PUBLIC SUMMARY DOCUMENT
Product: Trastuzumab, powder for I.V. infusion, 60 mg and 150 mg, Herceptin®
Sponsor: Roche Products Pty Ltd
Date of PBAC Consideration: July 2012

1. Purpose of Application

To extend the current Authority Required Section 100 Efficient Funding of Chemotherapy (Public Hospital or Private Hospital/Clinic) listing to include:

1. Initial and continuing treatment of human epidermal growth factor receptor-2 (HER2) positive early breast cancer (EBC) commencing concurrently with neoadjuvant chemotherapy; and
2. Initial and continuing treatment of HER2 positive locally advanced breast cancer (LABC) commencing concurrently with neoadjuvant chemotherapy.

2. Background

This drug had not previously been considered by the PBAC for this indication.

3. Registration Status

Trastuzumab was registered by the TGA on 29 June 2012 for the indication:

- Locally Advanced Breast Cancer - Trastuzumab is indicated for the treatment of HER2-positive locally advanced breast cancer in combination with neoadjuvant chemotherapy followed by adjuvant trastuzumab.

Trastuzumab is also registered by the TGA for the following indications:

- Localised Breast Cancer - Trastuzumab is indicated for the treatment of patients with HER2 positive localised breast cancer following surgery, and in association with chemotherapy and, if applicable, radiotherapy.
- Metastatic Breast Cancer - Trastuzumab is indicated for the treatment of patients with metastatic breast cancer who have tumours that overexpress HER2:
  a) as monotherapy for the treatment of those patients who have received one or more chemotherapy regimens for their metastatic disease,
  b) in combination with taxanes for the treatment of those patients who have not received chemotherapy for their metastatic disease; or
  c) in combination with an aromatase inhibitor for the treatment of post-menopausal patients with hormone-receptor positive metastatic breast cancer.
- Advanced Gastric Cancer - Trastuzumab is indicated in combination with cisplatin and either capecitabine or 5-FU for the treatment of patients with HER2 positive advanced adenocarcinoma of the stomach or gastro-oesophageal junction who have not received prior anti-cancer treatment for their metastatic disease.

4. Listing Requested and PBAC's View

Efficient Funding Of Chemotherapy
Section 100 Authority Required Private Hospital/Private Clinic
Section 100 Authority Required Public Hospital

Early breast cancer:

- Initial treatment for HER2 positive early breast cancer commencing concurrently with neoadjuvant chemotherapy.

- Initial treatment for HER2 positive early breast cancer commencing concurrently with adjuvant chemotherapy following surgery *(existing restriction)*.
- Continuing treatment for HER2 positive early breast cancer where the patient has previously received treatment with PBS-subsidised trastuzumab *(existing restriction).*

Locally advanced breast cancer:
- Initial treatment for HER2 positive locally advanced breast cancer commencing concurrently with neoadjuvant chemotherapy.
- Continuing treatment for HER2 positive locally advanced breast cancer where the patient has previously received treatment with PBS-subsidised trastuzumab.

To be eligible to receive treatment with trastuzumab, patients must undergo HER2 pathology testing. ISH testing of a tumour sample is mandatory.

The listing request for early breast cancer was not considered by the PBAC as the TGA Delegate did not support the application for this indication. For PBAC's view on the listing request for locally advanced breast cancer, see Recommendation and Reasons.

5. Clinical Place for the Proposed Therapy

Approximately 13,000 cases of breast cancer are diagnosed in Australia each year, about 10-20% of these are locally advanced breast cancer. Locally advanced breast cancer is invasive breast cancer that has one or more of the following features: may be large (typically bigger than 5cm), may have spread to several lymph nodes in the axilla or other areas near the breast, may have spread to other tissues around the breast such as the skin, muscle or ribs. Treatment for locally advanced breast cancer will usually involve a combination of treatments such as chemotherapy, breast surgery, radiotherapy, hormonal therapies or targeted therapies.

Early breast cancer is invasive cancer that is contained in the breast and may or may not have spread to the lymph nodes in the breast or armpit. Treatment for early breast cancer may involve breast surgery, radiotherapy, chemotherapy, hormonal therapies or targeted therapies.

Neoadjuvant chemotherapy is treatment given to the patient before the primary therapy. It can be given to shrink a tumor that is inoperable in its current state, so it can subsequently be surgically removed. A patient whose tumor can be removed by mastectomy may instead receive neoadjuvant chemotherapy to shrink the tumor enough to allow breast-conserving surgery. Neoadjuvant chemotherapy is given in the same manner as adjuvant chemotherapy.

