

7 August 2008

**Notification of a decision regarding the funding of 12 months treatments with trastuzumab (Herceptin) for HER2-positive early breast cancer**

Further to our 5 May 2008 consultation, the PHARMAC Board, at its 30 July 2008 meeting, decided to decline Roche Products (New Zealand) Limited's application to list 12 months treatments with trastuzumab (Herceptin) on the Pharmaceutical Schedule for the treatment of HER2-positive early breast cancer.

This decision does not mean that PHARMAC could never revisit the issue of funding 12 months trastuzumab (e.g. if there was substantial new clinical information or a new commercial offer(s) from Roche); rather, it means that PHARMAC is not actively working on proposals related to the funding of 12 months trastuzumab for HER2-positive early breast cancer at this time.

PHARMAC's decision of April 2007 to fund 9 weeks treatment with trastuzumab administered concurrently with chemotherapy ("concurrent 9 weeks treatment") remains in place for women with HER2-positive early breast cancer.

**Rationale for the Decision**

PHARMAC's statutory objective is to *"to secure for people in need of pharmaceuticals, the best health outcomes that are reasonably achievable from pharmaceutical treatment and from within the amount of funding provided."*

Adjuvant trastuzumab in early breast cancer can be given in two main ways: concurrently with, or sequentially after, other chemotherapy. The concurrent 9 weeks treatment is a complete and fully funded regimen on its own.

In order to recommend funding of 12 months treatment with trastuzumab, PHARMAC would need to be confident that it would be justifiable under its Decision Criteria, and in particular that it offered sufficient additional health benefits over the currently funded concurrent 9 weeks treatment, and that investing in those benefits would not displace other funding options associated with greater health gains. PHARMAC is not satisfied that this is the case.

The available clinical evidence for trastuzumab in HER-2 positive early breast cancer only allows for indirect comparisons of the risks and benefits of the various different treatment regimens; new clinical trials such as SOLD which compares the concurrent 9 weeks and 12 months treatments are needed for direct comparisons.

The Pharmacology and Therapeutics advisory committee (PTAC) and its Cancer Treatments subcommittee (CaTSoP) considered new clinical evidence at their 4 July 2008 and 13 June 2008 meetings respectively. PTAC considered that there was still uncertainty about the best way of administering trastuzumab in terms of optimal treatment sequencing, duration, minimising cardiovascular toxicity, and long-term clinical outcomes.

Indirect comparisons of current clinical trial data suggest that the funded 9 week treatment regimen has comparable benefit in terms of disease-free survival as the various 12 month regimens (concurrent or sequential), although it is not currently possible to say whether the 9 week treatment regimen would result in comparable overall survival benefits. Some of the 12 month treatment trials have demonstrated that disease-free survival gains are translated into overall survival benefits.

It is acknowledged that there is more confidence in the precision of the effect estimate in the 12 month treatment trial results when compared with no trastuzumab treatment, and that the 9 week concurrent treatment (FinHER) trial data have not demonstrated a statistically significant benefit for overall survival. However, although the FinHER trial involved a smaller number of patients, resulting in wider confidence intervals than the larger 12 month treatment studies, the results for disease free survival are statistically significant and the benefits shown are comparable to the 12 month treatment studies. PHARMAC, PTAC

and CaTSoP carefully considered these issues when evaluating the clinical evidence from the FinHER trial and the 12 month treatment studies. It is clear that trastuzumab has short-term benefits on clinical outcomes in patients with HER-2 positive early breast cancer when dosed concurrently with chemotherapy. It is not clear whether there are long-term benefits, or whether extending the time of treatment (and consequently exposure to risk from treatment) has additional benefits.

PTAC, having reviewed new evidence, recommended that funding of any 12 month regimens (either sequential or concurrent) should be declined. It also stated that no new information had been presented that demonstrated any additional health benefit for 12 months treatment (sequential or concurrent) over the currently funded concurrent 9 week treatment regimen. Emerging evidence is that sequential 12 months treatment is the least effective way to use trastuzumab. PTAC noted that although the weight of evidence supports the use of concurrent 12 months treatment with trastuzumab, there are on balance overriding concerns about its durability of efficacy, increased cardiotoxicity, its high cost, and the lack of conclusive evidence of additional health gain over the concurrent 9 week treatment regimen. Both PTAC and CaTSoP recommended that the funding for concurrent 9 weeks treatment with trastuzumab for HER-2 positive early breast cancer patients be continued.

PHARMAC is not confident that there would be additional health gains from funding any 12 month treatment regimen (concurrent or sequential) compared with the currently funded concurrent 9 week treatment regimen. On the basis of the indirect comparisons from current trial evidence and the advice we have received from PTAC, we think it is reasonable to assume that 12 month treatments may produce no additional health gain compared with the funded concurrent 9 week treatment regimen.

In April 2008 PHARMAC received a new 'bundled' commercial in confidence offer from Roche for the funding of 12 months treatment with trastuzumab for HER2-positive early breast cancer patients and funding of another product. PHARMAC's assessment of the incremental cost (over and above funding already allocated for concurrent 9 weeks trastuzumab and the SOLD study) of Roche's 'bundled' commercial offer for trastuzumab and one other product is that it would be at least \$9 million per annum initially in the first 4 years, increasing to \$17-19 million annually once enrolment into the SOLD study had completed.

PHARMAC considers that investing additional funds in trastuzumab, for treatment regimens that cannot be determined to improve health outcomes compared with the currently funded concurrent 9 week treatment regimen, is not a cost-effective use of resources in consideration of other pharmaceuticals that could be funded with that same money.

### **More information**

For further information regarding the background and rationale for this decision you can find a number of documents on our website ([www.pharmac.govt.nz](http://www.pharmac.govt.nz)) including the following:

- Media Release
- A summary of the clinical evidence
- A summary of submissions received in response to consultation
- Herceptin Q&A
- CaTSoP minutes from 13 June 2008
- PTAC minutes from 4 July 2008
- An updated cost utility analysis

The PHARMAC resources for patients will also be updated in the coming weeks to include new clinical evidence and information about the confidence in the evidence

If you have any questions about this decision please feel free contact me directly or call our toll-free number on 0800 66 00 50 (9am to 5pm, Monday to Friday).

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