Appendix Two:  
Rapid update of TAR 75 for HERA 23 month follow-up information

Updated Clinical Information – 12 months trastuzumab sequential regimen

The cost-utility analysis for 12 months sequential trastuzumab treatment has not been updated to include the new evidence (23 months follow-up data published in the Lancet in January 20071), because PHARMAC staff believe that inclusion of this new information would only serve to make the 12 month sequential regimen less cost-effective (than the current base case result of $70,000-$80,000/QALY).

Reasons for this include:

- The original model assumed a faster rate of disease progression for HER2 positive early breast cancer over a 10 year time horizon than that currently observed with standard chemotherapy (see ‘Validation of underlying survival in HER2-positive breast cancer’, page 35 TAR 75, and Appendix Five TAR 75b). Therefore, the original model overstates the benefit of treatment (treatment with trastuzumab prevents more disease recurrences), and thus favours trastuzumab.

- The hazard ratio for disease free survival (DFS) at median 23 months was 0.64 (95% CI 0.54-0.76). This is less than observed at 12 month median follow-up (an early efficacy interim analysis) hazard ratio of 0.54 (95% CI 0.43-0.67). As shown in graph A below, the 23 month follow-up data appear to show a convergence of the curves between trastuzumab treatment arm and the standard chemotherapy arm. These results cast doubt on the durability of efficacy with the 12 month sequential treatment regimen.

- The hazard ratio for overall survival at 23 months median follow-up was 0.66 (95% CI 0.47-0.91), with 2.7% fewer deaths in the trastuzumab group than the standard chemotherapy arm at three years follow-up. These results are shown in graph B, below. Because the original model used the 12 month median follow-up data (0.54 as the reduction in risk of a recurrence), and exaggerated the rate of disease progression, the original CUA implicitly overestimated the survival gains from treating with trastuzumab.

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While the majority of changes to the original model would be expected to make trastuzumab less cost effective, there are some modifications to the original model that may improve the cost-effectiveness of the 12 month sequential regimen. These include:

- Reducing the costs for metastatic cancer (in particular, whether the cost of a second course of trastuzumab in the metastatic setting is included for those patients that receive trastuzumab in early disease). It should be noted that CaTSoP considered that the original CUA may have underestimated the costs relating to the treatment of metastatic breast cancer (see Appendix One: Relevant minutes of clinical advisory committees meetings since mid-2006).

- Reducing the costs associated with palliative care. It should be noted that PTAC considered that these costs were overestimated in the original model, and CaTSoP considered these costs to be underestimated. As can be seen in the sensitivity analysis section of the original TAR 75, increasing these costs by 50% improves the cost-effectiveness of 12 months sequential trastuzumab to $66,000/QALY. However, as this is not a large change in the results, the model is not considered to be sensitive to changes in this input.

In conclusion, a formal update of the 12 month CUA analysis including the recently published 23 month median overall survival data is considered unlikely to make trastuzumab treatment any more cost-effective than reported in the Part 1, TAR 75, as the majority of changes would disfavour trastuzumab. Therefore, PHARMAC has not undertaken an update of this analysis.