The submission proposed that treatment with trastuzumab in the neoadjuvant setting in combination with chemotherapy followed by surgery then treatment with trastuzumab monotherapy will replace neoadjuvant chemotherapy followed by surgery followed by adjuvant chemotherapy plus trastuzumab in certain patients with early breast cancer and locally advanced breast cancer.

6. Comparator

The PBAC considered the comparators for HER-2 positive patients with LABC (large tumours and node involvement +/- inflammatory disease and skin or muscle involvement) were either:

- Neoadjuvant chemotherapy (without trastuzumab) followed by surgical resection and

adjuvant trastuzumab (PBS subsidised).

- Neoadjuvant chemotherapy (without trastuzumab) where patients are unable to have surgery.
    - These patients will become eligible for the Herceptin Program when they progress to metastatic disease.

Patients who have LABC and skin/muscle involvement and or inflammatory disease are eligible for trastuzumab in combination with a taxane-based therapy via the Herceptin Program. A proportion of these patients may have surgery and would be eligible for either continuing on the Herceptin Program or switching to PBS-funded trastuzumab after surgery. If patients cannot have surgery, they may remain on the Herceptin Program.

7. Clinical Trials

The submission presented an indirect comparison using one direct randomised trial (NOAH) comparing neoadjuvant trastuzumab plus chemotherapy to neoadjuvant chemotherapy (234 patients), and three direct randomised trials comparing adjuvant trastuzumab plus chemotherapy to adjuvant chemotherapy (B-31 (2101 patients), N9831 (2289 patients), BCIRG 006 (3222 patients)).

All four trials included in the submission were randomised, multicentre, controlled, open-label, phase III trials. The key difference in the inclusion criteria across the four trials related to stage of disease: the NOAH trial included a much greater number of patients with LABC, defined as T3N1 or T4 or any T plus N2 or N3 or any T plus involvement of ipsilateral supraclavicular nodes, while the three adjuvant trials included patients with tumours defined as T1-T3 and a very small number of patients with T3 staging (tumours greater than 5cm). The adjuvant studies did not include patients with more advanced early breast cancer. The results were not reported separately for operable EBC and LABC.

For PBAC's view, see Recommendation and Reasons.

Details of trials and associated reports published at the time of submission are in the table below.

Trial ID / First author	Protocol title / Publication title	Publication citation
Proposed drug regimen – Neo-adjuvant trastuzumab plus chemotherapy		
NOAH		
Clinical Study Report – MO16432	A multicenter, randomized, controlled, open-labelled trial of paclitaxel-containing chemotherapy followed by CMF versus the same chemotherapy plus Herceptin in women with locally advanced breast cancer and HER2/c-erbB-2 overexpression and amplification, with a parallel observational study of the same chemotherapy regimen alone, in patients with HER2-negative tumors (0 or 1+ by immunohistochemistry)	Report No. 1039285. March 2011.
Gianni L, Eiermann W, Semiglazov V et al, 2009	Neo-adjuvant trastuzumab in patients with HER2-positive locally advanced breast cancer: Primary efficacy analysis of the NOAH trial.	Cancer Research 2009; 69(2) Suppl: S.
Gianni L, Eiermann W, Semiglazov V et	Neo-adjuvant chemotherapy with trastuzumab followed by adjuvant trastuzumab versus neo-adjuvant chemotherapy alone, in patients with	Lancet 2010; 375(9712):377-84.

