



Australian Government

Medical Services Advisory Committee

Public Summary Document

Application No. 1230 – HER2 ISH testing for access to trastuzumab for neoadjuvant breast cancer

Applicant: Roche Products Pty Ltd Australia

Date of MSAC consideration: 2 August 2012

1. Purpose of application

The Department of Health and Ageing received an application from Roche Products Australia in March 2012 requesting an extension to the existing Medicare Benefits Schedule (MBS) listing for *in situ* hybridisation (ISH) testing of human epidermal growth receptor 2 (HER2) for patients diagnosed with breast cancer to enable consideration of neoadjuvant treatment with trastuzumab.

2. Background

HER2 ISH testing of tumour tissue from a patient with breast cancer for HER2 was added to the Medicare Benefits Schedule (MBS) on 1 May 2012 to help determine eligibility for government-subsidised trastuzumab (Herceptin[®]).

The MSAC Executive had accepted that a fully integrated submission across the co-dependent package of HER2 ISH testing and neoadjuvant trastuzumab was not required for this requested extension of HER2 ISH testing. A minor submission was therefore provided by the applicant.

3. Proposal for public funding

The applicant proposed testing for HER2 positivity in patients diagnosed with breast cancer to enable consideration of treatment with trastuzumab. The application sought listing of the HER2 ISH test to determine whether a patient with early and locally advanced breast cancer is HER2-positive and so eligible to start treatment with trastuzumab in the neoadjuvant setting (i.e., before surgery). The start of the neoadjuvant course of trastuzumab is given in combination with chemotherapy. The course of trastuzumab is completed as monotherapy in the adjuvant setting (i.e., following surgery). Between the lodgement of the application and its consideration by MSAC, the Therapeutic Goods Administration and the Pharmaceutical Benefits Advisory Committee (PBAC) both proposed excluding patients with early breast cancer from the eligible population for neoadjuvant trastuzumab, so MSAC likewise excluded this population from its consideration of HER2 ISH testing.

4. Proposed intervention's place in clinical management

The applicant proposed that patients would be ISH tested for HER2 positivity before surgery to determine suitability for neoadjuvant treatment with trastuzumab.

5. Comparator to the proposed intervention

The main comparator to HER2 ISH testing on a biopsy specimen taken before surgery is to wait until after surgery to obtain resected tissue and then conduct the HER2 ISH testing. However, not all HER2 ISH tests conducted on a biopsy specimen would result in a repeated test on resected tissue.

6. Comparative safety

MSAC recalled that it had agreed in 2009 that ISH testing is safe.

7. Comparative effectiveness

MSAC recalled that it had agreed in 2009 that HER2 ISH testing for all women with breast cancer is an effective strategy for identifying women who are likely to respond to trastuzumab.

8. Economic evaluation

MSAC noted that the present fee (as at 1 May 2012 amended Medicare Benefits Schedule) for ISH testing of HER2 is \$317.50, and considered that this would also be suitable for the extended use.

MSAC considered that the additional use of ISH testing for HER2 as a result of the extended listing would be small. The sponsor's original estimate of 725 in the first year of listing was no longer relevant because it included patients with early (stage II) disease. The submission's estimate of zero additional tests for patients with locally advanced (stage III) disease is based on the argument that all such patients are already receiving testing on core biopsy samples and re-testing if negative because all have subsidised access to trastuzumab via the Herceptin Program and subsidised access to testing via the MBS.

However, this is inconsistent with the view of the Medical Oncology Group of Australia that some patients are currently missing out. Stage III disease represents 12.6% of the 2006 and 2007 incidence of breast cancer from the Victorian Cancer Registry, and 85% of these are expected to test negative for HER2. When these percentages are applied to the submission's projected overall incidence of 14,288 breast cancer patients, together with the estimate from the submission that 80% of these patients will have their disease resected (i.e., excluding borderline inoperable patients), the maximum number of additional tests in the first year of listing is 1189. The true estimate will fall within this range of zero to 1189.

9. Summary of consideration and rationale for MSAC's advice

MSAC noted that the Government has reimbursed trastuzumab (on the Herceptin program) since 2001 for HER2 positive metastatic breast cancer and on the Pharmaceutical Benefits Scheme (PBS) since 2006 for treatment of HER2 positive early breast cancer in the adjuvant setting.

