed below:

Theme	PHARMAC Comment
One responder noted whilst the proposal for pazopanib did not impact the current Special Authority criteria applying another advanced renal cell carcinoma treatment sunitinib (Sutent) it may indirectly lead to sunitinib being used as a second line treatment after pazopanib treatment failure. They noted that there is no data to support sunitinib treatment after failure of pazopanib and requested that the Special Authority criteria for sunitinib be amended to avoid it being funded when used this way.	PHARMAC intends to progress a separate proposal to amend the criteria for sunitinib as requested. Consultation on this proposal will commence shortly (the consultation letter will be posted on www.pharmac.govt.nz).
One responder noted that because pazopanib comes in packs of 30 tablets if a pharmacy dispensed the 12 week maximum as proposed in criterion 6 of the proposed Initial Special Authority criteria it would be left with 6 unsold tablets. It requested that criteria be amended to enable 90 days or the nearest original pack to be dispensed.	The criteria has been amended to read "*Pazopanib to be used for a maximum of 3 months*"

Theme	PHARMAC Comment
One responder considered that lapatinib was not registered for the indication in which funding was being proposed and the evidence for lapatinib was poor quality.	The current registered indications for lapatinib include its use as a first line HER 2 mBC treatment in combination with an aromatase inhibitor in hormone receptor-positive post menopausal women.
They noted that there is no clinical trial evidence directly comparing lapatinib with trastuzumab in HER 2 positive metastatic breast cancer (HER2 mBC), although a study is underway. They considered that data in other breast cancer settings strongly suggested that lapatinib is likely to demonstrate lower efficacy and an inferior toxicity profile compared with trastuzumab. They considered that diarrhoea with lapatinib is very common and may lead to dehydration and/or treatment discontinuation.	The funding of lapatinib provides an alternative funded treatment option for HER 2 mBC patients and those patients experiencing intolerance to trastuzumab. We consider that oncologists are best placed to evaluate the relative risks and benefits of lapatinib and trastuzumab and choose appropriate treatment for their individual patients. Trastuzumab remains funded as a first line treatment option for patients with HER2 mBC, therefore, if an oncologist considers that trastuzumab, rather than lapatinib, is the best treatment option for their patient(s) it would be funded.
They noted that current international treatment guidelines recommend trastuzumab as the first line HER2 mBC treatment with lapatinib as an alternative second line option for patients who cannot tolerate trastuzumab and recommended that the funding proposal be amended as such.	Lapatinib will be funded for patients who experience early intolerance to trastuzumab as long as their disease had not progressed
They noted that the supplier of trastuzumab is currently providing, and paying for, confirmatory HER2 ISH testing for DHBs and that the introduction of lapatinib as an alternative treatment option to the market may affect the commercial viability of this service.	The costs to DHBs of funding confirmatory HER2 ISH tests would be significantly less than the savings to DHBs from funding lapatinib.

Theme	PHARMAC Comment
One responder considered that there may be some patients who would benefit from first line lapatinib treatment e.g. patients with extensive brain metastases, mutations indicating resistance to trastuzumab, or those unable to receive IV treatment. They supported first line funding of lapatinib where it is considered the most effective option given the patient's circumstances. However, they considered that the greatest clinical need and strongest clinical evidence for lapatinib was for its use as a salvage [second line] therapy in patients with HER2 mBC who have progressed after receiving trastuzumab. They requested that funding be extended such that both lapatinib and trastuzumab be funded as second-line treatments after disease progression on the first option.	We agree that there is a health need for effective second line treatments for patients with HER2 positive mBC, however, at this time, we do not consider that the funding of lapatinib in this setting would be a cost effective use of health funding. PTAC and its cancer treatments subcommittee, CaTSoP, have reviewed applications for the funding of lapatinib as a second line treatment in patients with HER 2 mBC whose disease has progressed on trastuzumab. PTAC and CaTSoP considered second line lapatinib treatment offered only modest benefits in terms of delaying disease progression without any survival advantage. Both PTAC and CaTSoP recommended such funding be declined (relevant minutes can be found at www.pharmac.govt.nz) We are unaware of any relevant new evidence in this setting, therefore, consider that the decline recommendations from PTAC and CaTSoP remain valid and therefore have not proposed to fund lapatinib for second line treatment at this time. We would welcome a further application for consideration should relevant new evidence become available.

More information

If you have any questions about this decision, you can call our toll free number (9 am to 5 pm, Monday to Friday) on 0800 66 00 50.