al, 2010	HER2-positive locally advanced breast cancer (the NOAH trial): a randomised controlled superiority trial with a parallel HER2-negative cohort.	
Semiglazov V, Eiermann W, Zambetti M et al, 2011	Surgery following neo-adjuvant therapy in patients with HER2-positive locally advanced or inflammatory breast cancer participating in the Neo-adjuvant Herceptin (NOAH) study.	European Journal of Surgical Oncology 2011; 37(10):856-863.
Comparator regimen - adjuvant trastuzumab plus chemotherapy		
B-31		
Tan-Chiu E, Yothers G, Romond E et al, 2005	Assessment of cardiac dysfunction in a randomized trial comparing doxorubicin and cyclophosphamide followed by paclitaxel, with or without trastuzumab as adjuvant therapy in node-positive, human epidermal growth factor receptor 2-overexpressing breast cancer: NSABP B-31.	Journal of Clinical Oncology 2005; 23(31):7811-9.
BCIRG 006		
Clinical Study Report for BCIRG 006	Multicenter phase III randomized trial comparing doxorubicin and cyclophosphamide followed by docetaxel with doxorubicin and cyclophosphamide and trastuzumab (HERCEPTIN) and with docetaxel, carboplatin, and trastuzumab in the adjuvant treatment of node-positive and high-risk node-negative patients with operable breast cancer containing the HER2 alteration.	June 2007
Ranganathan A, Moore Z and O'Shaughnessy, 2007	Second interim efficacy analysis of the BCIRG 006 trial: Adjuvant chemotherapy with or without trastuzumab in HER2-overexpressing breast cancer.	Clinical Breast Cancer 2007:7(6):449-50.
Slamon D, Eiermann W, Robert N et al, 2005	BCIRG 006: Superior cardiac safety of adjuvant docetaxel (T), carboplatin (C) and trastuzumab (H) compared to doxorubicin (A) and cyclophosphamide (Cyc) followed by TH in patients with early stage breast cancer and altered HER2 gene.	European Journal of Cancer 2005; 3(2):74.
Slamon et al. 2011	Adjuvant trastuzumab in HER2-positive breast cancer.	New England Journal of Medicine 2011; 365(14):1273-1283.
Joint analysis B-31 and N9831		
Clinical Study Report for Joint Analysis of B-31 and N9831 – NSABP B-31	A randomized trial comparing the safety and efficacy of ADRIAMYCIN and cyclophosphamide followed by TAXOL to that of ADRIAMYCIN and cyclophosphamide followed by TAXOL plus HERCEPTIN in node-positive breast cancer patients who have tumors that overexpress HER2. NCCTG N9831: Phase III trial of doxorubicin and cyclophosphamide followed by weekly paclitaxel with or without trastuzumab as adjuvant treatment for women with HER2 over-expressing or amplified node positive or high-risk node negative breast cancer.	February 2006.
Romond EH, Perez EA, Bryant J et al, 2005	Trastuzumab plus adjuvant chemotherapy for operable HER2-positive breast cancer.	New England Journal of Medicine 2005; 353(16):1673-84.
Romond EH, Perez EA, Bryant J et a, 2005a.	Doxorubicin and cyclophosphamide (AC) followed by paclitaxel (T) with or without trastuzumab (H) as adjuvant therapy for patients with HER2-positive operable breast cancer (BC): combined analysis of NSABP B-31 and NCCTG N9831.	European Journal of Cancer 2005a; 3(2):73.

Russell SD, Blackwell KL, Lawrence J et al, 2010	Independent adjudication of symptomatic heart failure with the use of doxorubicin and cyclophosphamide followed by trastuzumab adjuvant therapy: A combined review of cardiac data from the National Surgical Adjuvant Breast and Bowel Project B-31 and the North Central Cancer Treatment Group N9831 clinical trials.	Journal of Clinical Oncology 2010; 28(21):3416-21.
N9831		
Perez EA, Suman VJ, Davidson NE et al, 2008	Cardiac safety analysis of doxorubicin and cyclophosphamide followed by paclitaxel with or without trastuzumab in the North Central Cancer Treatment Group N9831 adjuvant breast cancer trial.	Journal of Clinical Oncology 2008; 26(8):1231-8.
Perez et al. 2011a	Sequential versus concurrent trastuzumab in adjuvant chemotherapy for breast cancer.	Journal of Clinical Oncology 2011; 29(34):4491-4497.
Perez et al. 2011	Four-year follow-up of trastuzumab plus adjuvant chemotherapy for operable human epidermal growth factor receptor 2-positive breast cancer: Joint analysis of data from NCCTG N9831 and NSABP B-31.	Journal of Clinical Oncology 2011; 29(25):3366-3373.

8. Results of Trials

The submission presented an indirect comparison of event-free/disease-free survival at four years and from NOAH, B-31, N9831 and BCIRG 006 as the primary outcome. There are limitations to the analysis in terms of the exchangeability of the trials and differences in event rates in the comparison arms of the trials. Furthermore, none of the trials were powered to detect differences in overall survival.

The submission presented an indirect comparison where the common comparator was chemotherapy alone. However, the chemotherapy regimens used in the common comparator arms differ. In the NOAH trial, the common comparator arm is neoadjuvant chemotherapy while in the three adjuvant trials it is adjuvant chemotherapy. Thus, there is an underlying assumption that adjuvant and neoadjuvant chemotherapy are equivalent in efficacy. The trials also administer different chemotherapy regimens and dosages. These issues affect the legitimacy of the indirect comparison and exchangeability of the trials.