MSAC noted that on 29 June 2012, the Therapeutic Goods Administration (TGA) approved a more restricted indication for the use of trastuzumab in HER2 positive breast cancer treatment than the applicant (Roche) had requested, i.e., only for patients diagnosed with locally advanced (stage III) HER2 positive breast cancer. MSAC further noted that at its July 2012 meeting, the Pharmaceutical Benefits Advisory Committee (PBAC) recommended PBS listing for neoadjuvant trastuzumab in these patients. In addition, MSAC noted that neither the TGA nor PBAC supported use of neoadjuvant trastuzumab in early (stage II) HER2 positive breast cancer.

MSAC noted that, in the neoadjuvant setting, testing is on a core biopsy sample taken from the patient, rather than on a surgical resected specimen. False negatives are more likely when testing core biopsies than surgical resections, so MSAC expected some repeat testing of patients initially testing negative once the surgically resected specimen becomes available.

10. MSAC's Advice to the Minister

After considering the strength of the available evidence in relation to the safety, effectiveness and cost effectiveness, MSAC advised the Minister that it supported the extension of the MBS listing of in situ hybridisation (ISH) testing of tumour tissue from a patient with breast cancer to include its use to support the PBAC-recommended extension of the PBS listing of trastuzumab to include trastuzumab use in the neoadjuvant setting.

MSAC advised the Minister that it supports amending the current item descriptor for MBS item 73332, which currently states:

MBS Item 73332 Category 6 – PATHOLOGY SERVICES

An in situ hybridization (ISH) test of tumour tissue from a patient with breast cancer (other than in the neoadjuvant setting) requested by, or on behalf of, a specialist or consultant physician to determine if the requirements relating to human epidermal growth factor receptor 2 (HER2) gene mutation status for access to trastuzumab under the Pharmaceutical Benefits Scheme (PBS) or the Herceptin Program are fulfilled.

Fee: \$317.50 Benefit: 75% = \$238.15 85% = \$269.90

by removing “(other than in the neoadjuvant setting)”, so that the item descriptor would read as follows:

MBS Item 73332 Category 6 – PATHOLOGY SERVICES

An in situ hybridization (ISH) test of tumour tissue from a patient with breast cancer requested by, or on behalf of, a specialist or consultant physician to determine if the requirements relating to human epidermal growth factor receptor 2 (HER2) gene mutation status for access to trastuzumab under the Pharmaceutical Benefits Scheme (PBS) or the Herceptin Program are fulfilled.

Fee: \$317.50 Benefit: 75% = \$238.15 85% = \$269.90

In addition to this, MSAC supported a further modification to this item, to enable this test to become a pathologist-determinable service, noting that this would require further investigation by the Department of Health and Ageing.

11. Applicant's Response to Public Summary Document

Roche is pleased that MSAC recommended the extension of the MBS listing of in situ hybridisation (ISH) testing of tumour tissue from a patient with breast cancer to include testing in the neoadjuvant setting.

Roche supports MSAC's recommendation that the item be modified to become a pathologist-determinable service.

12. Context for decision

This advice was made under the MSAC Terms of Reference.

MSAC is to:

- Advise the Minister for Health and Ageing on medical services that involve new or emerging technologies and procedures and, where relevant, amendment to existing MBS items, in relation to:
 - the strength of evidence in relation to the comparative safety, effectiveness, cost-effectiveness and total cost of the medical service;

- whether public funding should be supported for the medical service and, if so, the circumstances under which public funding should be supported;
 - the proposed Medicare Benefits Schedule (MBS) item descriptor and fee for the service where funding through the MBS is supported;
 - the circumstances, where there is uncertainty in relation to the clinical or cost-effectiveness of a service, under which interim public funding of a service should be supported for a specified period, during which defined data collections under agreed clinical protocols would be collected to inform a re-assessment of the service by MSAC at the conclusion of that period;
 - other matters related to the public funding of health services referred by the Minister.
- Advise the Australian Health Ministers' Advisory Council (AHMAC) on health technology assessments referred under AHMAC arrangements.
 - MSAC may also establish sub-committees to assist MSAC to effectively undertake its role. MSAC may delegate some of its functions to its Executive sub-committee.

13. Linkages to other documents

MSAC's processes are detailed on the MSAC Website at: www.msac.gov.au