The submission provided an indirect comparison of NOAH versus a meta-analysis of B-31, N9831 and BCIRG006 which showed no statistically significant difference in overall survival between neoadjuvant trastuzumab plus chemotherapy and adjuvant trastuzumab plus chemotherapy. The studies were not powered to determine a survival benefit.

The submission presented surgical events from the NOAH trial as the secondary outcome.

The submission reported that twice as many patients in the neoadjuvant trastuzumab + chemotherapy arm were able to have breast-conserving surgery than in the neoadjuvant chemotherapy alone arm and that this is one of the important advantages of neoadjuvant therapy

For PBAC's view, see Recommendation and Reasons.

The submission conducted an indirect comparison of treatment related cardiac events. The results of the indirect comparison indicated that cardiac events are similar in NOAH compared to adjuvant trial setting.

9. Clinical Claim

The submission described neoadjuvant trastuzumab plus chemotherapy as non-inferior in terms of comparative effectiveness and non-inferior in terms of comparative safety over adjuvant trastuzumab plus chemotherapy.

Although the quality of data is poor, the PBAC considered that there is a sufficient basis to accept that starting trastuzumab in the neoadjuvant setting plus chemotherapy for locally advanced breast cancer is unlikely to be inferior in terms of comparative effectiveness and safety as adjuvant trastuzumab plus chemotherapy for early (stage I/II) breast cancer through the existing PBS listing.

The PBAC recalled that it had previously considered the main safety results associated with trastuzumab in the adjuvant setting (July 2006 PBAC meeting). Results of the indirect comparison in the submission indicated that there was no statistically significant difference in the rate of cardiac events in the neoadjuvant setting compared to the adjuvant setting.

10. Economic Analysis

The submission presented a cost minimisation analysis for LABC, based on the comparison of:

- Neoadjuvant trastuzumab accessed via the PBS versus
    1. Neoadjuvant trastuzumab accessed via the Herceptin Program for 10% of patients, and
    2. Adjuvant trastuzumab accessed via the PBS for LABC patients who become resectable after neoadjuvant chemotherapy.

The equi-effective doses for LABC are based on the draft product information and estimated as:

- Currently:
    - Dose: trastuzumab three-weekly, 8 mg/kg initial dose and 6 mg/kg subsequent doses; weekly, 4 mg/kg initial dose and 2 mg/kg subsequent doses, either as an adjuvant regimen via the PBS or via the Herceptin Program.
    - Duration: 52 weeks if via the PBS or >12 months if via the Herceptin Program
    - Concomitant therapies: adjuvant chemotherapies, such as anthracycline and/or taxane-based (details not stated).
- Proposed:
    - Dose: as above but neoadjuvant.
    - Duration: 52 weeks (initial plus continuing) neoadjuvant.
    - Concomitant therapies: as above but neoadjuvant.

The submission argued that a proportion of patients with LABC would have commenced the Herceptin Program and, if given neoadjuvant therapy, more of these patients would be able to have surgery (and more would be able to have breast conserving surgery). Following surgery these patients would continue for up to 52 weeks and stop. The alternative, in the current

funding arrangement, is that these patients would have continued on the Herceptin Program for >12 months.

The submission also noted that a proportion of patients will advance to metastatic disease following adjuvant therapy and become eligible for the Herceptin Program.

For PBAC's view, see Recommendation and Reasons.

11. Estimated PBS Usage and Financial Implications

The submission estimated the likely number of patients prescribed neoadjuvant trastuzumab to be less than 1,000 in the fifth year of listing. There are additional patients treated beyond the usual market growth because of the assumption that 10% of LABC patients receiving trastuzumab via the Herceptin Program will be transferred to the PBS.

The submission estimated the total net cost to the PBS to be less than $10 million over the first 5 years (excluding co-payments). The principal uncertainties lie in the claim of cost offsets associated with PBS neoadjuvant therapy and in treatment of LABC patients.

The submission appropriately applied the pricing under s100 Efficient Funding of Chemotherapy Drugs, and pricing under the Herceptin Program.

The submission claimed that neoadjuvant trastuzumab is cost saving on the basis of the net cost to all health budgets. This estimate was based on a potentially optimistic duration of therapy in the Herceptin Program.

The PBAC noted that HER2 ISH testing to determine a patient's eligibility for trastuzumab as currently subsidised had been listed on the MBS from 1 May 2012. The PBAC was aware that the MSAC was scheduled to consider extending this to support trastuzumab in the neoadjuvant setting.

The PBAC advised that there was not a strong basis to expect substantial overall savings to Government and did not accept the submission's claim that there would be sufficient number of patients reduced to 52 weeks of trastuzumab to achieve this.

12. Recommendation and Reasons

The PBAC advised that the maximum amounts and numbers of repeats for the weekly and 3-weekly regimens in the adjuvant setting should apply for these initial and continuing restrictions.

In making its recommendation, the PBAC also took into account the multiple applications from the Medical Oncology Group in Australia highlighting that patient preferences for treatment sequencing was compromised in a small number of patients with locally advanced (stage III) breast cancer. The PBAC agreed that the recommended listing would address this unmet need by maximising the choice of timing of subsidised access to trastuzumab. Patients with locally advanced breast cancer already have access to government-subsidised trastuzumab for some of the duration of their cancer, so in making its recommendation, the PBAC sought to optimise the timing of this subsidised access, with little risk that this would expand the overall extent of trastuzumab use.

The PBAC also reaffirmed its previous advice that the subsidised use of trastuzumab through the Herceptin Program is not acceptably cost-effective. This is relevant to the recommended extension of the PBS listing of trastuzumab, which minimises the risk of cost-ineffective use by being limited to an overall duration of 52 weeks.

The PBAC recognised neoadjuvant systemic treatment as a standard of care, with flexibility in the sequencing of surgery, chemotherapy and radiotherapy, with the timing of chemotherapy tailored to the circumstances of the individual and their response to treatment. The optimal timing of surgery in relation to systemic HER2 blockade has not been determined. The recommended extension to the trastuzumab listing would facilitate flexibility in sequencing.

The PBAC accepted the NOAH trial as the primary source of clinical evidence for the submission. Despite the many limitations of this trial, the PBAC considered that it showed improved surgical rates in women treated with neoadjuvant trastuzumab plus chemotherapy compared with chemotherapy alone, excluding the Russian centre which violated standard surgical practice, and a significantly improved event-free/disease-free survival. Thus, although the quality of data is poor, the PBAC considered that there is a sufficient basis to accept that starting trastuzumab in the neoadjuvant setting plus chemotherapy for locally advanced breast cancer is unlikely to be inferior in terms of comparative effectiveness and safety as adjuvant trastuzumab plus chemotherapy for early (stage I/II) breast cancer through the existing PBS listing.

The PBAC considered that there was a biological rationale supporting this conclusion given its previous acceptance of the cost effectiveness of concomitant administration of six months of trastuzumab plus chemotherapy as adjuvant therapy for early breast cancer. In 2006, the PBAC noted the incremental benefit and cost effectiveness of the additional six months of trastuzumab monotherapy in the adjuvant setting was uncertain given that the similar effect size reported in the FINHERA trial (in which trastuzumab was not continued as monotherapy) compared with the other adjuvant trastuzumab trials (in which trastuzumab was continued as monotherapy treatment). Taking the totality of the trial evidence for adjuvant therapy, the PBAC recommended subsidy of adjuvant trastuzumab for up to 12 months. This has parallels to adding trastuzumab to neoadjuvant chemotherapy in those patients in whom no post-operative adjuvant chemotherapy is planned or is not subsequently given due to delays in surgery (or other things). Without a neoadjuvant listing, these patients are currently only exposed to monotherapy trastuzumab.

The PBAC noted that the submission estimated that an annual incidence of <1,000 patients with HER2 positive locally advanced breast cancer would be affected by the recommendation. For most of these patients, the substitution is expected to be for PBS-subsidised adjuvant trastuzumab after neoadjuvant chemotherapy and there is no reason to assume that effectiveness or safety would be compromised by availability of neoadjuvant trastuzumab. However, the total duration of systemic therapy would be reduced if trastuzumab is used as neoadjuvant therapy.

For the small number of patients for whom the substitution is expected to be for neoadjuvant trastuzumab subsidised through the PBS rather than the Herceptin Program, it is possible that the total duration of trastuzumab therapy in at least some of these patients might reduce to 52 weeks and thus reduce expenditure on the Herceptin Program. For the remaining patients

who would otherwise progress to metastatic disease before receiving trastuzumab subsidised through the Herceptin Program, the existing alternative is still trastuzumab for an indefinite duration after an initial delay.

The PBAC also noted the comparative incidence of locally advanced breast cancer (~20%) and early breast cancer (~80%). Thus the overall cost effectiveness of PBS-subsidised trastuzumab would not be adversely affected to a large extent even if neoadjuvant/adjuvant trastuzumab for locally advanced breast cancer is less effective than adjuvant trastuzumab for early breast cancer.

Altogether, this clinical conclusion provides the basis for a cost-minimisation approach to support adopting the same price of trastuzumab for neoadjuvant trastuzumab plus chemotherapy compared with adjuvant trastuzumab plus chemotherapy. The PBAC advised that there was not a strong basis to expect substantial overall savings to government and did not accept the submission's claim that there would be sufficient number of patients reduced to 52 weeks of trastuzumab to achieve this.

The PBAC noted that HER2 ISH testing to determine a patient's eligibility for trastuzumab as currently subsidised had been listed on the MBS from 1 May 2012. The PBAC was aware that MSAC was scheduled to consider extending this to support trastuzumab in the neoadjuvant setting, but had no specific matters to refer to MSAC for advice.

The PBAC therefore recommended listing trastuzumab for neoadjuvant therapy in patients with HER2 positive locally advanced breast cancer on the PBS on the basis that this would likely at least maintain the current overall effectiveness, cost-effectiveness and total financial implications to government of trastuzumab compared to the status quo.

The PBAC noted that some patients receiving a 52-week course of trastuzumab started in the neoadjuvant setting would subsequently become eligible for trastuzumab through the Herceptin Program and that this funding Program perversely remains an ongoing source of cost-ineffective trastuzumab. Therefore the PBAC advised that the establishment of the Herceptin Program has had long-term negative consequences for accommodating the subsidy of the evolving indications for trastuzumab particularly in relation to concomitant use with other drugs, including aromatase inhibitors and non-taxane cytotoxic therapies. Unfortunately this might have also subsequently resulted in worse patient outcomes and clinical management choices than would have been possible if trastuzumab had been originally subsidised within the PBS where changing treatment paradigms could be accommodated and subsidised. Therefore the PBAC noted that the Herceptin Program illustrated potential unintended consequences of subsidy outside the PBS in the future for medicines which do not meet the usual PBAC cost-effectiveness criteria.

Recommendation:
TRASTUZUMAB, powder for I.V infusion, 60 mg and 150 mg

The PBAC recommended that the current Section 100 Efficient Funding of Chemotherapy (Public Hospital or Private Hospital/Clinic) Authority Required restrictions be extended to include (distinguishing text from the existing restrictions is highlighted in bold text):

<u>Initial treatment</u>

Initial treatment for HER2 positive **locally advanced** breast cancer commencing concurrently with **neo**adjuvant chemotherapy.

The total duration of PBS-subsidised treatment (initial plus continuing) that will be authorised is 52 weeks.

HER2 positivity must be demonstrated by in situ hybridisation (ISH).

Trastuzumab must not be used in patients with a left ventricular ejection fraction (LVEF) of less than 45% and/or with symptomatic heart failure. Cardiac function must be tested by a suitable method including, for example ECHO or MUGA, prior to seeking the authority approval and then at 3 monthly intervals during treatment.

Authority applications for initial treatment must be made in writing and must include:
[as per current adjuvant restriction for HER2 positive early breast cancer.]

Note
[As per current adjuvant restriction for HER2 positive early breast cancer.]

Continuing treatment
Continuing treatment for HER2 positive **locally advanced** breast cancer where the patient has received treatment with PBS-subsidised trastuzumab.

The patient is eligible to receive sufficient trastuzumab to complete 52 weeks of combined PBS-subsidised and non-PBS-subsidised therapy.

Trastuzumab must not be used in patients with a left ventricular ejection fraction (LVEF) of less than 45% and/or with symptomatic heart failure. Cardiac function must be tested by a suitable method including, for example ECHO or MUGA at 3 monthly intervals during treatment.

Authority applications for initial treatment may be made [as per current adjuvant restriction for HER2 positive early breast cancer.]

Breaks in therapy.
[As per current adjuvant restriction for HER2 positive early breast cancer.]

Note
[As per current adjuvant restriction for HER2 positive early breast cancer.]

13. Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

14. Sponsor's Comment

Roche is pleased that the PBAC has recommended PBS listing of trastuzumab for neoadjuvant therapy for patients with HER2-positive locally advanced breast cancer. Roche hopes that listing for trastuzumab on the PBS and ISH testing in the neoadjuvant setting on the MBS will be able to occur at the earliest available opportunity.